DISSERTATION / DOCTORAL THESIS

Titel der Dissertation /Title of the Doctoral Thesis

„The Role of Testosterone in Social Status Seeking“

verfasst von / submitted by

Hana Hollá Kutlíková, MSc

angestrebter akademischer Grad / in partial fulfilment of the requirements for the degree of

Doktorin der Naturwissenschaften (Dr.rer.nat.)

Wien, 2023/ Vienna 2023

Studienkennzahl lt. Studienblatt / degree programme code as it appears on the student record sheet:	UA 796 605 298
Dissertationsgebiet lt. Studienblatt / field of study as it appears on the student record sheet:	Psychologie
Betreut von / Supervisor:	Univ.-Prof. Dr. Claus Lamm

TABLE OF CONTENTS

ACKNOWLEDGEMENT

I am grateful to many people who have accompanied, inspired, and supported me on my PhD journey. Here I would like to mention a few of them.

I wish to thank Claus Lamm. Thank you for your guidance and for being an extraordinary mixture of scientific and human qualities. I am grateful I could learn from you.

I would like to extend my thanks to the co-authors of my articles and mentors - Jack van Honk, Bettina Studer Pastore, Igor Riečanský, and Michael Naef. Thank you for sharing your expertise with me and showing me the strength of the scientific community.

I want to thank my colleagues, who became friends - Lisa Rosenberger, Nace Mikuš, and Jasminka Majdandžić. Thank you for your open minds and hearts.

Special thanks go to my parents, my family. Without you, this would not be possible.

Finally, I thank Chris Eisenegger. I wish you could see what grows from what you sowed.

Chapter 1

GENERAL INTRODUCTION

1.1 Overview

The evolution of the endocrine system has allowed organisms to orchestrate complex integrated actions across diverse types of cells, tissues, and organs. Such an efficient integration is essential not only for many critical biological processes, such as growth and metabolism, but it also enables organisms to navigate their social environment. Testosterone is an evolutionarily ancient neuromodulator and hormone long-known for its crucial role in reproductive processes. However, the last decade, mainly due to the establishment of non-invasive administration methods in humans, has witnessed burgeoning research on testosterone's effects on elaborate social behaviors and decision-making. The reported effects of testosterone administration range from aggression, through approach behavior, to prosociality (e.g., Dreher et al., 2016; Enter et al., 2014; Geniole et al., 2020). Consequently, contrary to the end of the 20th century, when testosterone was mainly seen as a promoter of aggressive behavior, researchers currently suggest that testosterone’s effects on a variety of social behaviors may be best understood in terms of seeking and maintenance of social status (Eisenegger et al., 2011).

The present dissertation aims to contribute to the ongoing debate and shed light on the role of testosterone in human behavior. To generate a deeper understanding of testosterone functioning, this dissertation addresses both ultimate and proximate explanations (Tinbergen, 1963). Adopting such a synergistic perspective allows us to not only address the question of testosterone's evolutionary significance and function, but also to uncover the hormone‘s operational mechanisms. Specifically, this thesis provides A) a direct test of testosterone's influence on status-seeking behavior; B) a systematic examination of the social contexts that shape testosterone’s effects; C) an investigation of the mechanisms through which testosterone may exert its actions, namely stress-response management, reward learning, control perception, and deliberate cognitive processes.

Chapter 1 starts with an overview of research on testosterone evolution and its biological functions, continues with a summary of related animal research, and finally summarizes current relevant findings on testosterone's role in human social behavior. The aim of this chapter is to provide a general introduction and theoretical foundation for the experimental work reported in the subsequent chapters. Chapters 2 – 6 covers the empirical work, as published in or submitted to scientific journals,and thus constitutes the core of this dissertation. These chapters also include additional exploratory analyses conducted to provide a comprehensive examination of testosterone's functioning. Chapter 7 discusses our findings and suggests implications for future experimental studies and theoretical conceptualizations in the field of testosterone research. I hope that by addressing both "why" and "how" questions, this dissertation fosters and broadens the understanding of testosterone's coordinating role in various physiological and psychological actions.

Collaboration is an essential aspect of research, and this applies also for the research presented in this thesis. To depict the collective work, when describing research reported in the articles that were written together with other co-authors, the pronouns "we" and "our" are used. In contrast, the pronouns "I" and "my" denote exclusively individual thoughts and endeavours.

Finally, it needs to be noted that this dissertation focuses particularly on the effects of testosterone in human males. We limited the focus of our work to males for two main reasons. First, there are substantial sex differences in the organs producing testosterone, its metabolism, organizational effects during prenatal development, and circulating levels in adulthood (Auyeung et al., 2013; Gurvich et al., 2018; Nieschlag & Behre, 1998). A minority of research includes both sexes in the same analysis, scaling the sex difference in testosterone by normalizing levels, but this tactic has been criticized due to poor statistical quality (Mazur, 2017). Notably, at the time of testing, the pharmacokinetic data pertaining to identical routes of administration in both sexes were not available (Eisenegger, 2013). Lastly, the methodology utilized in our study was selected to align with the ethical committee standards at the Medical University of Vienna. This involved using legally approved synthetic hormone preparations available during the experimental testing period and location.

1.2 Evolution of testosterone and its function

The modern understanding of testosterone began in the 1930s with the isolation and identification of androgen hormones. In 1935 Ernst Laqueur and his group at the University of Amsterdam and the company Organon extracted10 mg of 17β-hydroxy-4-androstene-3one ($C_{19}H_{28}O_2$) from 100 kg of bull testes and called the hormone "testosterone" (David et al., 1935). In the same year, research groups in Göttingen (Butenandt & Hanisch, 1935), as well as in Zurich and Basel (Ruzicka & Wettstein, 1935) synthesized testosterone, marking the beginning of testosterone

physiology and pharmacology research. In male testes and female ovaries and adrenal glands, testosterone is synthesized from cholesterol in five enzymatic steps. First, cholesterol is converted to pregnenolone in cell mitochondria. The following steps take place in the endoplasmatic reticulum and involve hydroxylation of pregnenolone to 7-hydroxy-pregnenolone, which is next converted to dehydroepiandrosterone. Dehydroepiandrosterone (DHEA) is then reduced to androstenedione, which can be further metabolized to either testosterone or estrone, depending on the action of specific enzymes and tissues. Testosterone and its androgenic metabolite, dihydrotestosterone (DHT), exert their effects through binding to the androgen receptors and through aromatization of testosterone to estradiol, which allows action via binding to the estrogen receptors (Davey & Grossmann, 2016).

Research suggests that this steroidogenesis pathway evolved in a forward direction through a successive appearance of these steps in consecutive generations of animals. Thus, from an evolutionary perspective, steroid synthesis should be viewed as a cholesterol degradation pathway rather than as a synthesis pathway (Markov et al., 2017). This also aligns with the nested position of steroidogenic enzymes within detoxification enzymes in phylogenetic trees based on genomic data (Markov et al., 2009). According to this view, steroidogenesis derived from catabolic pathways implicated in xenobiotic detoxification, hence steroid hormones, including testosterone, can be viewed as co-opted cholesterol metabolites (Baker, 2005). The exact appearance of testosterone in the evolutionary tree is not clarified. However, the presence of a vertebrate side-chain steroidogenic pathway indicates that the last common ancestor of gnathostomes and lampreys was already able to synthesize at least one sex or adrenal steroid between 500 and 475 million years ago (Janvier, 2007). The question remains why the steroidogenic side-chain cleavage completely replaced a more ancient paraestrol pathway. It seems that this side-chain cleavage of cholesterol to estradiol helped to increase the binding affinity to ERs. This gain in ER affinity may have facilitated the transition from a promiscuous food-sensing system to a highly specific coupling between nutritional status and reproduction, which likely presented an evolutionary advantage (Markov et al., 2017; Torre et al., 2014). Testosterone molecule thus originally appeared as an intermediate in the convertion of choresterol to estradiol, long before the evolution of androgen receptors (AR) (Thornton, 2001).

The evolution of ARs is believed to have occurred through a process of gene duplication and divergence. This means that an ancestral gene encoding a receptor with a different function was duplicated, and one of the copies acquired mutations that enabled it to recognize and bind androgens. Over time, these mutations accumulated and became fixed in the population, resulting in a new gene that encoded a functional androgen receptor. Functional AR genes likely appeared in the jawed vertebrate lineaged approximately 450 million years ago (Ogino et al., 2009). The emergence of ARs probably provided a selective advantage to animals by allowing them to respond to androgens that contributed to the regulation of metabolism and development, resulting in advantageous muscle mass and bone density (Johnson et al., 2018; Ogino et al., 2018). The

evolution of ARs and the function of steroids, including testosterone, likely continued through sexual selection, where individuals with higher androgen sensitivity had a competitive advantage in sexual dimorphism and sexually attractive display (Johnson et al., 2018). In this manner, testosterone and androgen receptors acquired a coordination function of physiological processes essential for successful reproduction and early forms of social behaviors.

In the following section, we shortly summarize comparative research conceptualizing the evolutionary significance and social function of the hormone testosterone in non-human vertebrate animals, which has critically influenced the study of testosterone's role in human social behaviors.

1.3 The role of testosterone in the social behavior of non-human vertebrates

Testosterone exerts both long-term organizational effects, also persisting in the absence of circulating hormone, and short-term activational effects, which require the presence of the hormone (Goel & Bale, 2008). Organizational effects occur during critical periods of development, such as prenatal development and early infancy. During fetal and neonatal life, testosterone is thought to influence sexual differentiation and brain development (Lombardo et al., 2012). Studies in rodents and primates have shown that the hypothalamus, the hippocampus, the preoptic-septal region, and the limbic system are essential target areas for sex steroid action during development. These brain structures are likely to be activated later in life when testosterone concentrations rise, as suggested by differences in the presence of ARs across different tissues (Collaer & Hines, 1995; McEwen, 1992). Thus, testosterone's influence on adult behavior depends on the interaction of long-term organizational and short-term activational effects (Mazur & Booth, 1998). In this dissertation, I focus mainly on the activational effects that can be experimentally manipulated by testosterone administration, while taking into account their interaction with the hormone's organizational effects.

Although the activational effects of testosterone bring organisms considerable benefits (Cunningham et al., 2016; Muller, 2017), there is a number of costs imposed by chronically elevated testosterone levels. These include, for instance, increased metabolic rate (Ketterson & Nolan, 1992; Marler & Moore, 1988), production of oxygen radicals (Zirkin & Chen, 2000), immunosuppression (Muehlenbein & Watts, 2010), and decreased parenting effort (Goymann et al., 2019). Such findings prompted researchers to examine the factors that lead to the acute increases in circulating levels of the hormone and, in turn, to investigate the behavioral function of these hormonal changes. The challenge hypothesis (Wingfield et al., 1990) has been one of the most influential attempts to explain seasonal and situational differences in androgens levels by relating them to male-male aggressive interactions in competition over territory or mating

partners, and it has been listed as one of the conceptual breakthroughs in ethology and animal behavior (Breed, 2017). The origins of the challenge hypothesis go back to the observation that androgens in male birds elevate during periods of intense competition for mates and territories and decline once the males engage in the parental care of the young (Wingfield & Farner, 1978). As the breeding season begins, males' androgen levels increase, typically triggered by photoperiod changes, to an elevated breeding baseline. This breeding baseline, however, remains below the physiological maximum and was considered to have little enhancing effects on male–male aggression or mate guarding. The rise in testosterone, which would lead to aggressive behavior, is, according to the original challenge hypothesis, caused mainly by social stimulations from rival males, such as territorial intrusions (Wingfield et al., 1990). The original challenge hypothesis was formulated to explain bird behavior. However, it was soon applied to explain the short-term testosterone rise and its activational effects in many species, such as fish (Desjardins et al., 2006), rodents (Soto-Gamboa et al., 2005), and primates, including humans (Archer, 2006; Muller, 2017). Although the early studies provided support for this concept, more recent research has noted numerous exceptions and demonstrated that the original formulation of the challenge hypothesis has some important limitations (DeVries et al., 2012; Landys et al., 2007; Villavicencio et al., 2013), leading to updates in the formulation of the hypothesis (Goymann et al., 2019; Wingfield et al., 2020). Specifically, it has been shown that increased testosterone, male-male aggression, and mating behavior are typically a response to available female mating opportunities rather than to mere social challenge from conspecific males (Goymann, 2009; Hirschenhauser & Oliveira, 2006; Pinxten et al., 2003). Furthermore, it has been suggested that the rise in testosterone and related behavioral change depends on whether the species lives in a social environment with well-separated mating and parenting roles (Goymann et al., 2019). For example, in many fish and some bird species, nest-tending males are the most attractive mating partners for females (Art, 2000; Avise et al., 2002). For such species, there is no conflict between mating and parenting because males can attract female mating partners and be caring fathers at the same time. In that case, rather than merely promoting aggression and decreasing parental care, acute testosterone increase may enhance a variety of social behaviors and phenotypes relevant to the status enhancement and consequent reproductive success (Moore et al., 2020; Sapolsky, 2017). Research across animal species supports the claim that the testosterone increase and its effects depend on the mating system and broader environmental context. For instance, in line with the so-called bipotential regulation hypothesis, testosterone was found to promote growth in male lizards in which sexual size dimorphism presents a competitive advantage (Cox et al., 2009) but inhibits growth in other reptiles, where large size is not advantageous (John-Alder & Cox, 2007; Sockman et al., 2008). Furthermore, research in mammals shows that testosterone increase is shaped by contextual factors, such as instability of the environment or social rank (e.g., in macaques (Higham et al., 2013) or capuchin monkeys (Mendonça-Furtado et al., 2014)) and that its

behavioral effects also depend on social context and individual life-history, for instance, previous sexual experience (Zhao et al., 2019) or familiarity of the environment (Zhao & Marler, 2016).

Although providing an exhaustive overview of testosterone's activational effects on social behaviors in non-human animals is beyond the scope of this dissertation, the research above demonstrates the richness of these effects, that range from territorial aggression (Wingfield, 1994) to courtship (Fusani, 2008), intersexual advertisement (McDonald et al., 2001) and increased paternal behavior (Trainor & Marler, 2001). Importantly, the exact form of testosterone's short-term effects appears to be impacted by the specific configuration of the individual's social environment. Such findings provide fertile ground for the investigation of the role of testosterone in humans, whose social behaviors and environments reach a complexity unparalleled by other animal species.

1.4 The role of testosterone in human social behavior

In 2010, Christoph Eisenegger published a study demonstrating that in humans, testosterone administration enhances fair behavior (Eisenegger et al., 2010). This research transformed the scientific discourse, which had hitherto been mainly centered, similar to research in animals, on studying testosterone's link to aggression (e.g., Dabbs et al., 1995, Archer, 2006, for review see Geniole et al., 2020) and mating (Gray & Campbell, 2009; M. Peters et al., 2008).

Based on their administration study, correlational studies (Coates & Herbert, 2008; Josephs et al., 2003; Newman et al., 2005) and previous theoretical frameworks (for testosterone reciprocal model and biosocial model of status see Mazur, 1985, 2005; Mazur & Booth, 1998), Eisenegger et al. (2011) argued that the role of testosterone in human social behavior is best understood in terms of the search for, and maintenance of, social status. Soon after the publication of the above research and review, testosterone administration research started to blossom, bringing evidence supportive of the claim that testosterone promotes a diverse spectrum of behaviors that may lead to social status enhancement. These behaviors included cooperation (van Honk et al., 2012), reciprocity (Boksem et al., 2013), approach behavior (Enter et al., 2016), and prosocial but also antisocial decision-making (Dreher et al., 2016). Despite the evidence and popularization of the idea that testosterone's primary role is to promote status-seeking (Sapolsky, 2017), this hypothesis wasn't directly tested. Therefore, this doctoral project's first aim was to provide the causal test of the hypothesis that in human males, testosterone promotes status-seeking behaviors. Furthermore, with the rising number of studies that highlight the diversity of testosterone effects, it became even more evident than in the studies of other vertebrates, that testosterone's effects are crucially shaped by contextual factors. Understanding the envornmental factors that influence the effects of change in teststoerone levels are an important step in our understanding of the current

and evolutionary function of variations in the hormone–behavior connections (Hau et al., 2008). The present thesis therefore sought to systematically test the interaction of testosterone's effects with different types of social context. Finally, the variety of testosterone's effects gives rise to an intriguing question, which is through what mechanisms testosterone promotes or modulates complex social behaviors. In the following subsection we discuss possible pathways through which testosterone may exert its activational effects and outline the experimental approaches that we employed to test these mechanisms.

1.5 Mechanisms underlying the role of testosterone in human social behavior

1.5.1 Fear and stress reduction

When an organism is facing a situation that threatens or, on the contrary, potentially elevates its social status, the individual typically exhibits a fear or stress response, which subsequently influences its social behaviors (Taylor, 2014). It has thus been suggested that testosterone may enhance status-seeking behaviors through the reduction of fear and stress (Eisenegger et al., 2011). Enhanced stress resilience and reduced fear responses can help an individual cope more effectively with challenging situations. Indeed, research in rodent stress models showed that testosterone replacement in gonadectomized rats reduced corticotrope stress response (Viau & Meaney, 2004) and reduced anxiety-like behavior (Fernández-Guasti & Martínez-Mota, 2005). Consistently, in humans, exogenous testosterone reduced unconscious attention to fear (van Honk et al., 2005) and fear-potentiated startle (Hermans et al., 2006). Yet, other studies show mixed effects of exogenous testosterone on cortisol and corticotropin release during pharmacological HPA axis stimulation (Rubinow et al., 2005) and enhanced cortisol in response to social stressor after testosterone administration (Knight et al., 2017a).

In Study 1 of this thesis, we aimed to address some of these inconsistencies and examine the effects of testosterone administration on the physiological stress response. Specifically, we were interested in whether testosterone impacts physiological stress response differentially when the stressor is purely biological (thus when no threat to social status is present) compared to situations where the stressor is embedded in a social context. For this reason, we employed and compared closely matched stress protocols: the cold-pressor test and the socially evaluated cold-pressor test, which differed only in one aspect: the presence or absence of an observer. To capture the multifaceted nature of the stress response, our study went beyond previous research, which typically focused on either the hypothalamic-pituitary-adrenal (HPA) axis (for reviews, see, e.g., Handa & Weiser, 2014; Stephens et al., 2016; Turan et al., 2015) or, to a lesser extent, the autonomic nervous system (ANS) (Chichinadze & Chichinadze, 2008; Toufexis et al., 2014).

Instead, we assessed established markers of HPA axis activity, as well as the activation of the sympathetic and parasympathetic branches of the ANS, along with psychological measures of subjectively perceived stress. By comparing the impact of testosterone on stress responses in social and non-social contexts, we took another step towards exploring the assertion that testosterone enhances social status via reducing stress responses.

1.5.2 Reward processing

Another possible mechanism through which testosterone might influence complex social behaviors is by modulation of reward processing in the dopaminergic system. In rodents, exogenous testosterone was found to increase dopamine levels in the ventral striatum (de Souza Silva et al., 2009), a part of the so-called "reward circuit". Furthermore, rodents exhibit place preferences for testosterone administration (Johnson & Wood, 2001); an effect that had been localized to the nucleus accumbens shell (Robbins & Everitt, 1996), and blocked by dopamine receptor antagonists (Packard et al., 1998). Such findings suggest that testosterone may exert its effects through modulation of the dopaminergic system in reward-related neural circuits. Beyond these insights from animal research, testosterone and reward processing have also been linked in humans. For example, testosterone administration enhanced neural responses measured by means of functional magnetic resonance imaging (fMRI) in the ventral striatum to cues signaling potential reward (Hermans et al., 2010), and endogenous testosterone levels correlated with ventral striatum activations in response to monetary rewards (Op de Macks et al., 2011). This evidence provided initial support for the hypothesis that testosterone modulates reward-related circuits. However, it remained unclear which specific aspects of reward processing testosterone acts on. To address this open questions, in Study 2 (see Chapter 3), we employed a novel, combined reinforcement-learning drift-diffusion modeling framework (RLDDM).

The reinforcement learning part of the framework (Sutton & Barto, 2018) posits that individuals learn to take actions that maximize their rewards on a trial-and-error basis by forming stimulus–outcome associations. The central component of this learning is the so-called prediction error (PE) which denotes the difference between the expected and actual outcome of a choice. There is substantial evidence (Cohen et al., 2012; Diederen et al., 2016) that PEs are encoded by the phasic activity of midbrain dopaminergic neurons projecting to the ventral striatum. These PEs guide the update of previously learned reward values and thus enable learning about the consequences of our actions. The learned reward values then inform future choice performance and allow us to navigate the social environments essential for our well-being and survival.

The temporal dynamics of these processes can be captured by drift-diffusion modeling. The DDM part of the framework (Ratcliff & McKoon, 2008) postulates that when making a decision, noisy evidence in favor of one over the other option is integrated over time until a certain pre-set threshold is reached. This threshold indicates how much of this relative evidence is enough to

initiate a response. Since the incoming evidence is noisy, the integrated evidence becomes more reliable as time passes. Therefore, higher thresholds typically lead to more accurate decisions. The combined RLDDM model takes into account that the speed of evidence integration is also influenced by the difference between the subjective reward values of the available options (Fontanesi et al., 2019). Leveraging the strengths of both RL and DDM frameworks provides a unique opportunity to elucidate the latent mechanisms underlying testosterone's effects on reward processing and related decision-making. This approach allows for the disentanglement of the influence of testosterone on the components of the learning and decision-making process, namely: the integration of prediction errors, the translation of learned values into choice behavior, the individual amount of evidence required to reach a decision, and the temporal dynamics of reward evidence accumulation. Chapter 3 describes the outcomes of our endeavor to examine whether testosterone administration modulates these processes and ultimately determine if testosterone bolsters the pursuit of social status by means of these mechanisms.

1.5.3 Threat and competence perception

The ability to accurately perceive potential threats in the social environment is essential not only for maintaining one's safety and avoiding harm but also for effective status-seeking strategies. The correct assessment of the social situation with regard to status-seeking involves both evaluations of one’s own competence and the assessment of the abilities and behavioral tendencies of others involved. Inadequate competence perception can lead to poor decision-making, unfavorable results of conflicts, and consequently to reduced social status. Research provides some evidence that testosterone modulates the subjective perception of oneself (Welling et al., 2016) and that it may modulate how an individual perceives and reacts to social cues present in his immediate environment. For example, testosterone administration enhanced amygdala responsiveness to viewing angry facial expressions (Hermans et al., 2008) yet diminished gaze aversion from angry faces viewed outside of awareness (Terburg et al., 2012, 2016). Other research shows that although testosterone reduced submissive behavior towards threatening individuals, it did not affect the subjective perception of threat (Geniole, Proietti, et al., 2019). In Chapter 4, we explain the link between the perception of competence and the perception of control, how this perception may motivate status-seeking behavior outside of aggressive interactions, and examine whether testosterone influences status-related behaviors through modulating the perception of own and opponent’s competence.

1.5.4. Deliberate and reflexive cognitive processes

Correlation studies have report a positive relationship between endogenous testosterone and impulse control disorders such as drug abuse, bulimia, and borderline personality disorder (Campbell et al., 2010; Naessén et al., 2019; Rausch et al., 2015). More recently, testosterone administration was shown to increase impulsivity for sexual and monetary rewards in an

intertemporal choice task (Wu et al., 2020, 2022). Importantly, prefrontal brain regions involved in impulse control contain ARs (Aubele & Kritzer, 2012; Lieberman et al., 2002), and several imaging studies have linked testosterone to reduced activation in the prefrontal regions and/or functional decoupling between them and regions of the limbic systems (e.g., Kaldewaij et al., 2019; Spielberg et al., 2015; Volman et al., 2016). Such findings led to the hypothesis that testosterone biases decision-making away from reflective and deliberate responses toward rapid and intuitive ones (Nave et al., 2017). This shift could serve as a potential mechanism by which testosterone enhances status-seeking behaviors, as facilitation of rapid, reflexive responses can be biologically adaptive in contexts where success depends on fast, instinctive behavior and when slow responding might be costly (e.g., physical challenges or mating). One of the aims of my dissertation was to rigorously examine whether testosterone affects cognitive processes underlying impulsive behaviors (Daw et al., 2005; Kahneman, 2011; Kool et al., 2016). In Chapter 5, I present the results of a multi-lab study that assessed whether exogenous testosterone impairs deliberate cognitive reflection (Frederick, 2005). Moreover, to further elucidate the involvement of testosterone in deliberate cognitive processes, Chapter 6 presents the outcomes of a study that used computational modeling to explore whether and how testosterone, in interaction with genetic polymorphisms, impacts the trade-off between deliberate and reflexive decision-making.

1.5.5 Genetic polymorphisms

The effects testosterone (and, for that matter, any other hormone) exerts do not depend merely on the released amount of the hormone but also on its interaction with all other agents in a signaling cascade. The respective elements in the androgenic system evolved when genetic mutations changed the amino acid sequence that defined a protein's structure and function, thereby turning up or down the regulatory capacity of the steroid system as a whole (Schuppe et al., 2020). In testosterone signaling, a crucial role is played by androgen receptors (De Gendt et al., 2004) encoded by the AR receptor gene containing a polymorphic cytosine-adenine-guanine (CAG) repeat sequence (Edwards et al., 1992). This triplet CAG, present in exon 1 of the AR gene, encodes a polyglutamine stretch in AR's N-terminal transactivating domain, such that a greater number of CAG repeats leads to the production of ARs with longer stretches of polyglutamine (Zitzmann & Nieschlag, 2003). In vitro, the length of the polyglutamine chain correlates inversely with transcriptional activity by the AR (Chamberlain et al., 1994). In line with this, men who possess exceptionally long CAG-repeat sequence experience clinical androgen insensitivity (Igarashi et al., 1992; La Spada et al., 1991), and more severe symptoms of hypoandrogenicity and an earlier onset of the disease were observed in individuals with longer CAG-repeat length (Choong et al., 1998; Mariotti et al., 2000). Crucially, a recent testosterone administration study showed that the hormone's enhancing effects on aggressive (Geniole, Procyshyn, et al., 2019) and competitive (Losecaat Vermeer et al., 2020) behavior were more pronounced in participants with fewer CAG repeats. Finding that testosterone administration interacts with the CAG-repeat

polymorphism is especially interesting because it may help characterize the exact role of the polymorphism in shaping AR function. As mentioned earlier, there is substantial evidence that the CAG-repeat polymorphism influences AR transcriptional activity (Chamberlain et al., 1994; Zitzmann & Nieschlag, 2003). However, short-term activational effects were not considered to depend on gene transcription and protein synthesis. Rather, these relatively fast activational effects were thought to occur through non-genomic pathways involving rapid extranuclear signaling (Michels & Hoppe, 2008; Simoncini & Genazzani, 2003). These discrepancies led to suggesting (Thomas, 2019) the existence of distinct membrane steroid receptors unrelated to nuclear steroid receptors that could initiate rapid increases in second messengers such as free calcium and activation of G proteins (Foradori et al., 2008). This dissertation aims to contribute to the understanding of testosterone signaling pathways by investigating whether the short-term effects of exogenous testosterone, reported across our four studies, depend on the CAG-repeat polymorphism of the AR gene.

As mentioned in subchapter 1.5.2 it has been suggested that testosterone may influence behavior by interacting with dopaminergic pathways. In rodents, exogenous testosterone increased dopamine concentration in the ventral striatum (de Souza Silva et al., 2009) and increased expression of the dopamine transporter (DAT) protein in the substantia nigra (Purves-Tyson et al., 2014). The expression of DAT, which regulates striatal dopamine, is linked to a 40 base-pair variable number tandem repeat (VNTR) polymorphism of the DAT1 gene (Vandenbergh et al., 1992). Homozygous 10/10-repeat carriers of this polymorphism have higher DAT expression (leading to lower striatal dopamine) than heterozygous individuals (Heinz et al., 2000). Importantly, DAT1 polymorphism was shown to determine the effects of pharmacological dopamine manipulation on reinforcement learning (Eisenegger et al., 2013). Therefore, our studies involving RL paradigms assessed DAT1 polymorphism and examined whether it modulated testosterone administration effects.

Besides examining the interaction between exogenous testosterone and polymorphisms determining striatal dopamine concentration, we also explored whether testosterone interacts with possible dopamine levels in the prefrontal cortex, indexed by the Catechol-O-methyl transferase (COMT) gene polymorphism. COMT is important to the degradation of several catecholamines, but it is especially relevant to the metabolism of dopamine in the prefrontal cortex (PFC), as it is assumed to be responsible for degrading more than 60% of PFC dopamine in the synaptic cleft (Käenmäki et al., 2010; Karoum et al., 1994). A nucleotide substitution (G to A) at codon 158 of the COMT gene creates a functional polymorphic variation of this enzyme - val158met, which has a degradation rate between ⅓ and ¼ slower than the enzyme val158val (Chen et al., 2004). Thus, individuals who are homozygous for the valine allele have higher COMT activity and lower concentrations of extracellular dopamine than the heterozygous individuals with intermediate enzyme activity and than homozygous met carriers who tend to have the lowest levels of COMT

activity (i.e., the highest dopamine bioavailability in the synaptic cleft). Multiple studies show a link between COMT genotype and cognitive function (Barkus et al., 2016; Gaysina et al., 2013; Satterfield et al., 2018), and there is preliminary evidence that the detrimental impact of declining testosterone levels on cognitive function in aging is mediated by COMT polymorphism (Buskbjerg et al., 2022). Therefore, to further elucidate mechanisms through which testosterone exerts its effects, in our computational study of testosterone effects on deliberate cognitive processes, we examined whether testosterone actions interact with the COMT gene polymorphism.

1.6 Outline

The following chapters of this dissertation report the findings of our single-dose testosterone administration studies rooted in the above-outlined research evidence and theoretical considerations. The studies aimed to test and characterize testosterone's causal role in status-seeking behavior, and to elucidate mechanisms by which the hormone exerts its effects. In Study 1, we address the assertion that testosterone enhances status-seeking via stress reduction by contrasting testosterone's impact on physiological stress responses in private versus socially evaluated settings. In study 2, we test whether testosterone promotes dominant or reputable status-seeking behaviors, once again by comparing testosterone's effects in private and socially visible situations. Moreover, by using a task embedded in a reinforcement-learning drift-diffusion modeling framework, we examine the claim that testosterone promotes status-seeking by impacting reward-related processes. In Study 3, we continue our inquiry into the mechanisms underlying testosterone's behavioral effects and examine whether testosterone boosts persistence by affecting the subjective perception of personal or opponent's control in a competitive setting. Finally, in Studies 4 and 5, we investigate whether testosterone promotes reflexive over deliberate cognitive processes, a mechanism that may foster rapid responses in status-challenging environments.

References

Archer, J. (2006). Testosterone and human aggression: An evaluation of the challenge hypothesis. *Neuroscience and Biobehavioral Reviews*, *30*(3), 319–345. https://doi.org/10.1016/j.neubiorev.2004.12.007

Art, S. H. M. B. (2000). Population structure and breeding system of the sex-role reversed, polyandrous Bronze-winged Jacana Metopidius indicus. *Ibis*, *142*(1), 93–102. https://doi.org/10.1111/j.1474-919X.2000.tb07688.x

Aubele, T., & Kritzer, M. F. (2012). Androgen Influence on Prefrontal Dopamine Systems in Adult Male Rats: Localization of Cognate Intracellular Receptors in Medial Prefrontal Projections to the Ventral Tegmental Area and Effects of Gonadectomy and Hormone Replacement on Glutamate-Stimulated Extracellular Dopamine Level. *Cerebral Cortex (New York, NY)*, *22*(8), 1799–1812. https://doi.org/10.1093/cercor/bhr258

Auyeung, B., Lombardo, M. V., & Baron-Cohen, S. (2013). Prenatal and postnatal hormone effects on the human brain and cognition. *Pflugers Archiv: European Journal of Physiology*, *465*(5), 557–571. https://doi.org/10.1007/s00424-013-1268-2

Avise, J. C., Jones, A. G., Walker, D., & DeWoody, J. A. (2002). Genetic Mating Systems and Reproductive Natural Histories of Fishes: Lessons for Ecology and Evolution. *Annual Review of Genetics*, *36*(1), 19–45. https://doi.org/10.1146/annurev.genet.36.030602.090831

Baker, M. E. (2005). Xenobiotics and the Evolution of Multicellular Animals: Emergence and Diversification of Ligand-Activated Transcription Factors1. *Integrative and Comparative Biology*, *45*(1), 172–178. https://doi.org/10.1093/icb/45.1.172

Barkus, C., Korn, C., Stumpenhorst, K., Laatikainen, L. M., Ballard, D., Lee, S., Sharp, T., Harrison, P. J., Bannerman, D. M., Weinberger, D. R., Chen, J., & Tunbridge, E. M. (2016). Genotype-Dependent Effects of COMT Inhibition on Cognitive Function in a Highly Specific, Novel Mouse Model of Altered COMT Activity. *Neuropsychopharmacology*, *41*(13), Article 13. https://doi.org/10.1038/npp.2016.119

Boksem, M. A. S., Mehta, P. H., Van den Bergh, B., van Son, V., Trautmann, S. T., Roelofs, K., Smidts, A., & Sanfey, A. G. (2013). Testosterone inhibits trust but promotes reciprocity. *Psychological Science*, *24*(11), 2306–2314. https://doi.org/10.1177/0956797613495063

Bos, P. A., Hermans, E. J., Ramsey, N. F., & van Honk, J. (2012). The neural mechanisms by which testosterone acts on interpersonal trust. *NeuroImage*, *61*(3), 730–737. https://doi.org/10.1016/j.neuroimage.2012.04.002

Breed, M. D. (2017). Chapter 64—1990 The Challenge Hypothesis. In M. D. Breed (Ed.), *Conceptual Breakthroughs in Ethology and Animal Behavior* (pp. 195–196). Academic Press. https://doi.org/10.1016/B978-0-12-809265-1.00064-2

Buskbjerg, C. R., Amidi, A., Buus, S., Gravholt, C. H., Hadi Hosseini, S. M., & Zachariae, R. (2022). Androgen deprivation therapy and cognitive decline—Associations with brain connectomes, endocrine status, and risk genotypes. *Prostate Cancer and Prostatic Diseases*, *25*(2), Article 2. https://doi.org/10.1038/s41391-021-00398-1

Butenandt, A., & Hanisch, G. (1935). *Über Testosteron. Umwandlung des Dehydro-androsterons in Androstendiol und Testosteron; ein Weg zur Darstellung des Testosterons aus Cholesterin. 237*(1–3), 89–97. https://doi.org/10.1515/bchm2.1935.237.1-3.89

Campbell, B. C., Dreber, A., Apicella, C. L., Eisenberg, D. T. A., Gray, P. B., Little, A. C., Garcia, J. R., Zamore, R. S., & Lum, J. K. (2010). Testosterone exposure, dopaminergic reward, and sensation-seeking in young men. *Physiology & Behavior*, *99*(4), 451–456. https://doi.org/10.1016/j.physbeh.2009.12.011

Carré, J. M., Geniole, S. N., Ortiz, T. L., Bird, B. M., Videto, A., & Bonin, P. L. (2017). Exogenous Testosterone Rapidly Increases Aggressive Behavior in Dominant and Impulsive Men. *Biological Psychiatry*, *82*(4), 249–256. https://doi.org/10.1016/j.biopsych.2016.06.009

Chamberlain, N. L., Driver, E. D., & Miesfeld, R. L. (1994). The length and location of CAG trinucleotide repeats in the androgen receptor N-terminal domain affect transactivation function. *Nucleic Acids Research*, *22*(15), 3181–3186. https://doi.org/10.1093/nar/22.15.3181

Chen, J., Lipska, B. K., Halim, N., Ma, Q. D., Matsumoto, M., Melhem, S., Kolachana, B. S., Hyde, T. M., Herman, M. M., Apud, J., Egan, M. F., Kleinman, J. E., & Weinberger, D. R. (2004). Functional Analysis of Genetic Variation in Catechol-O-Methyltransferase (COMT): Effects on mRNA, Protein, and Enzyme Activity in Postmortem Human Brain. *The American Journal of Human Genetics*, *75*(5), 807–821. https://doi.org/10.1086/425589

Chichinadze, K., & Chichinadze, N. (2008). Stress-induced increase of testosterone: Contributions of social status and sympathetic reactivity. *Physiology & Behavior*, *94*(4), 595–603. https://doi.org/10.1016/j.physbeh.2008.03.020

Choong, C. S., Kemppainen, J. A., & Wilson, E. M. (1998). Evolution of the primate androgen receptor: A structural basis for disease. *Journal of Molecular Evolution*, *47*(3), 334–342. https://doi.org/10.1007/pl00006391

Coates, J. M., & Herbert, J. (2008). Endogenous steroids and financial risk taking on a London trading floor. *Proceedings of the National Academy of Sciences*, *105*(16), 6167–6172. https://doi.org/10.1073/pnas.0704025105

Coccaro, E. F., McCloskey, M. S., Fitzgerald, D. A., & Phan, K. L. (2007). Amygdala and Orbitofrontal Reactivity to Social Threat in Individuals with Impulsive Aggression. *Biological Psychiatry*, *62*(2), 168–178. https://doi.org/10.1016/j.biopsych.2006.08.024

Cohen, J. Y., Haesler, S., Vong, L., Lowell, B. B., & Uchida, N. (2012). Neuron-type-specific signals for reward and punishment in the ventral tegmental area. *Nature*, *482*(7383), 85–88. https://doi.org/10.1038/nature10754

Collaer, M. L., & Hines, M. (1995). Human behavioral sex differences: A role for gonadal hormones during early development? *Psychological Bulletin*, *118*(1), 55–107. https://doi.org/10.1037/0033-2909.118.1.55

Cools, R., & D'Esposito, M. (2011). Inverted-U–Shaped Dopamine Actions on Human Working Memory and Cognitive Control. *Biological Psychiatry*, *69*(12), e113–e125. https://doi.org/10.1016/j.biopsych.2011.03.028

Cox, R. M., Stenquist, D. S., & Calsbeek, R. (2009). Testosterone, growth and the evolution of sexual size dimorphism. *Journal of Evolutionary Biology*, *22*(8), 1586–1598. https://doi.org/10.1111/j.1420-9101.2009.01772.x

Creutz, L. M., & Kritzer, M. F. (2004). Mesostriatal and mesolimbic projections of midbrain neurons immunoreactive for estrogen receptor beta or androgen receptors in rats. *Journal of Comparative Neurology*, *476*(4), 348–362. https://doi.org/10.1002/cne.20229

Cunningham, G. R., Stephens-Shields, A. J., Rosen, R. C., Wang, C., Bhasin, S., Matsumoto, A. M., Parsons, J. K., Gill, T. M., Molitch, M. E., Farrar, J. T., Cella, D., Barrett-Connor, E., Cauley, J. A., Cifelli, D., Crandall, J. P., Ensrud, K. E., Gallagher, L., Zeldow, B., Lewis, C. E., … Snyder, P. J. (2016). Testosterone Treatment and Sexual Function in Older Men With Low Testosterone Levels. *The Journal of Clinical Endocrinology and Metabolism*, *101*(8), 3096–3104. https://doi.org/10.1210/jc.2016-1645

Dabbs, J. M., Carr, T. S., Frady, R. L., & Riad, J. K. (1995). Testosterone, crime, and misbehavior among 692 male prison inmates. *Personality and Individual Differences*, *18*(5), 627–633. https://doi.org/10.1016/0191-8869(94)00177-T

Davey, R. A., & Grossmann, M. (2016). Androgen Receptor Structure, Function and Biology: From Bench to Bedside. *The Clinical Biochemist Reviews*, *37*(1), 3–15. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4810760/

David, K., Dingemanse, E., Freud, J., & Laqueur, E. (1935). Über krystallinisches männliches Hormon aus Hoden (Testosteron), wirksamer als aus Harn oder aus Cholesterin bereitetes Androsteron. *Hoppe-Seyler´s Zeitschrift Für Physiologische Chemie*, *233*(5–6), 281–283. https://doi.org/10.1515/bchm2.1935.233.5-6.281

Daw, N. D., Gershman, S. J., Seymour, B., Dayan, P., & Dolan, R. J. (2011). Model-based influences on humans' choices and striatal prediction errors. *Neuron*, *69*(6), 1204–1215. https://doi.org/10.1016/j.neuron.2011.02.027

Daw, N. D., Niv, Y., & Dayan, P. (2005). Uncertainty-based competition between prefrontal and dorsolateral striatal systems for behavioral control. *Nature Neuroscience*, *8*(12), 1704–1711. https://doi.org/10.1038/nn1560

De Gendt, K., Swinnen, J. V., Saunders, P. T. K., Schoonjans, L., Dewerchin, M., Devos, A., Tan, K., Atanassova, N., Claessens, F., Lécureuil, C., Heyns, W., Carmeliet, P., Guillou, F., Sharpe, R. M., & Verhoeven, G. (2004). A Sertoli cell-selective knockout of the androgen receptor causes spermatogenic arrest in meiosis. *Proceedings of the National Academy of Sciences of the United States of America*, *101*(5), 1327–1332. https://doi.org/10.1073/pnas.0308114100

de Souza Silva, M. A., Mattern, C., Topic, B., Buddenberg, T. E., & Huston, J. P. (2009). Dopaminergic and serotonergic activity in neostriatum and nucleus accumbens enhanced by intranasal administration of testosterone. *European Neuropsychopharmacology*, *19*(1), 53–63. https://doi.org/10.1016/j.euroneuro.2008.08.003

Delville, Y., Mansour, K. M., & Ferris, C. F. (1996). Testosterone facilitates aggression by modulating vasopressin receptors in the hypothalamus. *Physiology & Behavior*, *60*(1), 25–29. https://doi.org/10.1016/0031-9384(95)02246-5

Desjardins, J. K., Hazelden, M. R., Van der Kraak, G. J., & Balshine, S. (2006). Male and female cooperatively breeding fish provide support for the "Challenge Hypothesis." *Behavioral Ecology*, *17*(2), 149–154. https://doi.org/10.1093/beheco/arj018

DeVries, M. S., Winters, C. P., & Jawor, J. M. (2012). Testosterone elevation and response to gonadotropin-releasing hormone challenge by male northern cardinals (Cardinalis cardinalis) following aggressive behavior. *Hormones and Behavior*, *62*(1), 99–105. https://doi.org/10.1016/j.yhbeh.2012.05.008

Diederen, K. M. J., Spencer, T., Vestergaard, M. D., Fletcher, P. C., & Schultz, W. (2016). Adaptive Prediction Error Coding in the Human Midbrain and Striatum Facilitates Behavioral Adaptation and Learning Efficiency. *Neuron*, *90*(5), 1127–1138. https://doi.org/10.1016/j.neuron.2016.04.019

Dreher, J.-C., Dunne, S., Pazderska, A., Frodl, T., Nolan, J. J., & O'Doherty, J. P. (2016). Testosterone causes both prosocial and antisocial status-enhancing behaviors in human males. *Proceedings of the National Academy of Sciences*, *113*(41), 11633–11638. https://doi.org/10.1073/pnas.1608085113

Edwards, A., Hammond, H. A., Jin, L., Caskey, C. T., & Chakraborty, R. (1992). Genetic variation at five trimeric and tetrameric tandem repeat loci in four human population groups. *Genomics*, *12*(2), 241–253. https://doi.org/10.1016/0888-7543(92)90371-x

Eisenegger, C., Haushofer, J., & Fehr, E. (2011). The role of testosterone in social interaction. *Trends in Cognitive Sciences*, *15*(6), 263–271. https://doi.org/10.1016/j.tics.2011.04.008

Eisenegger, C., Naef, M., Linssen, A., Clark, L., Gandamaneni, P. K., Müller, U., & Robbins, T. W. (2014). Role of Dopamine D2 Receptors in Human Reinforcement Learning. *Neuropsychopharmacology*, *39*(10), 2366–2375. https://doi.org/10.1038/npp.2014.84

Eisenegger, C., Naef, M., Snozzi, R., Heinrichs, M., & Fehr, E. (2010). Prejudice and truth about the effect of testosterone on human bargaining behaviour. *Nature*, *463*(7279), 356–359. https://doi.org/10.1038/nature08711

Eisenegger, C., Pedroni, A., Rieskamp, J., Zehnder, C., Ebstein, R., Fehr, E., & Knoch, D. (2013). DAT1 Polymorphism Determines L-DOPA Effects on Learning about Others' Prosociality. *PLoS ONE*, *8*(7), e67820. https://doi.org/10.1371/journal.pone.0067820

Enter, D., Spinhoven, P., & Roelofs, K. (2014). Alleviating social avoidance: Effects of single dose testosterone administration on approach–avoidance action. *Hormones and Behavior*, *65*(4), 351–354. https://doi.org/10.1016/j.yhbeh.2014.02.001

Enter, D., Spinhoven, P., & Roelofs, K. (2016). Dare to approach: Single dose testosterone administration promotes threat approach in patients with social anxiety disorder. *Clinical Psychological Science*, *4*, 1073–1079. https://doi.org/10.1177/2167702616631499

Fernández-Guasti, A., & Martínez-Mota, L. (2005). Anxiolytic-like actions of testosterone in the burying behavior test: Role of androgen and GABA-benzodiazepine receptors. *Psychoneuroendocrinology*, *30*(8), 762–770. https://doi.org/10.1016/j.psyneuen.2005.03.006

Fontanesi, L., Gluth, S., Spektor, M. S., & Rieskamp, J. (2019). A reinforcement learning diffusion decision model for value-based decisions. *Psychonomic Bulletin & Review*, *26*(4), 1099–1121. https://doi.org/10.3758/s13423-018-1554-2

Foradori, C. D., Weiser, M. J., & Handa, R. J. (2008). Non-genomic Actions of Androgens. *Frontiers in Neuroendocrinology*, *29*(2), 169–181. https://doi.org/10.1016/j.yfrne.2007.10.005

Frederick, S. (2005). Cognitive Reflection and Decision Making. *Journal of Economic Perspectives*, *19*(4), 25–42. https://doi.org/10.1257/089533005775196732

Fusani, L. (2008). Testosterone control of male courtship in birds. *Hormones and Behavior*, *54*(2), 227–233. https://doi.org/10.1016/j.yhbeh.2008.04.004

Gaysina, D., Xu, M. K., Barnett, J. H., Croudace, T. J., Wong, A., Richards, M., & Jones, P. B. (2013). The catechol-O-methyltransferase gene (COMT) and cognitive function from childhood through adolescence. *Biological Psychology*, *92*(2), 359–364. https://doi.org/10.1016/j.biopsycho.2012.11.007

Geniole, S. N., Bird, B. M., McVittie, J. S., Purcell, R. B., Archer, J., & Carré, J. M. (2020). Is testosterone linked to human aggression? A meta-analytic examination of the relationship between baseline, dynamic, and manipulated testosterone on human aggression. *Hormones and Behavior*, *123*, 104644. https://doi.org/10.1016/j.yhbeh.2019.104644

Geniole, S. N., Procyshyn, T. L., Marley, N., Ortiz, T. L., Bird, B. M., Marcellus, A. L., Welker, K. M., Bonin, P. L., Goldfarb, B., Watson, N. V., & Carré, J. M. (2019). Using a Psychopharmacogenetic Approach To Identify the Pathways Through Which—And the People for Whom—Testosterone Promotes Aggression. *Psychological Science*, *30*(4), 481–494. https://doi.org/10.1177/0956797619826970

Geniole, S. N., Proietti, V., Bird, B. M., Ortiz, T. L., Bonin, P. L., Goldfarb, B., Watson, N. V., & Carré, J. M. (2019). Testosterone reduces the threat premium in competitive resource division. *Proceedings. Biological Sciences*, *286*(1903), 20190720. https://doi.org/10.1098/rspb.2019.0720

Goel, N., & Bale, T. L. (2008). Organizational and Activational Effects of Testosterone on Masculinization of Female Physiological and Behavioral Stress Responses. *Endocrinology*, *149*(12), 6399–6405. https://doi.org/10.1210/en.2008-0433

Goetz, S. M. M., Tang, L., Thomason, M. E., Diamond, M. P., Hariri, A. R., & Carré, J. M. (2014). Testosterone Rapidly Increases Neural Reactivity to Threat in Healthy Men: A Novel Two-Step Pharmacological Challenge Paradigm. *Biological Psychiatry*, *76*(4), 324–331. https://doi.org/10.1016/j.biopsych.2014.01.016

Goymann, W. (2009). Social modulation of androgens in male birds. *General and Comparative Endocrinology*, *163*(1–2), 149–157. https://doi.org/10.1016/j.ygcen.2008.11.027

Goymann, W., Moore, I. T., & Oliveira, R. F. (2019). Challenge Hypothesis 2.0: A Fresh Look at an Established Idea. *BioScience*, *69*(6), 432–442. https://www.jstor.org/stable/26732562

Gray, P. B., & Campbell, B. C. (2009). Human male testosterone, pair-bonding, and fatherhood. In *Endocrinology of social relationships* (pp. 270–293). Harvard University Press.

Gurvich, C., Hoy, K., Thomas, N., & Kulkarni, J. (2018). Sex Differences and the Influence of Sex Hormones on Cognition through Adulthood and the Aging Process. *Brain Sciences*, *8*(9), 163. https://doi.org/10.3390/brainsci8090163

Handa, R. J., & Weiser, M. J. (2014). Gonadal steroid hormones and the hypothalamo–pituitary–adrenal axis. *Frontiers in Neuroendocrinology*, *35*(2), 197–220. https://doi.org/10.1016/j.yfrne.2013.11.001

Hau, M., Gill, S. A., & Goymann, W. (2008). Tropical field endocrinology: Ecology and evolution of testosterone concentrations in male birds. *General and Comparative Endocrinology*, *157*(3), 241–248. https://doi.org/10.1016/j.ygcen.2008.05.008

Heany, S. J., Bethlehem, R. A. I., van Honk, J., Bos, P. A., Stein, D. J., & Terburg, D. (2018). Effects of testosterone administration on threat and escape anticipation in the orbitofrontal cortex. *Psychoneuroendocrinology*, *96*, 42–51. https://doi.org/10.1016/j.psyneuen.2018.05.038

Heinz, A., Goldman, D., Jones, D. W., Palmour, R., Hommer, D., Gorey, J. G., Lee, K. S., Linnoila, M., & Weinberger, D. R. (2000). Genotype Influences In Vivo Dopamine Transporter Availability in Human Striatum. *Neuropsychopharmacology*, *22*(2), 133–139. https://doi.org/10.1016/S0893-133X(99)00099-8

Hermans, E. J., Bos, P. A., Ossewaarde, L., Ramsey, N. F., Fernández, G., & van Honk, J. (2010). Effects of exogenous testosterone on the ventral striatal BOLD response during reward

anticipation in healthy women. *NeuroImage*, *52*(1), 277–283. https://doi.org/10.1016/j.neuroimage.2010.04.019
Hermans, E. J., Putman, P., Baas, J. M., Koppeschaar, H. P., & van Honk, J. (2006). A single administration of testosterone reduces fear-potentiated startle in humans. *Biological Psychiatry*, *59*(9), 872–874. https://doi.org/10.1016/j.biopsych.2005.11.015
Hermans, E. J., Ramsey, N. F., & van Honk, J. (2008). Exogenous testosterone enhances responsiveness to social threat in the neural circuitry of social aggression in humans. *Biological Psychiatry*, *63*(3), 263–270. https://doi.org/10.1016/j.biopsych.2007.05.013
Higham, J. P., Heistermann, M., & Maestripieri, D. (2013). The endocrinology of male rhesus macaque social and reproductive status: A test of the challenge and social stress hypotheses. *Behavioral Ecology and Sociobiology*, *67*(1), 19–30. https://doi.org/10.1007/s00265-012-1420-6
Hirschenhauser, K., & Oliveira, R. F. (2006). Social modulation of androgens in male vertebrates: Meta-analyses of the challenge hypothesis. *Animal Behaviour*, *71*(2), 265–277. https://doi.org/10.1016/j.anbehav.2005.04.014
Igarashi, S., Tanno, Y., Onodera, O., Yamazaki, M., Sato, S., Ishikawa, A., Miyatani, N., Nagashima, M., Ishikawa, Y., & Sahashi, K. (1992). Strong correlation between the number of CAG repeats in androgen receptor genes and the clinical onset of features of spinal and bulbar muscular atrophy. *Neurology*, *42*(12), 2300–2302. https://doi.org/10.1212/wnl.42.12.2300
Ishikawa, T., Glidewell-Kenney, C., & Jameson, J. L. (2006). Aromatase-independent testosterone conversion into estrogenic steroids is inhibited by a 5 alpha-reductase inhibitor. *The Journal of Steroid Biochemistry and Molecular Biology*, *98*(2–3), 133–138. https://doi.org/10.1016/j.jsbmb.2005.09.004
Ito, H., Takahashi, H., Arakawa, R., Takano, H., & Suhara, T. (2008). Normal database of dopaminergic neurotransmission system in human brain measured by positron emission tomography. *NeuroImage*, *39*(2), 555–565. https://doi.org/10.1016/j.neuroimage.2007.09.011
Janvier, P. (2007). Living Primitive Fishes and Fishes From Deep Time. In *Fish Physiology* (Vol. 26, pp. 1–51). Academic Press. https://doi.org/10.1016/S1546-5098(07)26001-7
John-Alder, H. B., & Cox, R. M. (2007). 195Development of sexual size dimorphism in lizards: Testosterone as a bipotential growth regulator. In *Sex, Size and Gender Roles: Evolutionary Studies of Sexual Size Dimorphism*. Oxford University Press. https://doi.org/10.1093/acprof:oso/9780199208784.003.0022
Johnson, L. R., & Wood, R. I. (2001). Oral testosterone self-administration in male hamsters. *Neuroendocrinology*, *73*(4), 285–292. https://doi.org/10.1159/000054645
Johnson, M. A., Kircher, B. K., & Castro, D. J. (2018). The evolution of androgen receptor expression and behavior in Anolis lizard forelimb muscles. *Journal of Comparative Physiology A*, *204*(1), 71–79. https://doi.org/10.1007/s00359-017-1228-y
Jönsson, E. G., Nöthen, M. M., Grünhage, F., Farde, L., Nakashima, Y., Propping, P., & Sedvall, G. C. (1999). Polymorphisms in the dopamine D2 receptor gene and their relationships to striatal dopamine receptor density of healthy volunteers. *Molecular Psychiatry*, *4*(3), Article 3. https://doi.org/10.1038/sj.mp.4000532
Josephs, R. A., Newman, M. L., Brown, R. P., & Beer, J. M. (2003). Status, testosterone, and human intellectual performance: Stereotype threat as status concern. *Psychological Science*, *14*(2), 158–163. https://doi.org/10.1111/1467-9280.t01-1-01435
Käenmäki, M., Tammimäki, A., Myöhänen, T., Pakarinen, K., Amberg, C., Karayiorgou, M., Gogos, J. A., & Männistö, P. T. (2010). Quantitative role of COMT in dopamine clearance in the prefrontal cortex of freely moving mice. *Journal of Neurochemistry*, *114*(6), 1745–1755. https://doi.org/10.1111/j.1471-4159.2010.06889.x
Kahneman, D. (2011). *Thinking, fast and slow* (p. 499). Farrar, Straus and Giroux.
Kaldewaij, R., Koch, S. B. J., Zhang, W., Hashemi, M. M., Klumpers, F., & Roelofs, K. (2019). High Endogenous Testosterone Levels Are Associated With Diminished Neural Emotional Control in Aggressive Police Recruits. *Psychological Science*, *30*(8), 1161–1173. https://doi.org/10.1177/0956797619851753

Ketterson, E. D., & Nolan, V. (1992). Hormones and life histories: An integrative approach. *The American Naturalist*, *140 Suppl 1*, S33-62. https://doi.org/10.1086/285396

Klebe, S., Golmard, J.-L., Nalls, M. A., Saad, M., Singleton, A. B., Bras, J. M., Hardy, J., Simon-Sanchez, J., Heutink, P., Kuhlenbäumer, G., Charfi, R., Klein, C., Hagenah, J., Gasser, T., Wurster, I., Lesage, S., Lorenz, D., Deuschl, G., Durif, F., … Corvol, J.-C. (2013). The Val158Met COMT polymorphism is a modifier of the age at onset in Parkinson's disease with a sexual dimorphism. *Journal of Neurology, Neurosurgery, and Psychiatry*, *84*(6), 666–673. https://doi.org/10.1136/jnnp-2012-304475

Knight, E. L., Christian, C. B., Morales, P. J., Harbaugh, W. T., Mayr, U., & Mehta, P. H. (2017a). Exogenous testosterone enhances cortisol and affective responses to social-evaluative stress in dominant men. *Psychoneuroendocrinology*, *85*, 151–157. https://doi.org/10.1016/j.psyneuen.2017.08.014

Knight, E. L., Christian, C. B., Morales, P. J., Harbaugh, W. T., Mayr, U., & Mehta, P. H. (2017b). Exogenous testosterone enhances cortisol and affective responses to social-evaluative stress in dominant men. *Psychoneuroendocrinology*, *85*, 151–157. https://doi.org/10.1016/j.psyneuen.2017.08.014

Kool, W., Cushman, F. A., & Gershman, S. J. (2016). When Does Model-Based Control Pay Off? *PLOS Computational Biology*, *12*(8), e1005090. https://doi.org/10.1371/journal.pcbi.1005090

Kwak, S., Huh, N., Seo, J.-S., Lee, J.-E., Han, P.-L., & Jung, M. W. (2014). Role of dopamine D2 receptors in optimizing choice strategy in a dynamic and uncertain environment. *Frontiers in Behavioral Neuroscience*, *8*. https://www.frontiersin.org/articles/10.3389/fnbeh.2014.00368

La Spada, A. R., Wilson, E. M., Lubahn, D. B., Harding, A. E., & Fischbeck, K. H. (1991). Androgen receptor gene mutations in X-linked spinal and bulbar muscular atrophy. *Nature*, *352*(6330), 77–79. https://doi.org/10.1038/352077a0

Lakshman, K. M., Kaplan, B., Travison, T. G., Basaria, S., Knapp, P. E., Singh, A. B., LaValley, M. P., Mazer, N. A., & Bhasin, S. (2010). The Effects of Injected Testosterone Dose and Age on the Conversion of Testosterone to Estradiol and Dihydrotestosterone in Young and Older Men. *The Journal of Clinical Endocrinology and Metabolism*, *95*(8), 3955–3964. https://doi.org/10.1210/jc.2010-0102

Landys, M. M., Goymann, W., Raess, M., & Slagsvold, T. (2007). Hormonal responses to male-male social challenge in the blue tit Cyanistes caeruleus: Single-broodedness as an explanatory variable. *Physiological and Biochemical Zoology: PBZ*, *80*(2), 228–240. https://doi.org/10.1086/510564

Lee, E., Seo, M., Dal Monte, O., & Averbeck, B. B. (2015). Injection of a Dopamine Type 2 Receptor Antagonist into the Dorsal Striatum Disrupts Choices Driven by Previous Outcomes, But Not Perceptual Inference. *The Journal of Neuroscience*, *35*(16), 6298–6306. https://doi.org/10.1523/JNEUROSCI.4561-14.2015

Lieberman, A. P., Harmison, G., Strand, A. D., Olson, J. M., & Fischbeck, K. H. (2002). Altered transcriptional regulation in cells expressing the expanded polyglutamine androgen receptor. *Human Molecular Genetics*, *11*(17), 1967–1976. https://doi.org/10.1093/hmg/11.17.1967

Litwack, G. (2022). Chapter 12—Androgens. In G. Litwack (Ed.), *Hormones (Fourth Edition)* (pp. 287–311). Academic Press. https://doi.org/10.1016/B978-0-323-90262-5.00004-4

Lombardo, M. V., Ashwin, E., Auyeung, B., Chakrabarti, B., Taylor, K., Hackett, G., Bullmore, E. T., & Baron-Cohen, S. (2012). Fetal Testosterone Influences Sexually Dimorphic Gray Matter in the Human Brain. *The Journal of Neuroscience*, *32*(2), 674–680. https://doi.org/10.1523/JNEUROSCI.4389-11.2012

Losecaat Vermeer, A. B., Krol, I., Gausterer, C., Wagner, B., Eisenegger, C., & Lamm, C. (2020). Exogenous testosterone increases status-seeking motivation in men with unstable low social status. *Psychoneuroendocrinology*, *113*, 104552. https://doi.org/10.1016/j.psyneuen.2019.104552

Luberti, F. R., Reside, T.-L., Bonin, P. L., & Carré, J. M. (2021). Development of a single-dose intranasal testosterone administration paradigm for use in men and women. *Hormones and Behavior*, *136*, 105046. https://doi.org/10.1016/j.yhbeh.2021.105046

Mariotti, C., Castellotti, B., Pareyson, D., Testa, D., Eoli, M., Antozzi, C., Silani, V., Marconi, R., Tezzon, F., Siciliano, G., Marchini, C., Gellera, C., & Donato, S. D. (2000). Phenotypic manifestations associated with CAG-repeat expansion in the androgen receptor gene in male patients and heterozygous females: A clinical and molecular study of 30 families. *Neuromuscular Disorders: NMD*, *10*(6), 391–397. https://doi.org/10.1016/s0960-8966(99)00132-7

Markov, G. V., Gutierrez-Mazariegos, J., Pitrat, D., Billas, I. M. L., Bonneton, F., Moras, D., Hasserodt, J., Lecointre, G., & Laudet, V. (2017). Origin of an ancient hormone/receptor couple revealed by resurrection of an ancestral estrogen. *Science Advances*, *3*(3), e1601778. https://doi.org/10.1126/sciadv.1601778

Markov, G. V., Tavares, R., Dauphin-Villemant, C., Demeneix, B. A., Baker, M. E., & Laudet, V. (2009). Independent elaboration of steroid hormone signaling pathways in metazoans. *Proceedings of the National Academy of Sciences*, *106*(29), 11913–11918. https://doi.org/10.1073/pnas.0812138106

Marler, C. A., & Moore, M. C. (1988). Evolutionary costs of aggression revealed by testosterone manipulations in free-living male lizards. *Behavioral Ecology and Sociobiology*, *23*(1), 21–26. https://doi.org/10.1007/BF00303053

Martinez, D., Orlowska, D., Narendran, R., Slifstein, M., Liu, F., Kumar, D., Broft, A., Van Heertum, R., & Kleber, H. D. (2010). D2/3 receptor availability in the striatum and social status in human volunteers. *Biological Psychiatry*, *67*(3), 275–278. https://doi.org/10.1016/j.biopsych.2009.07.037

Mazur, A. (1985). A biosocial model of status in face-to-face primate groups. *Social Forces*, *64*, 377–402. https://doi.org/10.2307/2578647

Mazur, A. (2005). *Biosociology of Dominance and Deference*. Rowman & Littlefield Publishers.

Mazur, A. (2017). Testosterone in biosociology: A memoir. *Hormones and Behavior*, *92*, 3–8. https://doi.org/10.1016/j.yhbeh.2015.12.004

Mazur, A., & Booth, A. (1998). Testosterone and dominance in men. *The Behavioral and Brain Sciences*, *21*(3), 353–363; discussion 363-397.

McDonald, P. G., Buttemer, W. A., & Astheimer, L. B. (2001). The influence of testosterone on territorial defence and parental behavior in male free-living rufous whistlers, Pachycephala rufiventris. *Hormones and Behavior*, *39*(3), 185–194. https://doi.org/10.1006/hbeh.2001.1644

McEwen, B. S. (1992). Steroid hormones: Effect on brain development and function. *Hormone Research*, *37 Suppl 3*, 1–10. https://doi.org/10.1159/000182393

McLeod, H. L., Syvänen, A. C., Githang'a, J., Indalo, A., Ismail, D., Dewar, K., Ulmanen, I., & Sludden, J. (1998). Ethnic differences in catechol O-methyltransferase pharmacogenetics: Frequency of the codon 108/158 low activity allele is lower in Kenyan than Caucasian or South-west Asian individuals. *Pharmacogenetics*, *8*(3), 195–199.

Mehta, P. H., & Beer, J. (2010). Neural Mechanisms of the Testosterone–Aggression Relation: The Role of Orbitofrontal Cortex. *Journal of Cognitive Neuroscience*, *22*(10), 2357–2368. https://doi.org/10.1162/jocn.2009.21389

Mendonça-Furtado, O., Edaes, M., Palme, R., Rodrigues, A., Siqueira, J., & Izar, P. (2014). Does hierarchy stability influence testosterone and cortisol levels of bearded capuchin monkeys (Sapajus libidinosus) adult males? A comparison between two wild groups. *Behavioural Processes*, *109 Pt A*, 79–88. https://doi.org/10.1016/j.beproc.2014.09.010

Michels, G., & Hoppe, U. C. (2008). Rapid actions of androgens. *Frontiers in Neuroendocrinology*, *29*(2), 182–198. https://doi.org/10.1016/j.yfrne.2007.08.004

Mikus, N., Korb, S., Massaccesi, C., Gausterer, C., Graf, I., Willeit, M., Eisenegger, C., Lamm, C., Silani, G., & Mathys, C. (2022). *Effects of dopamine D2 and opioid receptor antagonism on the trade-off between model-based and model-free behavior in healthy volunteers* (p. 2022.03.03.482871). bioRxiv. https://doi.org/10.1101/2022.03.03.482871

Moore, I. T., Hernandez, J., & Goymann, W. (2020). Who rises to the challenge? Testing the Challenge Hypothesis in fish, amphibians, reptiles, and mammals. *Hormones and Behavior*, *123*, 104537. https://doi.org/10.1016/j.yhbeh.2019.06.001

Morgan, D., Grant, K. A., Gage, H. D., Mach, R. H., Kaplan, J. R., Prioleau, O., Nader, S. H., Buchheimer, N., Ehrenkaufer, R. L., & Nader, M. A. (2002). Social dominance in

monkeys: Dopamine D2 receptors and cocaine self-administration. *Nature Neuroscience*, *5*(2), 169–174. https://doi.org/10.1038/nn798
Muehlenbein, M. P., & Watts, D. P. (2010). The costs of dominance: Testosterone, cortisol and intestinal parasites in wild male chimpanzees. *Biopsychosocial Medicine*, *4*, 21. https://doi.org/10.1186/1751-0759-4-21
Muller, M. N. (2017). Testosterone and reproductive effort in male primates. *Hormones and Behavior*, *91*, 36–51. https://doi.org/10.1016/j.yhbeh.2016.09.001
Nader, M. A., Nader, S. H., Czoty, P. W., Riddick, N. V., Gage, H. D., Gould, R. W., Blaylock, B. L., Kaplan, J. R., Garg, P. K., Davies, H. M., Morton, D., Garg, S., & Reboussin, B. A. (2012). SOCIAL DOMINANCE IN FEMALE MONKEYS: DOPAMINE RECEPTOR FUNCTION AND COCAINE REINFORCEMENT. *Biological Psychiatry*, *72*(5), 414–421. https://doi.org/10.1016/j.biopsych.2012.03.002
Naessén, S., Söderqvist, G., & Carlström, K. (2019). So similar and so different: Circulating androgens and androgen origin in bulimic women. *The Journal of Steroid Biochemistry and Molecular Biology*, *185*, 184–188. https://doi.org/10.1016/j.jsbmb.2018.08.013
Nathan, L., Shi, W., Dinh, H., Mukherjee, T. K., Wang, X., Lusis, A. J., & Chaudhuri, G. (2001). Testosterone inhibits early atherogenesis by conversion to estradiol: Critical role of aromatase. *Proceedings of the National Academy of Sciences*, *98*(6), 3589–3593. https://doi.org/10.1073/pnas.051003698
Nave, G., Nadler, A., Zava, D., & Camerer, C. (2017). Single-Dose Testosterone Administration Impairs Cognitive Reflection in Men. *Psychological Science*, *28*(10), 1398–1407. https://doi.org/10.1177/0956797617709592
Newman, M. L., Sellers, J. G., & Josephs, R. A. (2005). Testosterone, cognition, and social status. *Hormones and Behavior*, *47*(2), 205–211. https://doi.org/10.1016/j.yhbeh.2004.09.008
Nieschlag, E., & Behre, H. M. (Eds.). (1998). *Testosterone*. Springer. https://doi.org/10.1007/978-3-642-72185-4
Noble, E. P. (1998). The D2 Dopamine Receptor Gene: A Review of Association Studies in Alcoholism and Phenotypes. *Alcohol*, *16*(1), 33–45. https://doi.org/10.1016/S0741-8329(97)00175-4
Ogino, Y., Katoh, H., Kuraku, S., & Yamada, G. (2009). Evolutionary History and Functional Characterization of Androgen Receptor Genes in Jawed Vertebrates. *Endocrinology*, *150*(12), 5415–5427. https://doi.org/10.1210/en.2009-0523
Ogino, Y., Yamada, G., & Iguchi, T. (2018). Diversified Sex Characteristics Developments in Teleost Fishes: Implication for Evolution of Androgen Receptor (AR) Gene Function. In H. Hirata & A. Iida (Eds.), *Zebrafish, Medaka, and Other Small Fishes: New Model Animals in Biology, Medicine, and Beyond* (pp. 113–126). Springer. https://doi.org/10.1007/978-981-13-1879-5_7
Op de Macks, Z. A., Moor, B. G., Overgaauw, S., Güroğlu, B., Dahl, R. E., & Crone, E. A. (2011). Testosterone levels correspond with increased ventral striatum activation in response to monetary rewards in adolescents. *Developmental Cognitive Neuroscience*, *1*(4), 506–516. https://doi.org/10.1016/j.dcn.2011.06.003
Packard, M. G., Schroeder, J. P., & Alexander, G. M. (1998). Expression of Testosterone Conditioned Place Preference Is Blocked by Peripheral or Intra-accumbens Injection of α-Flupenthixol. *Hormones and Behavior*, *34*(1), 39–47. https://doi.org/10.1006/hbeh.1998.1461
Peters, M., Simmons, L. W., & Rhodes, G. (2008). Testosterone is associated with mating success but not attractiveness or masculinity in human males. *Animal Behaviour*, *76*(2), 297–303. https://doi.org/10.1016/j.anbehav.2008.02.008
Peters, S., Jolles, D. J., Duijvenvoorde, A. C. K. V., Crone, E. A., & Peper, J. S. (2015). The link between testosterone and amygdala–orbitofrontal cortex connectivity in adolescent alcohol use. *Psychoneuroendocrinology*, *53*, 117–126. https://doi.org/10.1016/j.psyneuen.2015.01.004
Pinxten, R., de Ridder, E., & Eens, M. (2003). Female presence affects male behavior and testosterone levels in the European starling (Sturnus vulgaris). *Hormones and Behavior*, *44*(2), 103–109. https://doi.org/10.1016/s0018-506x(03)00120-x

Pittman, Q. J., Lawrance, D., & McLean, L. (1982). Central effects of arginine vasopressin on blood pressure in rats, *110*(3), 1058–1060. https://doi.org/10.1210/endo-110-3-1058

Purves-Tyson, T. D., Owens, S. J., Double, K. L., Desai, R., Handelsman, D. J., & Weickert, C. S. (2014). Testosterone Induces Molecular Changes in Dopamine Signaling Pathway Molecules in the Adolescent Male Rat Nigrostriatal Pathway. *PLoS ONE*, *9*(3), e91151. https://doi.org/10.1371/journal.pone.0091151

Ratcliff, R., & McKoon, G. (2008). The Diffusion Decision Model: Theory and Data for Two-Choice Decision Tasks. *Neural Computation*, *20*(4), 873–922. https://doi.org/10.1162/neco.2008.12-06-420

Rausch, J., Gäbel, A., Nagy, K., Kleindienst, N., Herpertz, S. C., & Bertsch, K. (2015). Increased testosterone levels and cortisol awakening responses in patients with borderline personality disorder: Gender and trait aggressiveness matter. *Psychoneuroendocrinology*, *55*, 116–127. https://doi.org/10.1016/j.psyneuen.2015.02.002

Robbins, T. W., & Everitt, B. J. (1996). Neurobehavioural mechanisms of reward and motivation. *Current Opinion in Neurobiology*, *6*(2), 228–236. https://doi.org/10.1016/s0959-4388(96)80077-8

Roney, J. R. (2016). Theoretical frameworks for human behavioral endocrinology. *Hormones and Behavior*, *84*, 97–110. https://doi.org/10.1016/j.yhbeh.2016.06.004

Rubinow, D. R., Roca, C. A., Schmidt, P. J., Danaceau, M. A., Putnam, K., Cizza, G., Chrousos, G., & Nieman, L. (2005). Testosterone Suppression of CRH-Stimulated Cortisol in Men. *Neuropsychopharmacology*, *30*(10), Article 10. https://doi.org/10.1038/sj.npp.1300742

Ruzicka, L., & Wettstein, A. (1935). Sexualhormone VII. Über die künstliche Herstellung des Testikelhormons Testosteron (Androsten-3-on-17-ol). *Helvetica Chimica Acta*, *18*(1), 1264–1275. https://doi.org/10.1002/hlca.193501801176

Sapolsky, R. M. (2017). Behave: The biology of humans at our best and worst. In *Behave: The biology of humans at our best and worst*. Penguin Press, an imprint of Penguin Random House LLC.

Satterfield, B. C., Hinson, J. M., Whitney, P., Schmidt, M. A., Wisor, J. P., & Van Dongen, H. P. A. (2018). Catechol-O-methyltransferase (COMT) genotype affects cognitive control during total sleep deprivation. *Cortex*, *99*, 179–186. https://doi.org/10.1016/j.cortex.2017.11.012

Schroeder, J. P., & Packard, M. G. (2000). Role of dopamine receptor subtypes in the acquisition of a testosterone conditioned place preference in rats. *Neuroscience Letters*, *282*(1), 17–20. https://doi.org/10.1016/S0304-3940(00)00839-9

Schuppe, E. R., Miles, M. C., & Fuxjager, M. J. (2020). Evolution of the androgen receptor: Perspectives from human health to dancing birds. *Molecular and Cellular Endocrinology*, *499*, 110577. https://doi.org/10.1016/j.mce.2019.110577

Simoncini, T., & Genazzani, A. R. (2003). Non-genomic actions of sex steroid hormones. *European Journal of Endocrinology*, *148*(3), 281–292. https://doi.org/10.1530/eje.0.1480281

Sockman, K. W., Weiss, J., Webster, M. S., Talbott, V., & Schwabl, H. (2008). Sex-specific effects of yolk-androgens on growth of nestling American kestrels. *Behavioral Ecology and Sociobiology*, *62*(4), 617–625. https://doi.org/10.1007/s00265-007-0486-z

Soto-Gamboa, M., Villalón, M., & Bozinovic, F. (2005). Social cues and hormone levels in male Octodon degus (Rodentia): A field test of the Challenge Hypothesis. *Hormones and Behavior*, *47*(3), 311–318. https://doi.org/10.1016/j.yhbeh.2004.11.010

Soutschek, A., & Tobler, P. N. (2023). A process model account of the role of dopamine in intertemporal choice. *ELife*, *12*, e83734. https://doi.org/10.7554/eLife.83734

Spielberg, J. M., Forbes, E. E., Ladouceur, C. D., Worthman, C. M., Olino, T. M., Ryan, N. D., & Dahl, R. E. (2015). Pubertal testosterone influences threat-related amygdala–orbitofrontal cortex coupling. *Social Cognitive and Affective Neuroscience*, *10*(3), 408–415. https://doi.org/10.1093/scan/nsu062

Stephens, M. A. C., Mahon, P. B., McCaul, M. E., & Wand, G. S. (2016). Hypothalamic–pituitary–adrenal axis response to acute psychosocial stress: Effects of biological sex and circulating sex hormones. *Psychoneuroendocrinology*, *66*, 47–55. https://doi.org/10.1016/j.psyneuen.2015.12.021

Sutton, R. S., & Barto, A. G. (2018). *Reinforcement Learning, second edition: An Introduction*. MIT Press.
Szot, P., & Dorsa, D. M. (1994). Expression of cytoplasmic and nuclear vasopressin RNA following castration and testosterone replacement: Evidence for transcriptional regulation. *Molecular and Cellular Neurosciences*, *5*(1), 1–10. https://doi.org/10.1006/mcne.1994.1001
Taylor, C. J. (2014). Physiological stress response to loss of social influence and threats to masculinity. *Social Science & Medicine (1982)*, *103*, 51–59. https://doi.org/10.1016/j.socscimed.2013.07.036
Terburg, D., Aarts, H., & van Honk, J. (2012). Testosterone Affects Gaze Aversion From Angry Faces Outside of Conscious Awareness. *Psychological Science*, *23*(5), 459–463. https://doi.org/10.1177/0956797611433336
Terburg, D., Syal, S., Rosenberger, L. A., Heany, S. J., Stein, D. J., & Honk, J. van. (2016). Testosterone abolishes implicit subordination in social anxiety. *Psychoneuroendocrinology*, *72*, 205–211. https://doi.org/10.1016/j.psyneuen.2016.07.203
Terburg, D., & van Honk, J. (2013). Approach–Avoidance versus Dominance–Submissiveness: A Multilevel Neural Framework on How Testosterone Promotes Social Status. *Emotion Review*, *5*(3), 296–302. https://doi.org/10.1177/1754073913477510
Thomas, P. (2019). Membrane Androgen Receptors Unrelated to Nuclear Steroid Receptors. *Endocrinology*, *160*(4), 772–781. https://doi.org/10.1210/en.2018-00987
Thompson, J., Thomas, N., Singleton, A., Piggott, M., Lloyd, S., Perry, E. K., Morris, C. M., Perry, R. H., Ferrier, I. N., & Court, J. A. (1997). D2 dopamine receptor gene (DRD2) Taq1 A polymorphism: Reduced dopamine D2 receptor binding in the human striatum associated with the A1 allele. *Pharmacogenetics*, *7*(6), 479–484. https://doi.org/10.1097/00008571-199712000-00006
Thornton, J. W. (2001). Evolution of vertebrate steroid receptors from an ancestral estrogen receptor by ligand exploitation and serial genome expansions. *Proceedings of the National Academy of Sciences*, *98*(10), 5671–5676. https://doi.org/10.1073/pnas.091553298
Tinbergen, N. (1963). On aims and methods of Ethology. *Zeitschrift Für Tierpsychologie*, *20*(4), 410–433. https://doi.org/10.1111/j.1439-0310.1963.tb01161.x
Tobiansky, D. J., Wallin-Miller, K. G., Floresco, S. B., Wood, R. I., & Soma, K. K. (2018). Androgen Regulation of the Mesocorticolimbic System and Executive Function. *Frontiers in Endocrinology*, *9*, 279. https://doi.org/10.3389/fendo.2018.00279
Torre, S. D., Benedusi, V., Fontana, R., & Maggi, A. (2014). Energy metabolism and fertility—A balance preserved for female health. *Nature Reviews Endocrinology*, *10*(1), 13–23. https://doi.org/10.1038/nrendo.2013.203
Toufexis, D., Rivarola, M. A., Lara, H., & Viau, V. (2014). Stress and the Reproductive Axis. *Journal of Neuroendocrinology*, *26*(9), 573–586. https://doi.org/10.1111/jne.12179
Trainor, B. C., & Marler, C. A. (2001). Testosterone, paternal behavior, and aggression in the monogamous California mouse (Peromyscus californicus). *Hormones and Behavior*, *40*(1), 32–42. https://doi.org/10.1006/hbeh.2001.1652
Turan, B., Tackett, J. L., Lechtreck, M. T., & Browning, W. R. (2015). Coordination of the cortisol and testosterone responses: A dual axis approach to understanding the response to social status threats. *Psychoneuroendocrinology*, *62*, 59–68. https://doi.org/10.1016/j.psyneuen.2015.07.166
van Honk, J., Montoya, E. R., Bos, P. A., van Vugt, M., & Terburg, D. (2012). New evidence on testosterone and cooperation. *Nature*, *485*(7399), E4–E5. https://doi.org/10.1038/nature11136
van Honk, J., Peper, J. S., & Schutter, D. J. L. G. (2005). Testosterone reduces unconscious fear but not consciously experienced anxiety: Implications for the disorders of fear and anxiety. *Biological Psychiatry*, *58*(3), 218–225. https://doi.org/10.1016/j.biopsych.2005.04.003
van Wingen, G. A., Zylicz, S. A., Pieters, S., Mattern, C., Verkes, R. J., Buitelaar, J. K., & Fernández, G. (2009). Testosterone Increases Amygdala Reactivity in Middle-Aged Women to a Young Adulthood Level. *Neuropsychopharmacology*, *34*(3), Article 3. https://doi.org/10.1038/npp.2008.2

van Wingen, G., Mattern, C., Verkes, R. J., Buitelaar, J., & Fernández, G. (2010). Testosterone reduces amygdala–orbitofrontal cortex coupling. *Psychoneuroendocrinology*, *35*(1), 105–113. https://doi.org/10.1016/j.psyneuen.2009.09.007

Vandenbergh, D. J., Persico, A. M., Hawkins, A. L., Griffin, C. A., Li, X., Jabs, E. W., & Uhl, G. R. (1992). Human dopamine transporter gene (DAT1) maps to chromosome 5p15.3 and displays a VNTR. *Genomics*, *14*(4), 1104–1106. https://doi.org/10.1016/s0888-7543(05)80138-7

Viau, V., & Meaney, M. J. (2004). Testosterone-dependent variations in plasma and intrapituitary corticosteroid binding globulin and stress hypothalamic-pituitary-adrenal activity in the male rat. *Journal of Endocrinology*, *181*(2), 223–231. https://doi.org/10.1677/joe.0.1810223

Villavicencio, C. P., Apfelbeck, B., & Goymann, W. (2013). Experimental induction of social instability during early breeding does not alter testosterone levels in male black redstarts, a socially monogamous songbird. *Hormones and Behavior*, *64*(3), 461–467. https://doi.org/10.1016/j.yhbeh.2013.08.005

Volman, I., von Borries, A. K. L., Bulten, B. H., Verkes, R. J., Toni, I., & Roelofs, K. (2016). Testosterone Modulates Altered Prefrontal Control of Emotional Actions in Psychopathic Offenders. *ENeuro*, *3*(1), ENEURO.0107-15.2016. https://doi.org/10.1523/ENEURO.0107-15.2016

Welling, L. L. M., Moreau, B. J. P., Bird, B. M., Hansen, S., & Carré, J. M. (2016). Exogenous testosterone increases men's perceptions of their own physical dominance. *Psychoneuroendocrinology*, *64*, 136–142. https://doi.org/10.1016/j.psyneuen.2015.11.016

Wingfield, J. C. (1994). Regulation of Territorial Behavior in the Sedentary Song Sparrow, Melospiza melodia morphna. *Hormones and Behavior*, *28*(1), 1–15. https://doi.org/10.1006/hbeh.1994.1001

Wingfield, J. C., & Farner, D. S. (1978). The Endocrinology of a Natural Breeding Population of the White-Crowned Sparrow (Zonotrichia leucophrys pugetensis). *Physiological Zoology*, *51*(2), 188–205. https://www.jstor.org/stable/30157866

Wingfield, J. C., Hegner, R. E., Dufty, A. M., & Ball, G. F. (1990). The "Challenge Hypothesis": Theoretical Implications for Patterns of Testosterone Secretion, Mating Systems, and Breeding Strategies. *The American Naturalist*, *136*(6), 829–846. https://www.jstor.org/stable/2462170

Wingfield, J. C., Ramenofsky, M., Hegner, R. E., & Ball, G. F. (2020). Whither the challenge hypothesis? *Hormones and Behavior*, *123*, 104588. https://doi.org/10.1016/j.yhbeh.2019.104588

Wu, Y., Ou, J., Wang, X., Zilioli, S., Tobler, P. N., & Li, Y. (2022). Exogeneous testosterone increases sexual impulsivity in heterosexual men. *Psychoneuroendocrinology*, *145*, 105914. https://doi.org/10.1016/j.psyneuen.2022.105914

Wu, Y., Shen, B., Liao, J., Li, Y., Zilioli, S., & Li, H. (2020). Single dose testosterone administration increases impulsivity in the intertemporal choice task among healthy males. *Hormones and Behavior*, *118*, 104634. https://doi.org/10.1016/j.yhbeh.2019.104634

Xie, Z., Maddox, W. T., McGeary, J. E., & Chandrasekaran, B. (2015). The C957T polymorphism in the dopamine receptor D2 gene modulates domain-general category learning. *Journal of Neurophysiology*, *113*(9), 3281–3290. https://doi.org/10.1152/jn.01005.2014

Zak, P. J., Kurzban, R., Ahmadi, S., Swerdloff, R. S., Park, J., Efremidze, L., Redwine, K., Morgan, K., & Matzner, W. (2009). Testosterone Administration Decreases Generosity in the Ultimatum Game. *PLOS ONE*, *4*(12), e8330. https://doi.org/10.1371/journal.pone.0008330

Zhang, X., Hense, H.-W., Riegger, G. A. J., & Schunkert, H. (1999). Association of arginine vasopressin and arterial blood pressure in a population-based sample. *Journal of Hypertension*, *17*(3), 319. https://journals.lww.com/jhypertension/Abstract/1999/17030/Association_of_arginine_vasopressin_and_arterial.3.aspx

Zhao, X., Fuxjager, M. J., McLamore, Q., & Marler, C. A. (2019). Rapid effects of testosterone on social decision-making in a monogamous California mice (Peromyscus californicus). *Hormones and Behavior*, *115*, 104544. https://doi.org/10.1016/j.yhbeh.2019.06.008

Zhao, X., & Marler, C. A. (2016). Social and physical environments as a source of individual variation in the rewarding effects of testosterone in male California mice (Peromyscus californicus). *Hormones and Behavior*, *85*, 30–35. https://doi.org/10.1016/j.yhbeh.2016.07.007

Zirkin, B. R., & Chen, H. (2000). Regulation of Leydig Cell Steroidogenic Function During Aging1. *Biology of Reproduction*, *63*(4), 977–981. https://doi.org/10.1095/biolreprod63.4.977

Zitzmann, M., & Nieschlag, E. (2003). The CAG repeat polymorphism within the androgen receptor gene and maleness1. *International Journal of Andrology*, *26*(2), 76–83. https://doi.org/10.1046/j.1365-2605.2003.00393.x

Chapter 2

STUDY 1:
THE EFFECTS OF TESTOSTERONE ON THE PHYSIOLOGICAL RESPONSE TO SOCIAL AND SOMATIC STRESSORS

Original manuscript as published in Psychoneuroendocrinology, doi: 10.1016/j.psyneuen.2020.104693

Hana H. Kutlikova [a], Jaroslava Babková Durdiaková [b], Bernhard Wagner [c], Miroslav Vlček [d], Christoph Eisenegger [a,1], Claus Lamm [e], Igor Riečanský [e,f]

a. Neuropsychopharmacology and Biopsychology Unit, Department of Basic Psychological Research and Research Methods, Faculty of Psychology, University of Vienna. Liebiggasse 5, 1010 Vienna, Austria. hana.kutlikova@univie.ac.at
b. Institute of Physiology, Faculty of Medicine, Comenius University. Sasinkova 2, 811 08, Bratislava, Slovakia. durdiakova.jaroslava@gmail.com
c. Institute of Biomedical Science, FH JOANNEUM University of Applied Sciences. Eggenberger Allee 13, 8020 Graz, Austria. bernhard.wagner@fh-joanneum.at
d. Institute of Clinical and Translational Research, Biomedical Research Center, Slovak Academy of Sciences, Dúbravská cesta 9, 84505 Bratislava, Slovakia. miroslav.vlcek@savba.sk
e. Social, Cognitive and Affective Neuroscience Unit, Department of Basic Psychological Research and Research Methods, Faculty of Psychology, University of Vienna. Liebiggasse 5, 1010 Vienna, Austria. claus.lamm@univie.ac.at
f. Department of Behavioural Neuroscience, Institute of Normal and Pathological Physiology, Centre of Experimental Medicine, Slovak Academy of Sciences. Sienkiewiczova 1, 813 71 Bratislava, Slovakia. igor.riecansky@savba.sk

Notes:

1. Deceased February 27, 2017

Abstract

Higher testosterone levels in males have previously been linked to decreased stress reactivity, but in other cases, testosterone has been reported to increase the stress response. We addressed these inconsistencies in a placebocontrolled single-dose testosterone administration study, in which 120 male participants were randomly assigned to undergo a cold-pressor test (CPT, a non-social somatic stressor), a socially evaluated cold-pressor test (SECPT, a social-somatic stressor), or a lukewarm water test (LWT, a non-stressful control condition). Throughout the experiment, blood pressure and interbeat intervals were measured continuously, and saliva samples for hormonal analyses were taken repeatedly at predefined time points. When comparing the groups treated with a placebo, the SECPT elicited a larger increase in systolic blood pressure than CPT, in agreement with previous studies. However, testosterone administration altered this pattern. Compared to the placebo, testosterone increased systolic blood pressure during the CPT, whereas the opposite effect was found during the SECPT. Cortisol reactivity was not affected by testosterone administration. The CAG-repeat polymorphism of the androgen receptor gene was unrelated to the effects of testosterone on the stress response, but it was correlated with blood pressure across the whole sample. Our findings demonstrate that testosterone effects on the stress response are dependent on the social context. Testosterone's ability to flexibly influence the response to stressors may be an important mechanism through which the hormone promotes adaptive behavior. Our results are also in line with research showing that testosterone decreases social anxiety and suggest it may help to modulate the effects of stress in socially challenging situations.

Keywords: Sex hormones, Stress, Cold-pressor test, Autonomic nervous system, Heart rate variability, Cortisol

Introduction

Exposure of an organism to a stressful event, whether it is an oncoming predator or a job interview, triggers a well-orchestrated cascade of physiological changes. An adequate bodily response to a stressful situation is critical for an individual's survival and homeostasis. On the contrary, inappropriate stress response may lead to a number of endocrine, immune, cardiovascular, and psychiatric disorders. To prevent undesirable consequences of stress, it is important to understand the environmental and physiological factors that influence the functioning of the principal stress axes. In a stressful situation, two major systems play a role: autonomic nervous system (ANS) and the hypothalamic–pituitary–adrenal (HPA) axis. The ANS responds within seconds after the exposure to stressors via its sympathetic and parasympathetic branches. The sympathetic ANS promptly initiates the release of the catecholamines from the adrenal medulla, which trigger a change in multiple physiological functions and peripherally measurable biomarkers, such as an increase in systolic blood pressure and heart rate (Ulrich-Lei and Herman, 2009). The parasympathetic part of the ANS acts generally in the opposite way to the sympathetic ANS. It serves as a "brake" that calms the organism down and contributes to the high-frequency band of the heart rate variability (HF-HRV) (Rajendra et al., 2006). The reaction of HPA is slower than the ANS, it reaches its peak 20 - 40 minutes following stressor exposure and develops through a hormonal cascade that culminates in the release of cortisol from the adrenal cortex. The ANS thus plays a major role in the immediate "fight-or-flight" responses to threat, whereas the HPA axis shapes longer-term adaptation to the increased mental or physical load (Wetherell et al., 2006).

Both ANS and HPA act in a coordinated fashion with other physiological processes. A considerable body of research has examined their functional cross-talk with the hypothalamic–pituitary–gonadal axis, mainly the hormone testosterone (Heck and Handa, 2019). In rodents, testosterone administration was found to reduce HPA stress response (Viau and Meaney, 2004) and attenuate anxiety-like behavior (Aikey et al., 2002). Consistently with animal research, testosterone administration in men suppressed pharmacological stimulation of cortisol release (Rubinow et al., 2005), and cortisol response to a psychosocial stressor was weaker in males with high basal testosterone (Stephens et al., 2016). In contrast, in another study, social stress in form of a lost competition led to an increase in cortisol levels only in men with high basal testosterone levels, but not in men with low basal testosterone (Mehta et al, 2008). Additionally, a recent study reported that exogenous testosterone administration in healthy males increased cortisol response to a social stressor, although this effect was only observed in individuals with high trait dominance (Knight et al., 2017).

Although in mice the effect of testosterone on the sympathetic ANS neurons was demonstrated long time ago (Hartmann et al., 1986), majority of the human laboratory studies have focused on

the effects of testosterone on the HPA, neglecting the role of the ANS. The available findings on the ANS come mostly from correlational studies in clinical populations. Their conclusions remain contradictory: some interpret testosterone's role as protective, others as detrimental. A review of placebo-controlled randomized trials of testosterone therapy in elderly men revealed that exogenous testosterone increased the risk of cardiovascular adverse events (Xu et al., 2013). Similarly, another review of the impact of long-term testosterone therapy on blood pressure in transgender men reported that out of seven reviewed studies, three described modest increases in the systolic blood pressure and one study reported an onset of hypertension that was resolved after cessation of testosterone therapy (Velho et al., 2017). On the other hand, in a laboratory study, basal testosterone levels were found to be negatively associated with sympathetic response to a physiological stressor and positively associated with the parasympathetic response (Ramesh, 2015). Furthermore, testosterone administration in females reduced sympathetically mediated components of the stress response, as evidenced by lowered electrodermal activity to disturbing pictures (Hermans et al., 2007).

Although previous research has attempted to elucidate the role of testosterone in stress response by a single-dose testosterone administration approach (Hermans et al., 2007, Knight, et al., 2017), the causes and mechanisms underlying the inconsistent findings have not been addressed in a systematic manner. First, a possible cause of the conflicting results may be the differences in the used stressors. Importantly, recent studies have suggested that the role of testosterone in human behaviors is dependent on the social context and subtle differences in the environment (Carré and Archer, 2018). Second, testosterone might not interact equally with the two main axes of the stress response, ANS and HPA. Third, the effects of testosterone may be influenced by the genetic variability in the androgen receptor (AR). Namely, prior research has indicated that the neuroendocrine stress response (Hastings et al., 2018) and the effects of testosterone administration on social behaviors (Geniole et al., 2019) were related to the number cytosine-adenine-guanine (CAG) repeats in exon 1 of the AR gene, a polymorphism associated with AR activity (Bennett et al., 2010).

The goal of our study was to address these open questions and thus shed more light on testosterone role in stress. In healthy males, we compared the effects of testosterone on the physiological response to two types of stressors, somatic and social. For this purpose, we used the cold-pressor test (CPT) to elicit non-social somatic stress, the socially-evaluated cold-pressor test (SECPT) to elicit social-somatic stress, and the lukewarm water test (LWT) as a non-stressful control condition. Importantly, CPT and SECPT differ only in one parameter – the presence or absence of an observer, which allowed us to directly test the question of how the social component influences the testosterone effect on stress responsivity. We assessed the activation of both HPA and ANS using well-established endocrine and cardiovascular parameters: salivary cortisol, systolic blood pressure, interbeat interval, and HF-HRV (Thayer et al., 2012). We also assessed

stress-related psychological states and traits, and the AR gene CAG polymorphism. Due to the contradictory prior evidence of the testosterone's role in shaping the stress response, we did not make explicit predictions on the direction of the effects.

Method

Participants

The study sample consisted of 120 healthy adult men aged between 18 and 40 years (M = 23.88, SD = 4.42). Participants were recruited via flyers placed around university campuses and online advertisements. The volunteers, who replied to these advertisements, were screened via an online questionnaire and telephone interview for medical conditions that would prevent participation in the experiment. These conditions included neurological and psychiatric disorders, physical illness (including endocrine and other internal diseases), obesity, substance dependence or abuse, and use of steroids. All participants signed an informed consent and received a financial reward for study participation. All procedures were approved by the local research ethics board and conducted in accordance with the World Medical Association Declaration of Helsinki (2013).

Procedure and materials

For the purpose of the study, participants were randomly assigned to different levels of two between-subject factors: (1) Treatment (Testosterone/Placebo) and (2) Stress protocol (CPT/SCPT/LWT). These groups did not differ in their age, psychological trait measures or AR CAG repeat polymorphism (see Table S20 and S25 in the Supplementary material). The physiological measurements were taken repeatedly throughout the study, which is reflected by a within-subject factor (Pre/Post) (see section 2.3 for details). Participants arrived at the laboratory between 12:00 and 14:45 for a four-hour-long protocol (see Figure 1 for a schematic depiction of the experimental procedures). After providing informed consent, buccal swab samples were taken for the analysis of the AR CAG repeat polymorphism (for more details see Supplementary material). In addition, the participants provided hair samples for analysis, which we do not report here. In order to assess ANS activity, continuous arterial pressure and heart rate were measured at two time points: (1) 15 min after arrival to the laboratory - prior to gel administration and (2) during the exposure to the stressor. Each measurement lasted 5 min. In order to assess the HPA endocrine response, saliva samples were taken at four time points: (1) 15 min after arrival to the laboratory - prior to gel administration (time point -120), (2) shortly before the beginning of the stress protocol (time point 0), (3) 20 min after the end of the stress protocol (time point +20), and (4) 60 min after the end of the stress protocol (time point +60). Participants were asked to drool 2 mL of saliva directly into a polyethylene collection tube. The samples were frozen on-site and kept at -30°C until analysis by liquid chromatography tandem-mass spectrometry (for more details see Supplementary material). Immediately after the end of the stress protocol, subjective ratings of

the participants' experience were collected. Approximately 25 minutes after the end of the stress induction and after providing the third saliva sample, participants completed additional computer-based tasks, which will be reported elsewhere. At the end of the experiment, participants were debriefed.

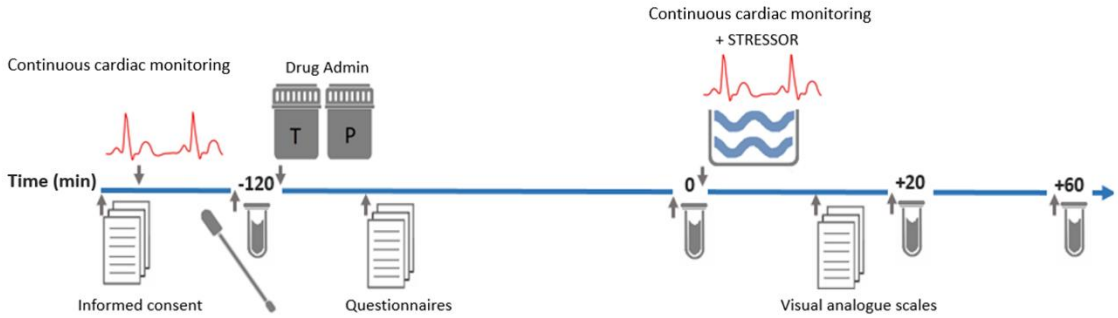


Figure 1. Time course of the experiment. Time 0 denotes the onset of the stressor.

Testosterone administration

Testosterone in a dose of 150 mg was administered via topical cream (Euro OTC Pharma GmbH, Bönen, Germany, see Supplementary material for more details) using a randomized, double-blind administration procedure. Both testosterone and placebo creams were prepared by a certified pharmacy and stored in disposable plastic containers. The only difference between the two creams was that the placebo cream was void of testosterone. Participants rubbed the cream onto their upper arms and shoulders in small increments using disposable latex gloves until the full sample was rubbed into their skin. The administration was followed by a 2-hour waiting period, during which the participants were offered leisure-time reading materials and were not allowed to leave the laboratory premises.

Stress protocols

A standard version of the cold-pressor test (CPT, Schwabe, et al., 2008) was used as a somatic non-social stressor. Participants were instructed to immerse their right hand and wrist up to elbow into continuously circulating ice water (0 – 3 °C) and keep their hand in the water as long as possible, but for a maximum of 5 min. The female experimenter monitored the screen with the blood pressure recording and did not directly observe the participant. A socially evaluated cold-pressor test (SECPT, Schwabe, et al., 2008) was used as a social-somatic stressor. The somatic component of the stressor was identical to the CPT: participants immersed their right hand into ice water (0–3 °C) and kept it there as long as possible (max. 5 min). On top of that, participants were informed that they would be video-recorded and that these recordings would be later used to analyze their facial expressions during the test. Furthermore, in contrast to the CPT, the female experimenter sat opposite to the participants and directly observed and monitored them all the time. The participants were asked to look in the camera lens and if they shifted their gaze away, they were reminded of it by the experimenter. A lukewarm water test (LWT) was used as a no-

stress control condition. Participants were instructed to immerse their right hand and wrist up to elbow into the water with a pleasant temperature (30 – 33 °C) and keep their hand in the water as long as they wished, but for a maximum of 5 min. During LWT, the female experimenter monitored the blood pressure measurement but did not look directly at the participant.

Cardio-vascular measurements

Arterial pressure was measured continuously ("beat-to-beat") by a non-invasive volume clamp method using finger plethysmography (Nexfin, Edwards Lifesciences BMEYE, the Netherlands). The finger cuff was placed between the two knuckles on the third finger of the participant's left hand and kept at heart level throughout the testing. Plethysmography was performed with a sampling rate of 2000 Hz by LabChart 7 (AD Instruments Pty Ltd., Castle Hill, Australia) and stored at a rate of 2 Hz for further analysis. The following parameters were computed by LabChart and analyzed offline: continuous systolic blood pressure (SBP) as a main biomarker of sympathetic ANS, continuous diastolic blood pressure (DBP), interbeat interval (i.e. the time interval between consecutive heartbeats, also termed heart period), and a high-frequency component of the heart rate variability (HF-HRV). HF-HRV, which reflects activity of the parasympathetic ANS (Cacioppo et al., 1994), was expressed in percentages as %HF-HRV = HF [μs^2]/TP[μs^2]*100%, where TP denotes the total spectral power density and HF the power within the 0.15-0.45 Hz frequency range.

Psychological measures

At the beginning of the waiting period, the participants filled in a demographic questionnaire, The Positive and Negative Affect Schedule (Watson et al., 1988, Slovak version: Ficková, 2000), The Behavioral Activation/Inhibition Scales (BIS/BAS) (Carver and White, 1994, Slovak adaptation for the purpose of the study), and the *NEO Five-Factor Inventory (*Costa and McCrae, 1989, Slovak version: Ruisel and Halama, 2007*).* The summed score of BAS-drive and BAS-reward responsiveness was used as a trait dominance measure in the subsequent analysis (Terburg et al., 2011). To assess subjective stress perception, visual analog scales were used. After completion of the stress protocols, participants were asked to rate how stressful, unpleasant, and painful their experience was using separate 10-cm *scales* with 1-cm increments.

Statistical analysis

Generalized linear mixed models (GLMMs) and analyses of variance (ANOVA) were used to examine the experimental effects. Ninety-five percent confidence intervals (95%CIs) of the model estimates (B) were used to determine the magnitude and direction of the effects. In the GLMMs, two between-subject factors: Treatment (Testosterone/Placebo), Stress protocol (CPT/SCPT/LWT), and one within-subject factor Time (Pre/Post) were entered as predictors. The observations were nested within participants, the models included random intercepts, and the factor Time was included as a random slope using polynomial contrasts. Saliva samples number 1

and 2 were entered into the GLMMs as separate pre-stressor onset values of the factor Time, while the saliva samples number 3 and 4 were entered as separate post-stressor onset values. Similarly, the values from the 5-minute long cardio-vascular measurement recorded shortly after the arrival to the laboratory were treated as pre-stressor onset levels of the factor Time, while the values recorded for the duration of 5 minutes from the onset of the stressor were entered as post-stressor onset values of the factor Time. For systolic blood pressure and diastolic blood pressure analysis, both Pre and Post cardiovascular measurements were analyzed at a sampling rate of 2 Hz, which resulted in the total number of 601 observations per participant and Time. Treatment contrasts were used to identify the pairwise differences in interactions.

To analyze HF-HRV, we used a 3-way ANOVA with the factors Treatment (Testosterone/Placebo), Stress protocol (CPT/SCPT/LWT), Time (Pre/Post), and their interactions, as HF-HRV contained only one value per Time and thus could not be entered into a multilevel model.

Similarly, self-reported stress, unpleasantness, and pain were tested using a 2-way ANOVA with the factors Treatment (Testosterone/Placebo), Stress protocol (CPT/SCPT/LWT), and their interaction.

Results

Manipulation check

One participant from the placebo group did not provide the necessary amount of saliva in any of the samples and was thus excluded from the hormone analyses (but retained in the analyses not including hormones). Two participants did not provide a sufficient amount of saliva in one of the samples, but their other samples were retained for the analyses. Due to a skewed distribution, testosterone values were winsorized to a score 3 SD above or below the mean for each time point (in total 2% of all observations were corrected this way).

No group differences in initial (pre-administration) testosterone levels were found (Testosterone group: $M_{Sample1}$ = 513 pg/ml, 95% CI [386, 639]; Placebo group: $M_{Sample1}$ = 460 pg/ml, 95% CI [333, 587]). Two hours after the drug administration, testosterone concentrations steeply increased in the testosterone group ($M_{Sample2}$ = 20024 pg/ml, 95% CI [12713, 27336]) and remained increased up to the last measurement (see Figure S1 in the Supplementary material). Testosterone levels of two participants in the testosterone group did not increase substantially after the administration of the cream (Sample 1/Sample 2: 1245/818 pg/ml; 262/301 pg/ml), and these participants were excluded from the analyses. Testosterone levels in the placebo group did not change considerably after the cream administration ($M_{Sample2}$= 435 pg/ml, 95% CI [365, 503]).

The time the participants kept their hand in the cold water did not differ significantly across the experimental conditions. There was no significant difference between the times in the group which

underwent CPT (M = 130 s, 95% CI [92.6, 166]) and SECPT (M = 140 s, 95% CI [102.3, 177]). There was neither a difference between the testosterone (M = 115 s, 95% CI [77.6, 152]) and the placebo group (M = 154 s, 95% CI [117.2, 191]), nor a significant Treatment x Stressor interaction (B = -28.52, 95% CI [-131.91 , 74.87]). Including the time spent in the cold water as an additional predictor to the statistical models assessing the experimental effects did not change the results considerably. In LWT condition, all but one participant kept the hand in the lukewarm bath for the maximum duration of 300 s (M = 293.7, 95% CI [-281.30, 306.10]).

Cardiovascular stress response

Analysis of the effect of testosterone administration on systolic blood pressure reactivity revealed a 3-way interaction between the factors Treatment, Stressor and Time. Testosterone compared with placebo administration increased SBP in CPT (Treatment x Time: B = 8.98, 95% CI [2.60, 15.36]), but decreased SBP in SECPT (Treatment x Time: B = -8.33, 95% CI [-14.71, -1.96]). No effects were found in LWT (Treatment x Time: B = 2.73, 95% CI [-3.57, 9.02]) (see Figure 2 and Tables S1- S4 in the Supplementary material).

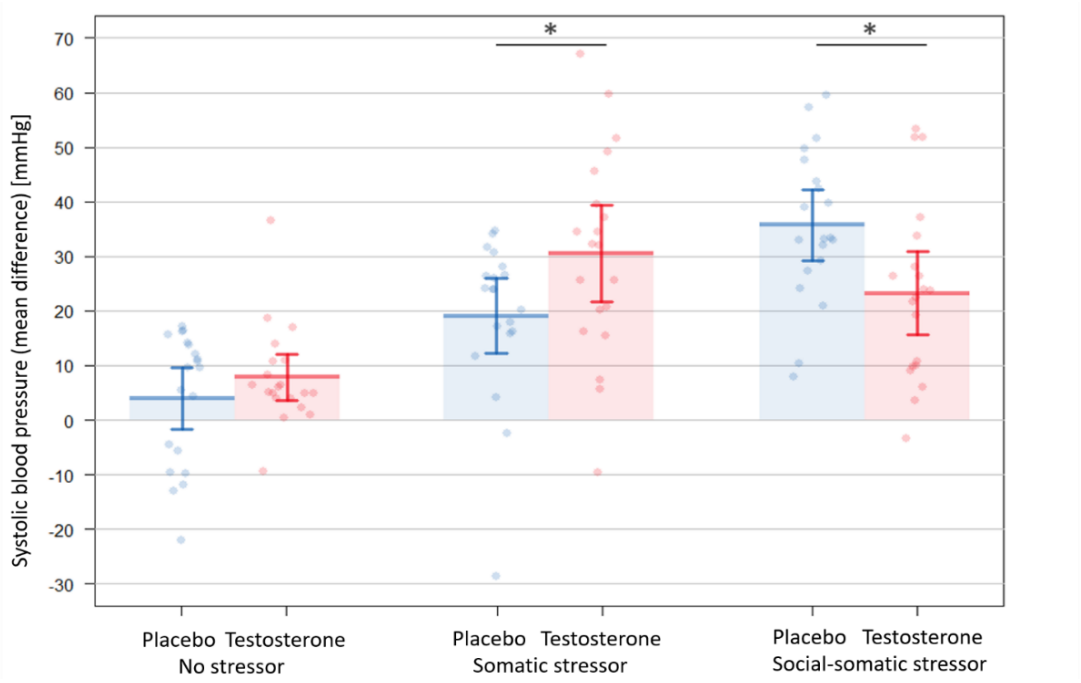


Figure 2. Differences in systolic blood pressure (SBP) across experimental conditions. The bars represent the difference in mean SBP *during* compared with *before* stressor exposure (Post-stressor onset – Pre-stressor onset) in mmHg. Asterisks mark the differences between Treatments (Testosterone/Placebo), colored dots depict data of individual participants. No stressor (LWT), Somatic stressor (CPT), Social stressor (SECPT). Error bars: 95% CI.

Including mean-centered trait dominance scores in the analysis did not improve the model fit, and trait dominance did not interact with the treatment effects in any experimental group (SECPT: B = -0.92, 95% CI [-3.42, 1.58]; CPT: B = -1.03, 95% CI [-3.65, 1.59], LWT: B = 0.91, 95% CI [-1.09, 2.92]).

Analysis of the effect of testosterone administration on the diastolic blood pressure reactivity also revealed a 3-way interaction between the factors Treatment, Stressor and Time. Testosterone administration compared to placebo increased DBP in response to CPT (Treatment x Time: B = 6.19, 95% CI [2.27, 10.10]), but did not have a considerable effect either in SECPT (Treatment x Time: B = -2.46, 95% CI [-6.37, 1.46]), or LWT (Treatment x Time: B = 2.08, 95% CI [-1.78, 5.94]) (see Tables S5 – S8 in the Supplementary material).

Analysis of the effect of testosterone administration on the interbeat intervals did not show a Treatment x Stressor x Time interaction. A two-way Treatment x Stressor interaction reflected that during SECPT, the interbeat interval was longer (i.e., heart rate was slower) in the testosterone group than in the placebo group (B = 89.04, 95% CI [5.00, 173.08]). On the contrary, during CPT, the interbeat interval was shorter (i.e., heart rate was faster) in the testosterone compared with the placebo group (B = -119.38, 95% CI [-202.22, -36.54]) (see Figure 3 and Tables S9 – S12 in the Supplementary material).

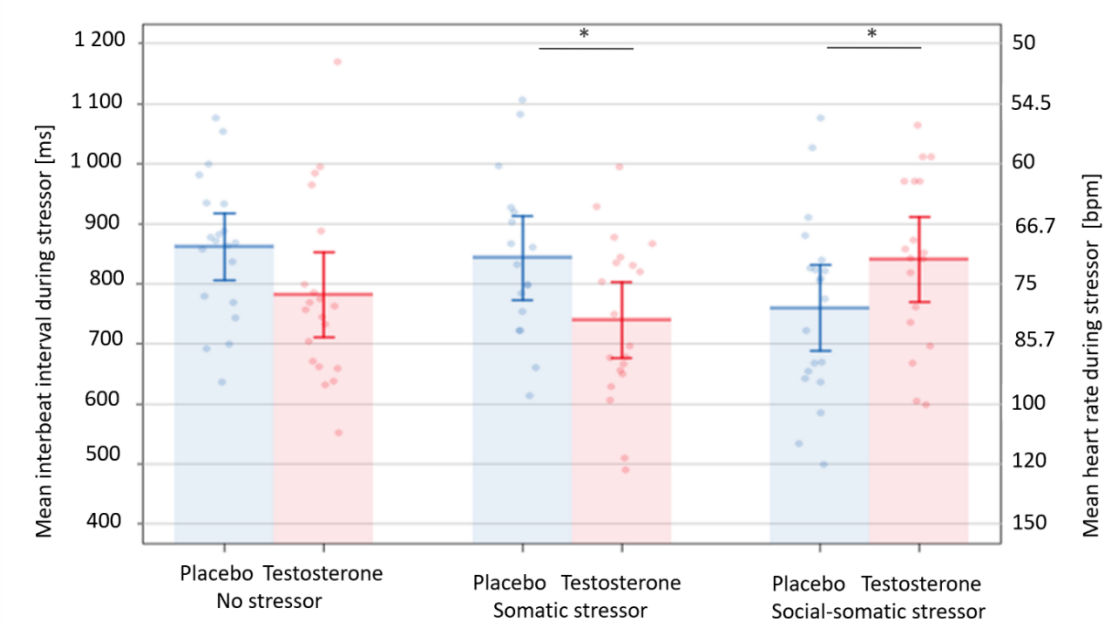


Figure 3. Interbeat intervals across experimental conditions. The bars represent the mean interbeat interval *during* stressor exposure (Post-stressor onset). Higher values of the interbeat interval mean slower heart rate. Asterisks mark the differences between Treatments (Testosterone/Placebo), colored dots depict data of individual participants. No stressor (LWT), Somatic stressor (CPT), Social-somatic stressor (SECPT). Error bars: 95% CI.

Repeated measures ANOVA on the high-frequency heart rate variability showed that across the whole experiment HF-HRV was lower in subjects treated with testosterone (M = 26.36%, 95% CI [23.46, 29.21]) compared with those treated with placebo (M = 30.92 %, 95% CI [28.10, 33.74]). Subsequent post-hoc analysis of the difference in HF-HRV before and during stressor exposure using Helmert contrasts revealed a significant Treatment x Stressor interaction when comparing the social-somatic stressor with the somatic stressor and the non-stressful control condition (B =

2.44, 95% CI [0.17, 4.71]). More specifically, in the placebo group, HF-HRV decreased during SECPT compared with CPT and LWT (B = -1.90, 95% CI [-3.48, -0.32]). However, this was not observed in the testosterone group (SECPT vs CPT&LWT: B = 0.54, 95% CI [-1.09, 2.17]) (see Figure 4 and Table S13 in the Supplementary material).

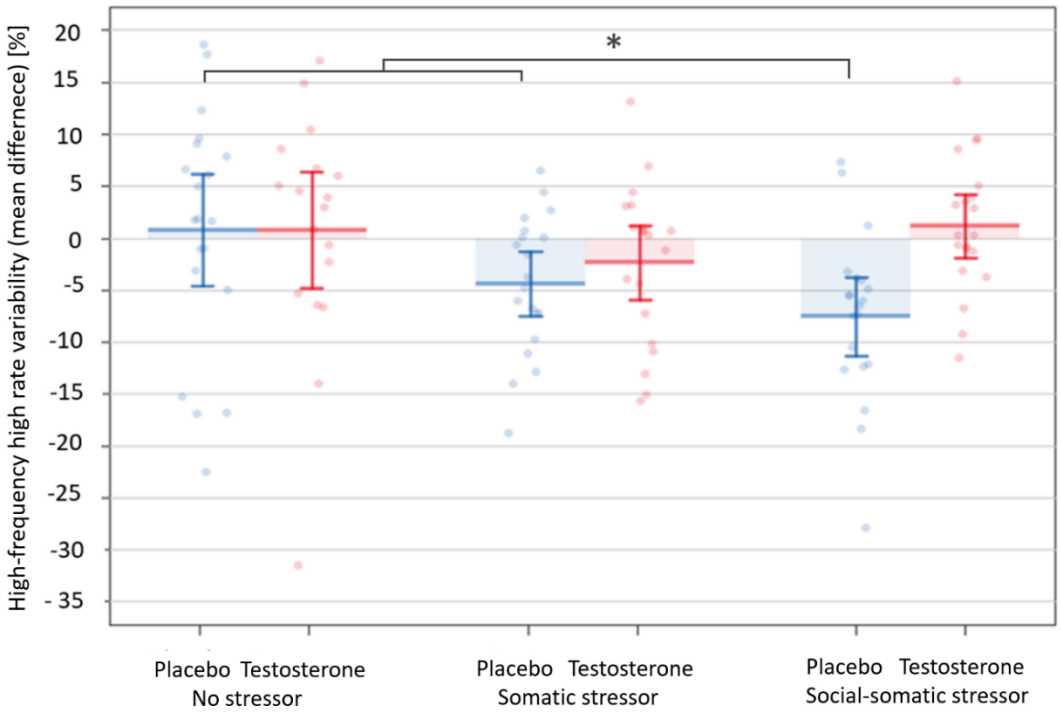


Figure 4. Differences in the high-frequency heart rate variability (HF-HRV) across experimental conditions. The bars represent the difference in %HF-HRV *during* compared with *before* stressor exposure (Post-stressor onset – Pre-stressor onset). Asterisk marks the decrease in %HF-HRV in the placebo group that is not present in the testosterone group. Colored dots depict data of individual participants. No stressor (LWT), Somatic stressor (CPT), Social stressor (SECPT). Error bars: 95% CI.

Cortisol stress response

As the cortisol values were not normally distributed, they were log-transformed, following winsorization to a score 3 SD above or below the mean for each time point. Winsorization led to a change of 2% measures in total. Analysis of the cortisol response did not reveal any effects of the testosterone administration. The Stressor x Time interaction showed that in the non-stressful condition, the cortisol levels decreased during the course of the experiment (B = - 0.24, 95% CI [-0.35, -0.13]). Following the exposure to stressors, the cortisol levels increased, but the increase was significant only in SECPT (B = 0.16, 95% CI [0.05, 0.28]), not in CPT (B = 0.10, 95% CI [-0.01, 0.21]) (see Figure 5, Tables S14 - S18, and Figure S2 in the Supplementary material). Including mean-centered trait dominance scores in the statistical analysis did not improve the model fit and trait dominance did not interact with any effects of the experimental groups on the cortisol responses to the stressors. (SECPT: B = 0.02, 95% CI [-0.04, 0.08]; CPT: B = 0.03, 95% CI [-0.03, 0.09], LWT: B = -0.02, 95% CI [-0.07, 0.03]).

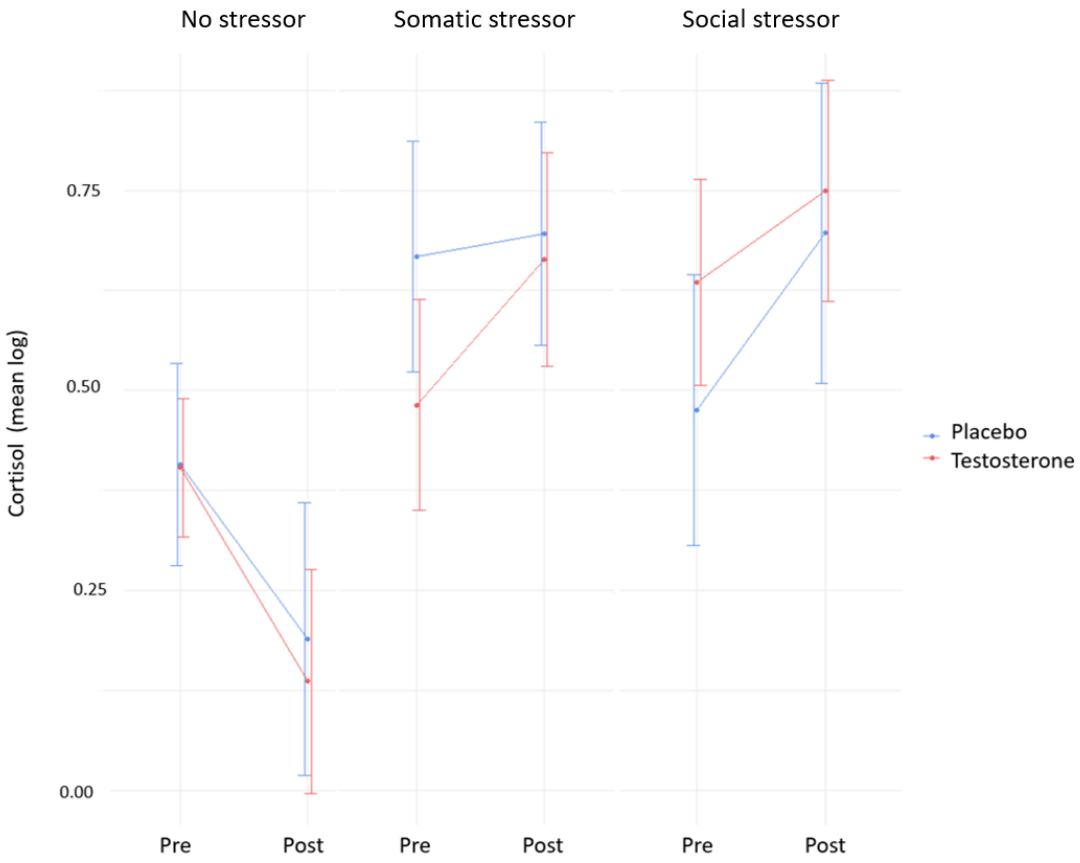


Figure 5. Mean cortisol levels (in log ng/mL) across the experimental conditions and time course of the experiment. Pre values are mean values from the measurements taken after the arrival to the laboratory (time = -120) and immediately before the onset of the stressor (time = 0). Post values are means of the measurements taken 20 (time = +20) and 60 minutes (time = +60) after the end of the exposure to the stressor. For a more detailed depiction of dynamics see Supplementary material. Error bars: 95% CI.

CAG-repeat polymorphism

Adding the mean-centered CAG repeat number as a predictor without interaction to the GLMMs of systolic and diastolic blood pressure improved the fit of the models. A higher number of the CAG repeats was associated with higher systolic (B = 0.89, 95% CI [0.07, 1.70]), and diastolic blood pressure (B = 0.63, 95% CI [0.10, 1.15]), regardless of Treatment, Stressor, or Time of the measurement. Including CAG repeat number as a predictor in interaction with other predictors did not improve the fit of any of the models of cardiovascular response. CAG repeat number did not predict the cortisol response (B= -0.00, 95%CI [- 0.02, 0.02]) and it did not interact with any of the predictors in the cortisol reactivity GLMM.

Stress perception

Participants in the SECPT condition rated their experience as more stressful (B = 23.6, 95% CI [13.9, 33.29]), unpleasant (B = 51.58, 95% CI [39.9, 63.28]), and painful (B = 49.4, 95% CI [38.5, 60.28]) than the participants in the non-stressful LWT condition. Similarly, participants in the CPT condition rated their experience as more stressful (B = 33.9, 95% CI [24.1, 43.69]), unpleasant (B = 59.46, 95% CI [47.7, 71.24]), and painful (B = 61.3, 95% CI [50.3, 72.25]) than

the participants in LWT. The participants in the SECPT condition rated the experience as less stressful than the participants in the CPT (B = -10.3, 95% CI [-20.2, -0.]). Participants in SCPT and CPT condition did not differ in their rating of unpleasantness and pain. There was no difference between testosterone and placebo participants, and no interaction of the experimental groups (See Tables S21 – 23 in the Supplementary material). Including the ratings as predictors either independently or in interaction with other predictors in GLMMs of the cardiovascular response and cortisol did not improve the fit of any of the models. For correlations among self-report measures, cardiovascular measures and cortisol levels see Table S24 in the Supplementary material.

Discussion

The aim of the present study was to examine how exogenous testosterone affects the response of the autonomic nervous system and hypothalamic–pituitary–adrenal axis to different types of acute stressors. We found that testosterone's influence on the cardiovascular response was different when exposed to a somatic (CPT) and a social-evaluative stressor (SECPT). Testosterone administration, compared with placebo, potentiated an increase in systolic blood pressure (an index of the sympathetic arousal) in CPT. However, in SECPT testosterone attenuated the elevation of blood pressure and inhibited reduction of heart rate variability in the high-frequency band, indicating an elevation of the parasympathetic arousal. We found no effects of testosterone on the cortisol stress response and no role of psychological traits or genetic variability of the androgen receptor in moderating the effects of testosterone on the physiological markers of the stress response.

An immediate encounter with a stressor increases the activity of the sympathetic ANS, resulting in the release of catecholamines, which stimulate glycogenolysis, lipolysis, and suppress the immune response (Chrousos, 2009). This promotes fast behavioral reactions, i.e. the fight-or-flight response. Testosterone-induced increase in SBP during somatic threat indicates a potentiation of the sympatho-adrenergic activation, which may, by increasing mobilization of energetic resources for skeletomuscular activity, support successful coping with a physical load. This may be viewed in the light of the positive effects of testosterone on physical activity, muscular physiology and function (e.g. Handelsman et al., 2018). The activity of the parasympathetic division of the ANS, on the other hand, counteracts the sympathetic activation and functions as a *brake that* can rapidly calm down an individual (Porges, 2001). Our data suggest that testosterone increases parasympathetic activity during exposure to a social-evaluative load, as indicated by dampening both the cardiovascular pressor response and the reduction of heart rate variability in the high-frequency band. Higher parasympathetic activation (the "vagal brake") has been linked with better ability to adjust physiological arousal and regulate emotions in response to situational demands

(Appelhans and Luecken, 2006). Testosterone thus may help to respond adaptively in social challenge situations, where appropriate emotion regulation plays a major role. Moreover, our data suggest that testosterone may also act as a protective factor against adverse health consequences of chronic social stress. However, whether and how the present experimental findings can be translated into persistent stress regulation in everyday life requires further research and validation.

Which physiological mechanisms are involved in mediating the effects of testosterone on the stress response? Testosterone can potentiate vasoconstrictive effects of epinephrine (Ammar et al., 2004) but also cause vasodilation via inactivation of the L-type voltage-gated calcium channels of smooth muscle cells (English et al., 2002) or increased nitric oxide synthesis in the endothelial cells (Miller and Mulvagh, 2007). These peripheral vasoactive actions of testosterone cannot, however, fully explain our findings, which are more complex and indicate the involvement of central mechanisms. Androgen receptors are present in the medulla and the brain stem (Sheridan and Weaker, 1982), the areas involved in the regulation of cardiovascular activity. Furthermore, androgen receptors are expressed in the hippocampus, the amygdala (Simerly et al., 1990), and the prefrontal cortex (PFC) (Tobiansky et al., 2018) that play a critical role in the regulation of behavioral and physiological responses to stressors (Ulrich-Lai and Herman, 2009). For instance, a meta-analysis by Thayer et al. (2012) suggests that HF-HRV indexes the degree to which inhibitory top-down appraisals from the medial PFC guide the brain stem regulation of the heart action. It seems thus probable that testosterone acting on medial PFC androgen receptors supports the inhibitory vagal function and thus contributes to adaptive coping with social stress. Furthermore, testosterone might influence the stress response via arginine vasopressin system in the amygdala (de Vries, 2008), or through the modulation of the dopaminergic signaling (Aubele and Kritzer, 2012; Ely et al. 2011). In the absence of direct or indirect measures of neural processes, this discussion of the putative neural mechanisms of our findings necessarily remains speculative. Future research should, therefore, combine the methods of testosterone-administration, stress induction, and neuroimaging as well as neurophysiological techniques. This way we could address the question of how the brain distinguishes between different types of the stressor and orchestrates the appropriate response.

Although our study shows that testosterone influences ANS activation, we did not find evidence for the effect of testosterone on the stress response of the HPA axis. Similarly to Schwabe et al. (2008), we have found that the cortisol increase was significant after SECPT, but not after CPT. This effect was not affected by testosterone treatment. Previous studies on the testosterone's influence on HPA reactivity are contradictory. Some report testosterone reduces HPA reactivity to stress (Viau and Meaney, 2004; Mhaouty-Kodja, 2018), while others show that testosterone correlates with increased cortisol response to threat (Mehta et al., 2008). Recently, Knight et al. (2017) showed that testosterone enhanced cortisol response to social-evaluative stressor only for men high in dominance. Our data do not show that trait dominance interacts with testosterone

effects. We, however, used a different measure of dominance (Terburg et al., 2011*)*, therefore it is difficult to directly compare our results to those of Knight et al. (2017).
In addition, we also examined whether CAG-repeat polymorphism in exon 1 of the AR gene moderates the effect of testosterone administration on the stress response, but we found no evidence for such an effect. We did not find support for the negative relationship between CAG polymorphism and cortisol stress reactivity (Hastings et al. 2018) either. On the other hand, we found that the CAG-repeat length was overall positively related to SBP and DBP, which fits with a previously reported association between CAG-repeat length and hypertension in men treated with testosterone (Zitzmann and Nieschlag, 2007).

Our results do not indicate that testosterone administration affects self-report ratings of stress, pain, and unpleasantness. As expected, the participant in the non-stressful condition rated their experience as less stressful, painful, and unpleasant than the participants in the conditions involving stressor. Interestingly, participants rated SECPT as less stressful than CPT, which does not correspond to the physiological response that was generally higher in SECPT than in CPT. Such a discrepancy between physiological and psychological measures is not uncommon in stress research (Lupien et al. 2019). We may speculate that social factors, such as desirability, lowered the self-reported stress in the SECPT participants. It is also conceivable that the presence of the experimenter in SECPT might have served as a distractor that diverted the attention of the participant and led to a decrease in the subjective perception of stress.

Limitations

Our study was limited to male participants, due to sex differences in the established testosterone administration methods and sex differences in the endogenous levels of testosterone and stress response (Eisenegger et al., 2013; Kajantie and Phillips, 2006). Future research is thus needed to test whether testosterone has similar effects in females. Sample size may also be considered as a limitation not allowing us to detect some small effects, despite the robust statistical approach adopted for the analyses.
Based on our results and the nature of the administered tasks, we interpret the testosterone's effects on the stress response as dependent on the social context. An alternative explanation could be, however, considered. In the placebo group, the physiological response was stronger in SECPT than CPT, indicating that SECPT was a stronger stressor than CPT. The effects of testosterone could thus depend not only on the presence or absence of the social component but also on stressor intensity. Future studies are needed to address this possibility in a systematic manner.

Conclusion

Our study shows that testosterone affects acute stress response depending on the stressor type. A single-dose administration of testosterone, compared with placebo, increased the cardiovascular pressor response to a somatic stressor. In contrast, testosterone decreased pressor response and prevented reduction of heart rate variability when confronted with a social-evaluative stressor. This indicates that testosterone may shape, increase or decrease, the activation of the ANS according to specific requirements in order to adaptively cope with the challenge. Rapid mobilization and an increase in sympathetic reactivity would provide a benefit when facing a biological threat and preparing for an efficient fight-or-flight response. On the other hand, when facing a social-evaluative threat, the desired coping strategy would be to persist, rather than to shy away, which is why the parasympathetic response that dampens the sympathetic arousal ("calming-down") might be a more adaptive reaction.

Acknowledgments

We wish to thank Karina Rerichová for her help with data collection, Štefan Bendžala for technical support and Richard Imrich for helpful comments. This work was supported by the Vienna Science and Technology Fund (WWTF VRG 13-007), uni:docs fellowship, as well as partially supported by the Slovak Research and Development Agency (APVV-14-0840).

References

Aikey, J.L., Nyby, J.G., Anmuth, D.M., James, P.J., 2002. Testosterone rapidly reduces anxiety in male house mice (Mus musculus). Horm Behav 42, 448–460.

Ammar, E.M., Said, S.A., Hassan, M.S., 2004. Enhanced vasoconstriction and reduced vasorelaxation induced by testosterone and nandrolone in hypercholesterolemic rabbits. Pharmacological Research 50, 253–259. https://doi.org/10.1016/j.phrs.2004.03.010

Appelhans, B.M., Luecken, L.J., 2006. Heart rate variability as an index of regulated emotional responding. Review of General Psychology 10, 229–240. https://doi.org/10.1037/1089-2680.10.3.229

Aubele, T., Kritzer, M.F., 2012. Androgen influence on prefrontal dopamine systems in adult male rats: localization of cognate intracellular receptors in medial prefrontal projections to the ventral tegmental area and effects of gonadectomy and hormone replacement on glutamate-stimulated extracellular dopamine level. Cereb. Cortex 22, 1799–1812. https://doi.org/10.1093/cercor/bhr258

Bennett, N.C., Gardiner, R.A., Hooper, J.D., Johnson, D.W., Gobe, G.C., 2010. Molecular cell biology of androgen receptor signalling. The International Journal of Biochemistry & Cell Biology 42, 813–827. https://doi.org/10.1016/j.biocel.2009.11.013

Cacioppo, J.T., Berntson, G.G., Binkley, P.F., Quigley, K.S., Uchino, B.N., Fieldstone, A., 1994. Autonomic cardiac control. II. Noninvasive indices and basal response as revealed by autonomic blockades. Psychophysiology 31, 586–598

Carré, J.M., Archer, J., 2018. Testosterone and human behavior: the role of individual and contextual variables. Current Opinion in Psychology, Aggression and violence 19, 149–153. https://doi.org/10.1016/j.copsyc.2017.03.021

Carver, C.S., White, T.L., 1994. Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: The BIS/BAS Scales. Journal of Personality and Social Psychology 67, 319–333. https://doi.org/10.1037/0022-3514.67.2.319

Chrousos, G.P., 2009. Stress and disorders of the stress system. Nat Rev Endocrinol 5, 374–381. https://doi.org/10.1038/nrendo.2009.106

Costa P.T., McCrae R.R.,1992. Revised NEO Personality Inventory (NEO PI-R) and NEO Five Factor Inventory (NEO-FFI). Professional Manual. Odessa, FL: Psychological Assessment Resources.

de Vries, G.J., 2008. Sex differences in vasopressin and oxytocin innervation of the brain. Prog. Brain Res. 170, 17–27. https://doi.org/10.1016/S0079-6123(08)00402-0

Eisenegger, C., von Eckardstein, A., Fehr, E., von Eckardstein, S., 2013. Pharmacokinetics of testosterone and estradiol gel preparations in healthy young men. Psychoneuroendocrinology 38, 171–178. https://doi.org/10.1016/j.psyneuen.2012.05.018

Ely, D., Toot, J., Salisbury, R., Ramirez, R., 2011. Androgens Alter Brain Catecholamine Content and Blood Pressure in the Testicular Feminized Male Rat. Clinical and Experimental Hypertension 33, 124–132. https://doi.org/10.3109/10641963.2010.531840

English, K.M., Jones, R.D., Jones, T.H., Morice, A.H., Channer, K.S., 2002. Testosterone acts as a coronary vasodilator by a calcium antagonistic action. J. Endocrinol. Invest. 25, 455–458. https://doi.org/10.1007/BF03344037

Ficková, E. 2000. Negatívna afektivita/emocionalita a sebahodnotenie adolscentov. In: Z. Ruiselová (Ed.), Adjustačné roblémy,charakteristiky zvládania a osobnosť adolescentov. Bratislava, Ústav experimentálnej psychológie SAV, 55-64.

Geniole, S.N., Procyshyn, T.L., Marley, N., Ortiz, T.L., Bird, B.M., Marcellus, A.L., Welker, K.M., Bonin, P.L., Goldfarb, B., Watson, N.V., Carré, J.M., 2019. Using a psychopharmacogenetic approach to identify the pathways through which-and the people for whom-testosterone promotes aggression. Psychol Sci 30, 481–494. https://doi.org/10.1177/0956797619826970

Hartmann, G., Addicks, K., Donike, M., Schänzer, W., 1986. Testosterone application influences sympathetic activity of intracardiac nerves in non-trained and trained mice. Journal of the Autonomic Nervous System 17, 85–100. https://doi.org/10.1016/0165-1838(86)90084-6

Hastings, W.J., Chang, A.M., Ebstein, R.P., Shalev, I., 2018. Neuroendocrine stress response is moderated by sex and sex hormone receptor polymorphisms. Horm Behav 106, 74–80. https://doi.org/10.1016/j.yhbeh.2018.10.002

Handelsman, D.J., Hirschberg, A.L., Bermon, S., 2018. Circulating Testosterone as the Hormonal Basis of Sex Differences in Athletic Performance. Endocr. Rev. 39, 803–829. https://doi.org/10.1210/er.2018-00020

Heck, A.L., Handa, R.J., 2019. Sex differences in the hypothalamic-pituitary-adrenal axis' response to stress: an important role for gonadal hormones. Neuropsychopharmacology 44, 45–58. https://doi.org/10.1038/s41386-018-0167-9

Hermans, E.J., Putman, P., Baas, J.M., Gecks, N.M., Kenemans, J.L., van Honk, J., 2007. Exogenous testosterone attenuates the integrated central stress response in healthy young women. Psychoneuroendocrinology 32, 1052–1061. https://doi.org/10.1016/j.psyneuen.2007.08.006

Kajantie, E., Phillips, D.I.W., 2006. The effects of sex and hormonal status on the physiological response to acute psychosocial stress. Psychoneuroendocrinology 31, 151–178. https://doi.org/10.1016/j.psyneuen.2005.07.002

Knight, E.L., Christian, C.B., Morales, P.J., Harbaugh, W.T., Mayr, U., Mehta, P.H., 2017. Exogenous testosterone enhances cortisol and affective responses to social-evaluative stress in dominant men. Psychoneuroendocrinology 85, 151–157. https://doi.org/10.1016/j.psyneuen.2017.08.014

Lupien, S.J., Leclaire, S., Majeur, D., Raymond, C., 2019. Are we good judges of our stress? A study of the association between subjective reports of stress and physiological stress markers. Psychoneuroendocrinology 100, S57. https://doi.org/10.1016/j.psyneuen.2018.12.193

Mehta, P.H., Jones, A.C., Josephs, R.A., 2008. The social endocrinology of dominance: basal testosterone predicts cortisol changes and behavior following victory and defeat. J Pers Soc Psychol 94, 1078–1093. https://doi.org/10.1037/0022-3514.94.6.1078

Mhaouty-Kodja, S., 2018. Role of the androgen receptor in the central nervous system. Molecular and Cellular Endocrinology, Androgens – revisiting their role as pleiotropic regulators of tissue function beyond the le reproductive system 465, 103–112. https://doi.org/10.1016/j.mce.2017.08.001

Miller, V., Mulvagh, S., 2007. Sex steroids and endothelial function: translating basic science to clinical practice. Trends in Pharmacological Sciences 28, 263–270. https://doi.org/10.1016/j.tips.2007.04.004

Porges, S.W., 2001. The polyvagal theory: phylogenetic substrates of a social nervous system. International Journal of Psychophysiology 42, 123–146. https://doi.org/10.1016/S0167-8760(01)00162-3

Rajendra Acharya, U., Paul Joseph, K., Kannathal, N., Lim, C.M., Suri, J.S., 2006. Heart rate variability: a review. Med Biol Eng Comput 44, 1031–1051. https://doi.org/10.1007/s11517-006-0119-0

Ramesh, S., Wilton, S.B., Holroyd-Leduc, J.M., Turin, T.C., Sola, D.Y., Ahmed, S.B., 2015. Testosterone is associated with the cardiovascular autonomic response to a stressor in healthy men. Clin. Exp. Hypertens. 37, 184–191. https://doi.org/10.3109/10641963.2014.933966

Rubinow, D.R., Roca, C.A., Schmidt, P.J., Danaceau, M.A., Putnam, K., Cizza, G., Chrousos, G., Nieman, L., 2005. Testosterone Suppression of CRH-Stimulated Cortisol in Men. Neuropsychopharmacology 30, 1906–1912. https://doi.org/10.1038/sj.npp.1300742

Ruisel, I. , Halama, P., 2007. NEO päťfaktorový osobnostný inventár (podľa NEO Five-Factor Inventory P.T. Costu a R.R. McCraeho). Praha, Testcentrum, Hogrefe, 45.

Schwabe, L., Haddad, L., Schachinger, H., 2008. HPA axis activation by a socially evaluated cold-pressor test. Psychoneuroendocrinology 33, 890–895. https://doi.org/10.1016/j.psyneuen.2008.03.001

Sheridan, P.J., Weaker, F.J., 1982. Androgen receptor systems in the brain stem of the primate. Brain Research 235, 225–232. https://doi.org/10.1016/0006-8993(82)91002-2

Simerly, R.B., Chang, C., Muramatsu, M., Swanson, L.W., 1990. Distribution of androgen and estrogen receptor mRNA-containing cells in the rat brain: an in situ hybridization study. J. Comp. Neurol. 294, 76–95. https://doi.org/10.1002/cne.902940107

Stephens, M.A.C., Mahon, P.B., McCaul, M.E., Wand, G.S., 2016. Hypothalamic-pituitary-adrenal axis response to acute psychosocial stress: Effects of biological sex and circulating sex hormones. Psychoneuroendocrinology 66, 47–55. https://doi.org/10.1016/j.psyneuen.2015.12.021

Terburg, D., Hooiveld, N., Aarts, H., Kenemans, J.L., van Honk, J., 2011. Eye Tracking Unconscious Face-to-Face Confrontations: Dominance Motives Prolong Gaze to Masked Angry Faces. Psychological Science 22, 314–319. https://doi.org/10.1177/0956797611398492

Thayer, J.F., Åhs, F., Fredrikson, M., Sollers, J.J., Wager, T.D., 2012. A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. Neuroscience & Biobehavioral Reviews 36, 747–756. https://doi.org/10.1016/j.neubiorev.2011.11.009

Tobiansky, D.J., Wallin-Miller, K.G., Floresco, S.B., Wood, R.I., Soma, K.K., 2018. Androgen regulation of the mesocorticolimbic system and executive function. Front. Endocrinol. 9, 279. https://doi.org/10.3389/fendo.2018.00279

Ulrich-Lai, Y.M., Herman, J.P., 2009. Neural Regulation of Endocrine and Autonomic Stress Responses. Nat Rev Neurosci 10, 397–409. https://doi.org/10.1038/nrn2647

Velho, I., Fighera, T.M., Ziegelmann, P.K., Spritzer, P.M., 2017. Effects of testosterone therapy on BMI, blood pressure, and laboratory profile of transgender men: a systematic review. Andrology 5, 881–888. https://doi.org/10.1111/andr.12382

Viau, V., Meaney, M.J., 2004. Testosterone-dependent variations in plasma and intrapituitary corticosteroid binding globulin and stress hypothalamic-pituitary-adrenal activity in the male rat. J. Endocrinol. 181, 223–231. https://doi.org/10.1677/joe.0.1810223

Watson, D., Clark, L.A., Tellegen, A., 1988. Development and validation of brief measures of positive and negative affect: the PANAS scales. J Pers Soc Psychol 54, 1063–1070.

Wetherell, M.A., Crown, A.L., Lightman, S.L., Miles, J.N.V., Kaye, J., Vedhara, K., 2006. The four-dimensional stress test: psychological, sympathetic-adrenal-medullary, parasympathetic and hypothalamic-pituitary-adrenal responses following inhalation of 35% CO2. Psychoneuroendocrinology 31, 736–747. https://doi.org/10.1016/j.psyneuen.2006.02.005

Xu, L., Freeman, G., Cowling, B.J., Schooling, C.M., 2013. Testosterone therapy and cardiovascular events among men: a systematic review and meta-analysis of placebo-controlled randomized trials. BMC Med 11, 108. https://doi.org/10.1186/1741-7015-11-108

Zitzmann, M., Nieschlag, E., 2007. Androgen receptor gene CAG repeat length and body mass index modulate the safety of long-term intramuscular testosterone undecanoate therapy in hypogonadal men. J. Clin. Endocrinol. Metab. 92, 3844–3853. https://doi.org/10.1210/jc.2007-0620

Supplementary Materials for: The effects of testosterone on the physiological response to social and somatic stressors

Supplementary tables and figures for the analysis of the cardiovascular and hormonal stress response

Predictors	*Estimates*	*CI*	*p*
(Intercept)	131.37	125.93 – 136.81	**<.001**
Treatment	-6.29	-14.08 – 1.51	.117
Stressor (CPT vs SECPT)	-3.90	-11.59 – 3.79	.322
Stressor (LWT vs SECPT)	-7.07	-14.76 – 0.63	.075
Time	25.29	20.84 – 29.74	**<.001**
Treatment x Stressor (CPT vs SECPT)	10.43	-0.59 – 21.45	.066
Treatment x Stressor (LWT vs SECPT)	7.78	-3.18 – 18.73	.167
Treatment x Time (Stressor = SECPT)	-8.33	-14.71 – -1.96	**.012**
Stressor (CPT vs SECPT) x Time	-11.77	-18.06 – -5.47	**<.001**
Stressor (LWT vs SECPT) x Time	-22.47	-28.77 – -16.18	**<.001**
Treatment x Stressor (CPT vs SECPT) x Time	17.32	8.30 – 26.34	**<.001**
Treatment x Stressor (LWT vs SECPT) x Time	11.06	2.10 – 20.02	**.017**
Random Effects			
σ^2	72.79		
$\tau_{00\ id}$	136.46		
$\tau_{11\ id.Orderpost}$	206.14		
$\rho_{01\ id}$	-0.20		
ICC $_{id}$	0.65		
Observations	141834		
Marginal R^2 / Conditional R^2	.410 / .795		

Table S1. Systolic blood pressure, Treatment x Stressor x Time model. Reference categories: Stressor: SECPT, Time: Pre, Treatment: Placebo.

Predictors	*Estimates*	*CI*	*p*
(Intercept)	127.47	122.03 – 132.90	**<.001**
Treatment	4.14	-3.65 – 11.93	.300
Stressor (SECPT vs CPT)	3.90	-3.79 – 11.59	.322
Stressor (LWT vs CPT)	-3.16	-10.85 – 4.53	.422
Time	13.52	9.07 – 17.98	**<.001**
Treatment x Stressor (SECPT vs CPT)	-10.43	-21.45 – 0.59	.066
Treatment x Stressor (LWT vs CPT)	-2.65	-13.60 – 8.29	.636
Treatment x Time (Stressor = CPT)	8.98	2.60 – 15.36	**.007**
Stressor (SECPT vs CPT) x Time	11.77	5.47 – 18.06	**<.001**
Stressor (LWT vs CPT) x Time	-10.71	-17.00 – -4.41	**.001**
Treatment x Stressor (SECPT vs CPT) x Time	-17.32	-26.34 – -8.30	**<.001**
Treatment x Stressor (LWT vs CPT) x Time	-6.26	-15.22 – 2.71	.174
Random Effects			
σ^2	72.79		
$\tau_{00\ id}$	136.30		
$\tau_{11\ id.Orderpost}$	206.14		
$\rho_{01\ id}$	-0.20		
ICC_{id}	0.65		
Observations	141834		
Marginal R^2 / Conditional R^2	.410 / .795		

Table S2. Systolic blood pressure, Treatment x Stressor x Time model. Reference categories: Stressor: CPT, Time: Pre, Treatment: Placebo.

Predictors	*Estimates*	*CI*	*p*
(Intercept)	124.30	118.86 – 129.74	**<.001**
Treatment	1.49	-6.20 – 9.18	.705
Stressor (SECPT vs LWT)	7.07	-0.62 – 14.76	.074
Stressor (CPT vs LWT)	3.16	-4.53 – 10.85	.422
Time	2.82	-1.63 – 7.27	.217
Treatment x Stressor (SECPT vs LWT)	-7.78	-18.72 – 3.17	.167
Treatment x Stressor (CPT vs LWT)	2.65	-8.29 – 13.60	.636
Treatment x Time (Stressor = LWT)	2.73	-3.57 – 9.02	.398
Stressor (SECPT vs LWT) x Time	22.47	16.18 – 28.77	**<.001**
Stressor (CPT vs LWT) x Time	10.71	4.41 – 17.00	**.001**
Treatment x Stressor (SECPT vs LWT) x Time	-11.06	-20.02 – -2.10	**.017**
Treatment x Stressor (CPT vs LWT) x Time	6.26	-2.71 – 15.22	.174
Random Effects			
σ^2	72.79		
$\tau_{00\ id}$	136.30		
$\tau_{11\ id.Orderpost}$	206.14		
$\rho_{01\ id}$	-0.20		
ICC $_{id}$	0.65		
Observations	141834		
Marginal R^2 / Conditional R^2	.410 / .795		

Table S3. Systolic blood pressure, Treatment x Stressor x Time model. Reference categories: Stressor: LWT, Time: Pre, Treatment: Placebo.

Predictors	*Chisq*	*Df*	*p*
(Intercept)	2242.18	1	**<.001**
Treatment	2.50	1	.114
Stressor	3.25	2	.197
Time	123.97	1	**<.001**
Treatment x Stressor	3.72	2	.156
Treatment x Time	6.56	1	.010
Stressor x Time	48.98	2	**<.001**
Treatment x Stressor x Time	14.53	2	**<.001**

Table S4. Type III Wald chi-square tests of the model with the factors Treatment, Stressor, Time, their interaction and dependent variable systolic blood pressure.

Predictors	*Estimates*	*CI*	*p*
(Intercept)	78.14	74.76 – 81.51	**<.001**
Treatment	-3.09	-7.92 – 1.75	.213
Stressor (CPT vs SECPT)	-1.95	-6.72 – 2.82	.425
Stressor (LWT vs SECPT)	-3.19	-7.95 – 1.58	.193
Time	13.97	11.23 – 16.70	**<.001**
Treatment x Stressor (CPT vs SECPT)	6.14	-0.70 – 12.97	.081
Treatment x Stressor (LWT vs SECPT)	3.50	-3.29 – 10.29	.314
Treatment x Time (Stressor = SECPT)	-2.46	-6.37 – 1.46	.221
Stressor (CPT vs SECPT) x Time	-7.73	-11.60 – -3.87	**<.001**
Stressor (LWT vs SECPT) x Time	-11.80	-15.66 – -7.94	**<.001**
Treatment x Stressor (CPT vs SECPT) x Time	8.64	3.11 – 14.18	**.003**
Treatment x Stressor (LWT vs SECPT) x Time	4.54	-0.96 – 10.03	.109
Random Effects			
σ^2	41.90		
$\tau_{00\ id}$	68.20		
$\tau_{11\ id.Orderpost}$	77.55		
$\rho_{01\ id}$	-0.39		
ICC $_{id}$	0.62		
Observations	141834		
Marginal R^2 / Conditional R^2	.301 / .734		

Table S5. Diastolic blood pressure, Treatment x Stressor x Time model. Reference categories: Stressor: SECPT, Time: Pre, Treatment: Placebo.

Predictors	*Estimates*	*CI*	*p*
(Intercept)	76.19	72.82 – 79.56	**<.001**
Treatment	3.05	-1.78 – 7.88	.218
Stressor (SECPT vs CPT)	1.95	-2.82 – 6.71	.425
Stressor (LWT vs CPT)	-1.24	-6.01 – 3.53	.612
Time	6.23	3.50 – 8.96	**<.001**
Treatment x Stressor (SECPT vs CPT)	-6.14	-12.97 – 0.70	.081
Treatment x Stressor (LWT vs CPT)	-2.64	-9.42 – 4.15	.448
Treatment x Time	6.19	2.27 – 10.10	**.002**
Stressor (SECPT vs CPT) x Time	7.73	3.87 – 11.60	**<.001**
Stressor (LWT vs CPT) x Time	-4.07	-7.93 – -0.21	**.041**
Treatment x Stressor (SECPT vs CPT) x Time	-8.64	-14.18 – -3.11	**.003**
Treatment x Stressor (LWT vs CPT) x Time	-4.11	-9.61 – 1.39	.146
Random Effects			
σ^2	41.90		
$\tau_{00\ id}$	68.20		
$\tau_{11\ id.Timepost}$	77.54		
$\rho_{01\ id}$	-0.39		
ICC_{id}	0.62		
Observations	141834		
Marginal R^2 / Conditional R^2	.301 / .734		

Table S6. Diastolic blood pressure, Treatment x Stressor x Time model. Reference categories: Stressor: CPT, Time: Pre, Treatment: Placebo.

Predictors	*Estimates*	*CI*	*p*
(Intercept)	74.95	71.58 – 78.32	**<.001**
Treatment	0.41	-4.35 – 5.18	.865
Stressor (SECPT vs LWT)	3.19	-1.58 – 7.95	.193
Stressor (CPT vs LWT)	1.24	-3.53 – 6.01	.612
Time	2.16	-0.57 – 4.90	.123
Treatment x Stressor (SECPT vs LWT)	-3.50	-10.29 – 3.29	.314
Treatment x Stressor (CPT vs LWT)	2.64	-4.15 – 9.42	.448
Treatment x Time	2.08	-1.78 – 5.94	.293
Stressor (SECPT vs LWT) x Time	11.80	7.94 – 15.66	**<.001**
Stressor (CPT vs LWT) x Time	4.07	0.21 – 7.93	**.041**
Treatment x Stressor (SECPT vs LWT) x Time	-4.54	-10.03 – 0.96	.109
Treatment x Stressor (CPT vs LWT) x Time	4.11	-1.39 – 9.61	.146
Random Effects			
σ^2	41.90		
$\tau_{00\ id}$	68.19		
$\tau_{11\ id.Timepost}$	77.54		
$\rho_{01\ id}$	-0.39		
ICC $_{id}$	0.62		
Observations	141834		
Marginal R^2 / Conditional R^2	.301 / .734		

Table S7. Diastolic blood pressure, Treatment x Stressor x Time model. Reference categories: Stressor: LWT, Time: Pre, Treatment: Placebo.

Predictors	*Chisq*	*Df*	*p*
(Intercept)	1961.27	1	**<.001**
Treatment	1.53	1	.216
Stressor	1.74	2	.418
Time	20.01	1	**<.001**
Treatment x Stressor	3.12	2	.210
Treatment x Time	9.60	1	.002
Stressor x Time	37.01	2	**<.001**
Treatment x Stressor x Time	9.38	2	**.009**

Table S8. Type III Wald chi-square tests of the model with the factors Treatment, Stressor, Time, their interaction and dependent variable diastolic blood pressure.

Predictors	*Estimates*	*CI*	*p*
(Intercept)	736.96	680.78 – 793.13	**<.001**
Treatment	89.04	5.00 – 173.08	**.040**
Stressor (CPT vs SECPT)	71.85	-10.87 – 154.57	.091
Stressor (LWT vs SECPT)	80.72	0.40 – 161.04	.051
Time	-28.81	-58.83 – 1.20	.063
Treatment x Stressor (CPT vs SECPT)	-208.42	-326.43 – -90.42	**.001**
Treatment x Stressor (LWT vs SECPT)	-167.45	-284.30 – -50.61	**.006**
Treatment x Time (Stressor = SECPT)	-12.38	-57.43 – 32.66	.591
Stressor (CPT vs SECPT) x Time	-23.00	-67.27 – 21.27	.311
Stressor (LWT vs SECPT) x Time	-33.00	-75.53 – 9.53	.131
Treatment x Stressor (CPT vs SECPT) x Time	-4.68	-68.16 – 58.80	.885
Treatment x Stressor (LWT vs SECPT) x Time	14.66	-47.35 – 76.66	.644
Random Effects			
σ^2	7236.77		
$\tau_{00\ ID}$	18873.19		
$\tau_{11\ ID.Timepre}$	9392.67		
$\rho_{01\ ID}$	-0.31		
$ICC_{\ ID}$	0.72		
Observations	62915		
Marginal R^2 / Conditional R^2	.139 / .761		

Table S9. Interbeat intervals. Treatment x Stressor x Time model. Reference categories: Stressor: SECPT, Time: During stressor, Treatment: Placebo.

Predictors	*Estimates*	*CI*	*p*
(Intercept)	808.81	748.09 – 869.52	**<.001**
Treatment	-119.38	-202.22 – -36.54	**.006**
Stressor (LWT vs CPT)	8.87	-74.68 – 92.42	.836
Stressor (SECPT vs CPT)	-71.85	-154.57 – 10.87	.091
Time	-51.81	-84.36 – -19.27	**.002**
Treatment x Stressor (LWT vs CPT)	40.97	-75.01 – 156.95	.490
Treatment x Stressor (SECPT vs CPT)	208.42	90.42 – 326.43	**.001**
Treatment x Time (Stressor = CPT)	-17.06	-61.79 – 27.67	.456
Stressor (LWT vs CPT) x Time	-10.00	-54.35 – 34.36	.660
Stressor (SECPT vs CPT) x Time	23.00	-21.27 – 67.27	.311
Treatment x Stressor (LWT vs CPT) x Time	19.33	-42.44 – 81.11	.541
Treatment x Stressor (SECPT vs CPT) x Time	4.68	-58.80 – 68.16	.885
Random Effects			
σ^2	7236.77		
$\tau_{00\ ID}$	18875.86		
$\tau_{11\ ID.Timepre}$	9393.67		
$\rho_{01\ ID}$	-0.31		
ICC_{ID}	0.72		
Observations	62915		
Marginal R^2 / Conditional R^2	.139 / .761		

Table S10. Interbeat intervals. Treatment x Stressor x Time model. Reference categories: Stressor: CPT, Time: During stressor, Treatment: Placebo.

Predictors	*Estimates*	*CI*	*p*
(Intercept)	817.68	760.28 – 875.08	**<.001**
Treatment	-78.41	-159.59 – 2.76	.061
Stressor (CPT vs LWT)	-8.87	-92.42 – 74.68	.836
Stressor (SECPT vs LWT)	-80.72	-161.04 – -0.40	.051
Time	-61.81	-91.94 – -31.68	**<.001**
Treatment x Stressor (CPT vs LWT)	-40.97	-156.95 – 75.01	.490
Treatment x Stressor (SECPT vs LWT)	167.45	50.61 – 284.30	**.006**
Treatment x Time (Stressor = LWT)	2.27	-40.33 – 44.88	.917
Stressor (CPT vs LWT) x Time	10.00	-34.36 – 54.35	.660
Stressor (SECPT vs LWT) x Time	33.00	-9.53 – 75.52	.131
Treatment x Stressor (CPT vs LWT) x Time	-19.33	-81.11 – 42.44	.541
Treatment x Stressor (SECPT vs LWT) x Time	-14.66	-76.66 – 47.35	.644
Random Effects			
σ^2	7236.77		
$\tau_{00\ ID}$	18873.19		
$\tau_{11\ ID.Timepre}$	9392.976		
$\rho_{01\ ID}$	-0.31		
$ICC_{\ ID}$	0.72		
Observations	62915		
Marginal R^2 / Conditional R^2	0.139 / 0.761		

Table S11. Interbeat intervals. Treatment x Stressor x Time model. Reference categories: Stressor: LWT, Time: During stressor, Treatment: Placebo.

Predictors	*Chisq*	*Df*	*p*
(Intercept)	852.59	1	**<.001**
Treatment	4.31	1	.038
Stressor	4.6389	2	.098
Time	3.5409	1	.060
Treatment x Stressor	13.4374	2	**<.001**
Treatment x Time	0.2902	1	.590
Stressor x Time	2.42	2	.298
Treatment x Stressor x Time	0.4147	2	.813

Table S12. Type III Wald chi-square tests of the model with the factors Treatment, Stressor, Tim e, their interaction and dependent variable interbeat intervals.

Predictors	*Estimates*	*CI*	*p*
(Intercept)	-3.73	-5.96 – -1.49	**.001**
Stressor (LWT vs CPT)	2.61	-0.12 – 5.35	.064
Stressor (SECPT vs LWT&CPT)	-1.90	-3.48 – -0.32	**.020**
Treatment	3.38	0.16 – 6.59	**.042**
Stressor (LWT vs CPT) x Treatment	-0.98	-4.92 – 2.97	.629
Stressor (SECPT vs LWT&CPT) x Treatment	2.44	0.17 – 4.71	**.037**
Observations	116		
R^2 / adjusted R^2	.120 / .080		

Table S13. High frequency-heart rate variability. Post-hoc analysis (Treatment x Stressor) of the difference in HF-HRV before and during stressor using Helmert contrasts.

Predictors	*Estimates*	*CI*	*p*
(Intercept)	0.58	0.47 – 0.69	**<.001**
Treatment	0.11	-0.05 – 0.27	.173
Time	0.15	0.04 – 0.26	**.008**
Stressor (CPT vs SECPT)	0.10	-0.06 – 0.26	.212
Stressor (LWT vs SECPT)	-0.28	-0.44 – -0.13	**.001**
Treatment x Time (Stressor = SECPT)	-0.07	-0.23 – 0.09	.385
Treatment x Stressor (CPT vs SECPT)	-0.22	-0.44 – 0.00	.053
Treatment x Stressor (LWT vs SECPT)	-0.14	-0.36 – 0.08	.220
Stressor (CPT vs SECPT) x Time	-0.13	-0.28 – 0.02	.101
Stressor (LWT vs SECPT) x Time	-0.30	-0.46 – -0.15	**<.001**
Treatment x Stressor (CPT vs SECPT) x Time	0.17	-0.05 – 0.40	.121
Treatment x Stressor (LWT vs SECPT) x Time	0.03	-0.18 – 0.25	.757
Random Effects			
σ^2	0.12		
$\tau_{00\ ID}$	0.02		
$\tau_{11\ ID.TimePost}$	0.00		
$\rho_{01\ ID}$	1.00		
ICC_{ID}	0.16		
Observations	466		
Marginal R^2 / Conditional R^2	.217 / .341		

Table S14. Cortisol levels, Treatment x Stressor x Time model. Reference categories: Stressor: SECPT, Time: Pre, Treatment: Placebo.

Predictors	*Estimates*	*CI*	*p*
(Intercept)	0.68	0.57 – 0.79	**<.001**
Treatment	-0.11	-0.27 – 0.05	.167
Time	-0.02	-0.13 – 0.09	.707
Stressor (LWT vs CPT)	-0.38	-0.54 – -0.23	**<.001**
Stressor (SECPT vs CPT)	-0.10	-0.26 – 0.06	.212
Treatment x Time (Stressor = CPT)	-0.11	-0.26 – 0.05	.184
Treatment x Stressor (LWT vs CPT)	0.08	-0.14 – 0.30	.461
Treatment x Stressor (SECPT vs CPT)	0.22	-0.00 – 0.44	.053
Stressor (LWT vs CPT) x Time	0.17	0.02 – 0.33	**.025**
Stressor (SECPT vs CPT) x Time	-0.13	-0.28 – 0.02	.101
Treatment x Stressor (LWT vs CPT) x Time	0.14	-0.08 – 0.36	.207
Treatment x Stressor (SECPT vs CPT) x Time	0.17	-0.05 – 0.40	.121
Random Effects			
σ^2	0.12		
$\tau_{00\ ID}$	0.05		
$\tau_{11\ ID.TimePre}$	0.00		
$\rho_{01\ ID}$	-1.00		
ICC_{ID}	0.28		
Observations	466		
Marginal R^2 / Conditional R^2	.191 / .418		

Table S15. Cortisol levels, Treatment x Stressor x Time model. Reference categories: Stressor: CPT, Time: Pre, Treatment: Placebo.

Predictors	*Estimates*	*CI*	*p*
(Intercept)	0.30	0.19 – 0.41	**<.001**
Treatment	-0.03	-0.18 – 0.13	.720
Time	0.15	0.05 – 0.26	**.005**
Stressor (CPT vs LWT)	0.38	0.23 – 0.54	**<.001**
Stressor (SECPT vs LWT)	0.28	0.13 – 0.44	**.001**
Treatment x Time (Stressor = LWT)	0.04	-0.12 – 0.19	.653
Treatment x Stressor (CPT vs LWT)	-0.08	-0.30 – 0.14	.461
Treatment x Stressor (SECPT vs LWT)	0.14	-0.08 – 0.36	.220
Stressor (CPT vs LWT) x Time	-0.17	-0.33 – -0.02	**.025**
Stressor (SECPT vs LWT) x Time	-0.30	-0.46 – -0.15	**<.001**
Treatment x Stressor (CPT vs LWT) x Time	-0.14	-0.36 – 0.08	.207
Treatment x Stressor (SECPT vs LWT) x Time	0.03	-0.18 – 0.25	.757
Random Effects			
σ^2	0.12		
$\tau_{00\ ID}$	0.05		
$\tau_{11\ ID.TimePre}$	0.00		
$\rho_{01\ ID}$	-1.00		
ICC_{ID}	0.28		
Observations	466		
Marginal R^2 / Conditional R^2	0.191 / 0.418		

Table S16. Cortisol levels, Treatment x Stressor x Time model. Reference categories: Stressor: LWT, Time: Pre, Treatment: Placebo.

Predictors	*Chisq*	*Df*	*p*
(Intercept)	103.34	1	**<.001**
Treatment	1.88	1	.170
Stressor	25.60	2	**<.001**
Time	7.04	1	**.008**
Treatment x Stressor	3.90	2	.143
Treatment x Time	0.76	1	.38
Stressor x Time	15.01	2	**<.001**
Treatment x Stressor x Time	2.73	2	.255

Table S17. Type III Wald chi-square tests of the model with the factors Treatment, Stressor, Tim e, their interaction and dependent cortisol levels.

Factor level	*Estimates*	*CI*	*p*
SECPT	0.164	0.05 – 0.28	**.005**
CPT	0.104	-0.01 – 0.21	.066
LWT	-0.242	-0.35 – - 0.13	**<.001**

Table S18. Pairwise comparison of cortisol levles Pre – Post stressor onset. Results are averaged o ver the levels of the factor Treatment. Confidence level: 0.95.

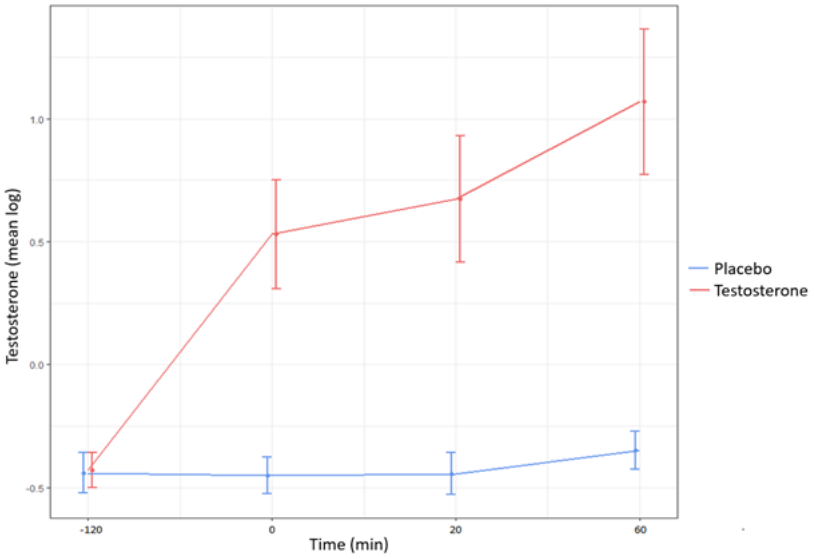


Figure S1. Testosterone levels [pg/ml] during the experiment (log-transformed). 0 denotes the time point when the stressor was administered. Error bars: 95% CI.

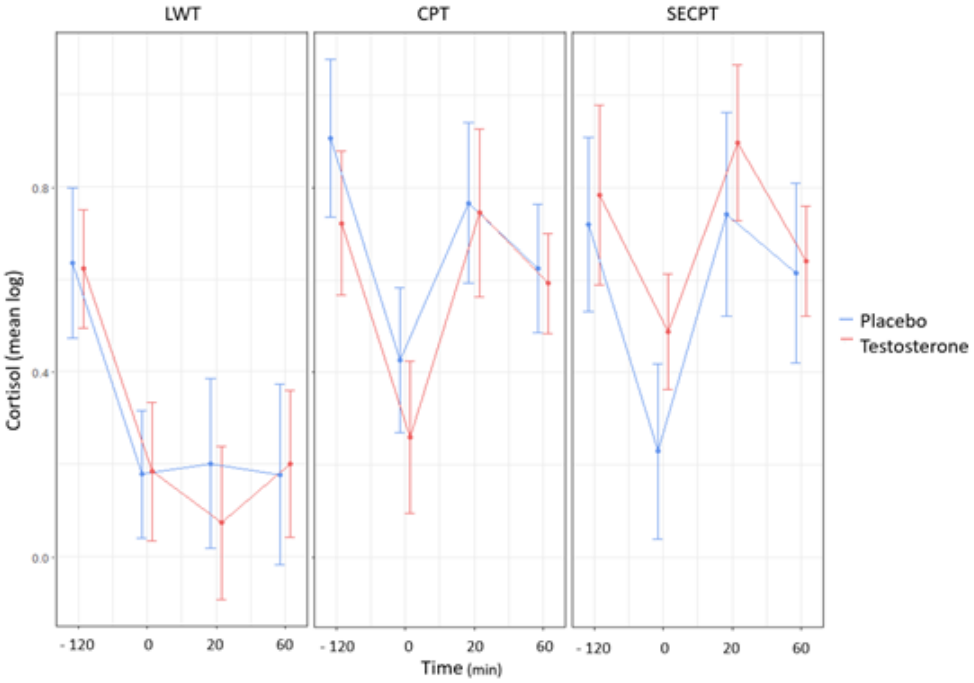


Figure S2. Cortisol levels in [ng/mL] during the experiment (log-transformed). 0 denotes the time point when the stressor was administered. Error bars: 95% CI.

	Placebo group			Testosterone group		
	SECPT	CPT	WWT	SECPT	CPT	WWT
Cortisol sample 1	7.44 (1.31)	10.87 (1.28)	5.76 (1.28)	8.71 (1.31)	6.55 (1.31)	4.87 (1.28)
Cortisol sample 2	2.55 (0.45)	3.42 (0.44)	2.07 (0.45)	3.63 (0.45)	2.31 (0.45)	2.07 (0.45)
Cortisol sample 3	8.12 (1.29)	7.90 (1.25)	2.19 (1.25)	10.35 (1.29)	7.40 (1.29)	2.87 (1.25)
Cortisol sample 4	5.87 (0.66)	5.15 (0.63)	2.21 (0.63)	4.78 (0.64)	4.31 (0.66)	2.07 (0.63)

Table S19. Salivary cortisol levels. Due to non-normal distribution of the cortisol levles, we used log-transformed data in our analysis. Here we provide means of the original values of cortisol levels in ng/mL (SE).

Supplementary analysis of the self-report measures

The group differences in the age, personality traits and affective states were tested using 2-way ANOVA with the factors Treatment (Testosterone/Placebo), Stress protocol (CPT/ SCPT / WWT), and their interaction. There were no differences in age, Positive and Negative Affect Schedule subscales, NEO *Five-Factor Inventory subscales or trait dominance* across the experimental groups *(all p-values > .07).*

	Placebo group			Testosterone group		
	SECPT	CPT	LWT	SECPT	CPT	LWT
Age	24.3 (0.98)	24.8 (0.98)	21.6 (0.98)	25.1 (0.98)	23.9 (0.98)	23.6 (0.98)
Positive Affect	36.1 (1.18)	39.0 (1.09)	37.0 (1.12)	35.8 (1.12)	36.3 (1.12)	35.3 (1.09)
Negative Affect	18.9 (1.70)	20.4 (1.58)	19.4 (1.62)	22.0 (1.62)	21.2 (1.62)	20.9 (1.58)
NEO-FFI Neuroticism	17.2 (1.74)	16.5 (1.74)	14.7 (1.79)	20.1 (1.79)	16.6 (1.79)	18.2 (1.74)
NEO-FFI Extraversion	31.6 (1.68)	33.2 (1.64)	31.6 (1.68)	28.2 (1.68)	30.7 (1.69)	28.5 (1.64)
NEO-FFI Openness	25.0 (1.27)	25.8 (1.27)	25.3 (1.29)	23.4 (1.31)	25.8 (1.30)	26.2 (1.24)
NEO-FFI Agreeableness	30.9 (1.39)	30.4 (1.39)	29.4 (1.43)	30.6 (1.43)	27.9 (1.3)	29.1 (1.43)
Dominance	30.1 (0.69)	31.9 (0.66)	31.2 (0.67)	30.0 (0.66)	31.1 (0.66)	30.1 (0.66)

Table S20. Mean values (SE) of the self-report measures administered during the waiting period.

Predictors	*Estimates*	*CI*	*p*
(Intercept)	19.16	15.87– 22.46	**<.001**
Treatment	-1.51	-4.81 – 2.78	.370
SECPT	-19.16	-23.79 – -14.53	**<.001**
CPT	14.74	10.06 – 19.43	**<.001**
Treatment x SECPT	1.51	-3.11 – 6.14	.523
Treatment x CPT	-3.03	-7.71 – 1.66	.209
R^2 / adjusted R^2	.406 / .378		

Table S21. Model with the factors Treatment (Testosterone/Placebo), Stressor type (LWT/CPT/SECPT), their interaction and a dependent variable of self-reported stress. Participants were asked to rate how stressful their experience was immediately after the offset of the stressor. 2-way ANOVA revealed a main effect of Stressor ($F(2,107) = 35.89$, $p = <.001$).

Predictors	*Estimates*	*CI*	*p*
(Intercept)	36.90	33.21 – 40.58	**<.001**
Treatment	-2.65	-6.34 – 1.04	.162
SECPT	-36.90	-42.08 – 31.71	**<.001**
CPT	24.40	19.14 – 29.65	**<.001**
Treatment x SECPT	2.65	-2.53 – 7.83	.319
Treatment x CPT	-0.12	-5.37 – 5.14	.966
R^2 / adjusted	.653 / .637		

Table S22. Model with the factors Treatment (Testosterone/Placebo), Stressor type (LWT/CPT/SECPT), their interaction, and a dependent variable of self-reported pain. Participants were asked to rate how painful their experience was immediately after the offset of the stressor. 2-way ANOVA revealed a main effect of Stressor ($F(2,107) = 100.33$, $p = <.001$).

Predictors	*Estimates*	*CI*	*p*
(Intercept)	38.06	34.10 – 42.03	**<.001**
Treatment	0.65	-3.31 – 4.62	.747
SECPT	-37.01	-42.59 – -31.44	**<.001**
CPT	22.44	16.80 – 28.09	**<.001**
Treatment x SECPT	0.40	-5.18 – 5.97	.889
Treatment x CPT	0.52	-5.13 – 6.17	.857
R^2 / adjusted R^2	.614 / .597		

Table S23. Model with the factors Treatment (Testosterone/Placebo), Stressor type (LWT/CPT/ SECPT), their interaction, and a dependent variable of self-reported unpleasantness. Participants were asked to rate how unpleasant their experience was immediately after the offset of the stressor. 2-way ANOVA revealed a main effect of Stressor ($F(2,108) = 85.76$, $p = <.001$).

	1	*2*	*3*
1. Self-reported stress			
2.Self-reported pain	.738***		
3. Self-reported unpleasantness	.665***	.824***	
4. Δ Systolic blood pressure	.313***	.412***	.424***
5. Δ Diastolic blood pressure	.200*	.326***	.375***
6. Δ Interbeat interval	-.020	.047	-.148
7. Δ HF-HRV	-.047	-.061	.-025
8. Δ Cortisol	.246*	.364***	.345***

Table S24. Overall Pearson correlations among self-report measures and stress-related change in the physiological measures. *Δ* = (Post stressor onset measurement) – (Pre stressor onset measurement).

Testosterone and placebo cream composition

Testosterone cream was composed of 5000 mg of cremor anionicus, 150 mg of 96% alcohol and 150 mg of testosterone (Euro OTC Pharma GmbH, Bönen, Germany). Placebo cream contained 5000 mg of cremor anionicus and 150 mg of 96% alcohol.

Salivary hormones analysis

Testosterone, cortisol, and androstenedione were measured from the saliva samples by liquid chromatography tandem-mass spectrometry (LC-MS/MS) using an Agilent 6460 with electrospray ionization coupled to a 1290 UHPLC system. 100 µl internal standards (5 ng/mL) were added to 500 µL plasma or saliva and the steroids were extracted using 4 mL MTBE. After 10 minutes overhead shacking, the samples were centrifuged for 5 minutes at 3000 rpm and the top MTBE layer was transferred to a test tube. MTBE was evaporated using a centrivap concentrator (Labconco). The residual sample was then re-dissolved in 30% methanol and analyzed by LC-MS/MS. Agilent Poroshell 120 EC-C18 was used for chromatographic separation.

CAG repeat polymorphism analysis

DNA was extracted from buccal swabs and isolated using a resin-based method with Chelex®100 (Sigma Aldrich, USA). The CAG repeat polymorphism in exon 1 of the AR gene was amplified using PCR in 20 µL reaction volume with 250 nmol/L primers: forward: 5’ GCGCGAAGTGATCCAGAAC 3’ tagged with 6–carboxyfluorescein and reverse 5’ CTCATCCAGGACCAGGTAGC 3’, 1× Taq buffer (Fermentas, Vilnius, Lithuania) and 1U of Taq DNA polymerase (Fermentas, Vilnius, Lithuania). The following PCR program was used: initial denaturation step at 94°C for 4 min, followed by 35 cycles each consisting of denaturation at 94°C for 45 s, annealing at 59.5°C for 45 s and polymerization at 72°C for 45 s. The length of the final fragment was 181 bp. The number of repeats was analyzed by capillary electrophoresis. The analysis was not completed in five samples due to lack of the provided sample availability. The number of CAG repeats in exon 1 of the AR gene did not differ significantly between testosterone (M = 21.54, 95% CI [20.8, 22.3]) and placebo group (M = 22.46, 95% CI [21.7, 23.2]), or across any experimental groups (See table S24).

Predictors	*Estimates*	*CI*	*p*
(Intercept)	22.00	21.50 – 22.50	**<.001**
Treatment	-0.46	-0.96 – 0.05	.078
CPT	0.21	-0.50 – 0.92	.562
SECPT	0.05	-0.63 – 0.74	.876
Treatment x CPT	-0.02	-0.73 – 0.69	.959
Treatment x SECPT	-0.17	-0.86 – 0.52	.625
R^2 / adjusted R^2	.038 / .006		

Table S25. Model with the factors Treatment (Testosterone/Placebo) and Stressor type (LWT/CPT/ SECPT), their interaction and a dependent variable of the number of CAG repeats.

Chapter 3

STUDY 2: TESTOSTERONE ELIMINATES STRATEGIC PROSOCIAL BEHAVIOR THROUGH IMPACTING CHOICE CONSISTENCY IN HEALTHY MALES

Original manuscript, as published in Neuropsychopharmacology,
doi: 10.1038/s41386-023-01570-y

Hana H. Kutlikova*[a,b, 1], Lei Zhang[a,c,d,1], Christoph Eisenegger [a †], Jack van Honk[b,e], Claus Lamm[a,f]

[a] Department of Cognition, Emotion, and Methods in Psychology, University of Vienna, Vienna, Austria

[b] Department of Experimental Psychology, Helmholtz Institute, Utrecht University, Utrecht, the Netherlands

[c] Centre for Human Brain Health, School of Psychology, University of Birmingham, Birmingham, UK

[d] Institute for Mental Health, School of Psychology, University of Birmingham, Birmingham, UK

[e] Department of Psychiatry and Mental Health, University of Cape Town, Cape Town, South Africa

[f] Vienna Cognitive Science Hub, University of Vienna, Vienna, Austria

[1] Equal contribution.

[†] Deceased February 27, 2017.

*Corresponding author: Hana H. Kutlikova, Liebiggasse 5, University of Vienna, Vienna 1010, Austria, hana.kutlikova@univie.ac.at.

Abstract

Humans are strategically more prosocial when their actions are being watched by others than when they act alone. Using a psychopharmacogenetic approach, we investigated the endocrinological and computational mechanisms of such audience-driven prosociality. 192 male participants received either a single dose of testosterone (150 mg) or a placebo and performed a prosocial and self-benefitting reinforcement learning task. Crucially, the task was performed either in private or when being watched. Rival theories suggest that the hormone might either diminish or strengthen audience-dependent prosociality. We show that exogenous testosterone fully eliminated strategic, i.e., feigned, prosociality and thus decreased submission to audience expectations. We next performed reinforcement-learning drift-diffusion computational modeling to elucidate which latent aspects of decision-making testosterone acted on. The modeling revealed that testosterone compared to placebo did not deteriorate reinforcement learning per se. Rather, when being watched, the hormone altered the degree to which the learned information on choice value translated to action selection. Taken together, our study provides novel evidence of testosterone's effects on implicit reward processing, through which it counteracts conformity and deceptive reputation strategies.

Introduction

Humans behave more prosocially when their actions are watched by others [1]. This phenomenon has been demonstrated across a variety of social behaviors, such as blood donations [2], church offerings [3], or monetary donations to charitable organizations [4], and is often referred to as strategic prosociality [5], or the audience effect [6]. From an evolutionary perspective, making one's generosity visible to others has an important signaling value, in that it advertises an individual's qualities as a potential partner or a valuable group member [7]. In the present study, we propose and investigate whether the steroid hormone testosterone plays a crucial role in shaping such audience effects.

Research in the past decade has demonstrated that testosterone is implicated in a wide spectrum of socially dominant behaviors [8,9]. Exogenous testosterone alleviates subordination to the dominance of others [10-12] and reduces the physiological response to being evaluated by others [13]. Given that enhanced submission to audience expectations has been associated with intense apprehension about social evaluation [14], one possible prediction is that testosterone administration will decrease audience effects.

Contrasting with this view, the hypothesis that testosterone drives status-seeking via reputation building rather than dominance [15, 16] would predict that based on the social context, testosterone might conditionally promote prosocial and especially socially desirable behavior to build up a reputation and increase status.

The present paper is the first that aimed to distinguish between these two alternatives of boosting one's social status that testosterone may act on. One option is that, in line with the social dominance hypothesis [17], the hormone prioritizes dominant status-seeking and would hence diminish the submission to audience expectations. The other option is that testosterone primarily promotes reputable status-seeking [15, 16]. If true, the hormone could increase strategic prosocial behavior.

Through what neurobiological pathways could testosterone modulate such complex social behaviors? Previously, exogenous testosterone was found to increase dopamine levels in the rat ventral striatum [18], suggesting that the hormone exerts its effects through the modulation of dopaminergic activity in reward-related neural circuits. Besides this insight from animal research, testosterone and reward processing have also been linked in humans [19, 20]. It remains to be shown, though, which specific aspects of reward processing testosterone acts on. For one, during value learning, testosterone may influence the incorporation of so-called prediction errors (PE), which track the difference between predicted and actual outcome [21] and are encoded by the phasic activity of midbrain dopaminergic neurons projecting to the ventral striatum [22, 23].

Alternatively, testosterone may impact the conversion of the learned values into action selection, or the temporal dynamics of the evidence accumulation.

The present study thus not only aimed to investigate if testosterone influences strategic prosociality, but also whether this is achieved by impacting reward-related computations. We employed a novel modeling approach, by combining reinforcement learning with diffusion decision models (RLDDM). This provided a more comprehensive account of the latent processes involved in prosocial decision-making than previous separate RL and DDM approaches [21,24]. Besides describing how subjective values of the choice options are learned through PEs (*learning rate parameters*) and converted to actions (*choice consistency parameter*), the new combination of reinforcement learning and diffusion decision modeling also enabled us to explore the temporal dynamics of these latent processes (*decision threshold and drift-scaling parameters,* see *SM Table S4* for parameter description) [24].

Male participants underwent a double-blind, between-subject, placebo-controlled, testosterone administration and then performed a reinforcement learning task (Figure 1). To compare self- and other-oriented decision-making, participants completed the task for themselves and for an NGO of their choice. While charitable donation tasks [16] and neuroeconomic games [8, 9] classically measure participants' overall prosociality using deliberated decisions, such as deciding how much money to share with another person, the RL task allowed us to furthermore characterize the hidden individual steps in the process of learning about the consequences actions have for oneself and others (see [25, 26] for similar recent approaches). Critically, the task was performed either in private or when being watched (see *Materials and Methods*).

Based on previous audience-effect research [2-6], we predicted that when the participants are watched, they will be relatively more prosocial (i.e., make more correct choices for the other vs self) than in private. Crucially, we expected that such an audience effect will be underpinned by relatively faster incorporation of the PEs (captured by the learning rate parameter α in RL); higher consistency in converting values to action probability (captured by the inverse temperature parameter tau in RL, also known as value sensitivity, exploration parameter, or $1/\beta$); and more integrated evidence necessary for making a decision (captured by the threshold parameter in DDM). In other words, participants would learn more efficiently, learned values would inform their behavior more consistently, and their decisions would be more cautious.

Our main hypothesis was that the effects of being watched on other- vs. self-benefitting behavior will be modulated by testosterone administration. Given that testosterone reduces submission signals and stress responses to the social evaluation, allowing for dominant status-seeking [10-13], we hypothesized that testosterone would reduce the audience effect expected in the placebo group. As an alternative prediction, we reasoned that if testosterone does not primarily cause dominant status-seeking, but instead, in non-threatening environments, promotes more agreeable and

reputable status-enhancing behaviors [15, 16], participants in the testosterone (vs placebo) group should show a larger audience effect. Irrespective of whether testosterone would increase or decrease prosocial behavior under the audience effect, we also predicted that testosterone's effects will be associated with changes in the efficiency of PE-based value updating (α in RL), choice consistency (tau in RL), and evidence necessary for making a decision (threshold parameter in DDM).

Previous research has suggested that testosterone possibly modulates social behavior through both androgenic and dopaminergic pathways and that testosterone effects on status-seeking behavior are moderated by CAG repeat polymorphism of the androgen receptor [27], and DAT1 polymorphism of the dopamine transporter [28]. We, therefore, examined whether these polymorphisms interact with testosterone administration effects on strategic prosociality. Furthermore, as research has shown that testosterone effects on status-seeking and decision-making are influenced by endogenous cortisol levels [29, 30], we examined whether testosterone administration effects interact with salivary cortisol levels measured at baseline and with cortisol reactivity to being watched. Moreover, as it has been suggested that sensitivity of dopaminergic pathways is heightened among highly dominant individuals [31] and that these individuals show more pronounced effects of testosterone administration [27, 32], we tested whether testosterone effects on strategic prosociality vary as a function of self-reported trait dominance [33]. Lastly, we sought to shed light on the motivational aspects [15, 34], of testosterone's actions. We, therefore, conducted an exploratory post-hoc analysis that tested whether testosterone effects on strategic prosociality interact with self-reported value system, based on a questionnaire that captures the motivational bases of human attitudes and behavior [35, 36].

Materials and Methods

Participants

The study sample consisted of 192 healthy adult men aged between 18 and 40 years (M = 24.89, SD = 4.08). The sample size was determined based on previous testosterone administration studies [8, 13, 32] and our pilot study. In the applied linear mixed models, our sample size gave us 90% power to detect three-way and 86% power to detect 4-way interaction effects of size $f \geq 0.15$. Using Monte Carlo simulation [37], we also calculated the probability of detecting a significant effect in the generalized linear mixed models (GzLMM) given our sample, experimental design, and the expected effect size based on previous research (B = 0.231) [16, 28]. The probability of a significant 3-way interaction was 93.68% (95% CI [89.08, 98.28]) and the probability of a significant 4-way interaction was 88.40% (95% CI [86.87, 89.31]. Participants were recruited via flyers placed around university campuses and online advertisements. The exclusion criteria comprised a history of neurological or psychiatric disorders, endocrine or other internal diseases, substance dependence, body mass index outside the healthy weight range (18.5 -

24.9), and the use of steroids. Only male participants were included as testosterone metabolism is subject to sex differences and the pharmacokinetics of topical administration of testosterone are unclear in women [38]. Two participants were excluded from the original sample N=192 because they continually clicked on the same response key irrespective of changing stimuli and reward probabilities for more than 80% of the block trials, and thus were classified as non-compliant. This led to a final sample size N = 190. All participants gave written consent and received a financial reward for their participation consisting of a flat fee and a bonus based on their task performance. All procedures were approved by the Ethics committee of the Medical University of Vienna and conducted following the latest revision of the Declaration of Helsinki [39]. No side-effects or adverse events were reported during or after the experimental sessions.

Procedure and experimental design

Testing took place in groups of three to five participants, who were seated individually in small cubicles within the same testing room. All experimental sessions started between 01:00 and 02:30 p.m. First, a buccal smear sample for CAG repeat and DAT1 polymorphisms analysis was taken (see *SM*: *Supplementary information on the analysis of genetic data*). 20 min after arrival, participants were asked to drool 2 mL of saliva into a polyethylene collection tube. All salivary samples were frozen on-site and stored at - 30 °C until analysis. Afterward, participants were administered topical testosterone or placebo gel in a double-blind between-subjects design with random group allocation. Those allocated to the testosterone group received a single dose of testosterone gel, containing 150 mg testosterone [Androgel®]; participants in the placebo group received an equivalent amount of placebo gel. The only difference between the testosterone and placebo gel was that the placebo gel did not contain testosterone. Participants rubbed the gel onto their upper arms and shoulders using disposable latex gloves. Gel administration was followed by a 2-hour waiting period, during which participants remained in the laboratory premises, completed personality and demographic questionnaires, and were offered leisure-time reading materials. The testosterone dose and timing of the experiment were based on the previously established pharmacokinetic study of testosterone gel preparations in healthy young males [38]. One hour and 50 minutes after the gel application, participants provided a second saliva sample and subsequently began the experimental task (see Figure 1). Two more saliva samples were taken during the course of the study: 20 and 60 minutes after the end of the experimental task. After data collection was complete, saliva samples were analyzed by liquid chromatography-tandem mass spectrometry.

Participants performed the experimental task under one of the two randomly assigned between-subject conditions: either in private or when being observed. In the private condition, participants were informed that their performance is completely anonymous and no one (including the experimenter) would know how much money they would earn for themselves and the charitable organization. In the observed condition, two female observers, introduced as NGO association

representatives entered the room and watched participants perform the task. The observers were seated at a desk with a laptop and had an equal view of all the participants. In addition, when participants were observed, a red frame was shown on their computer‘s screen and the displays of the participants' computers were transmitted onto the observers‘ laptop screens.

Participants were thus randomly assigned into four experimental groups corresponding to the levels of two between-subject factors: (1) treatment (testosterone/placebo) and (2) visibility (observed/private). These groups did not differ in age, trait dominance, basal hormone levels, or distribution of AR CAG and DAT1 genotype (see *SM: Table S1*).

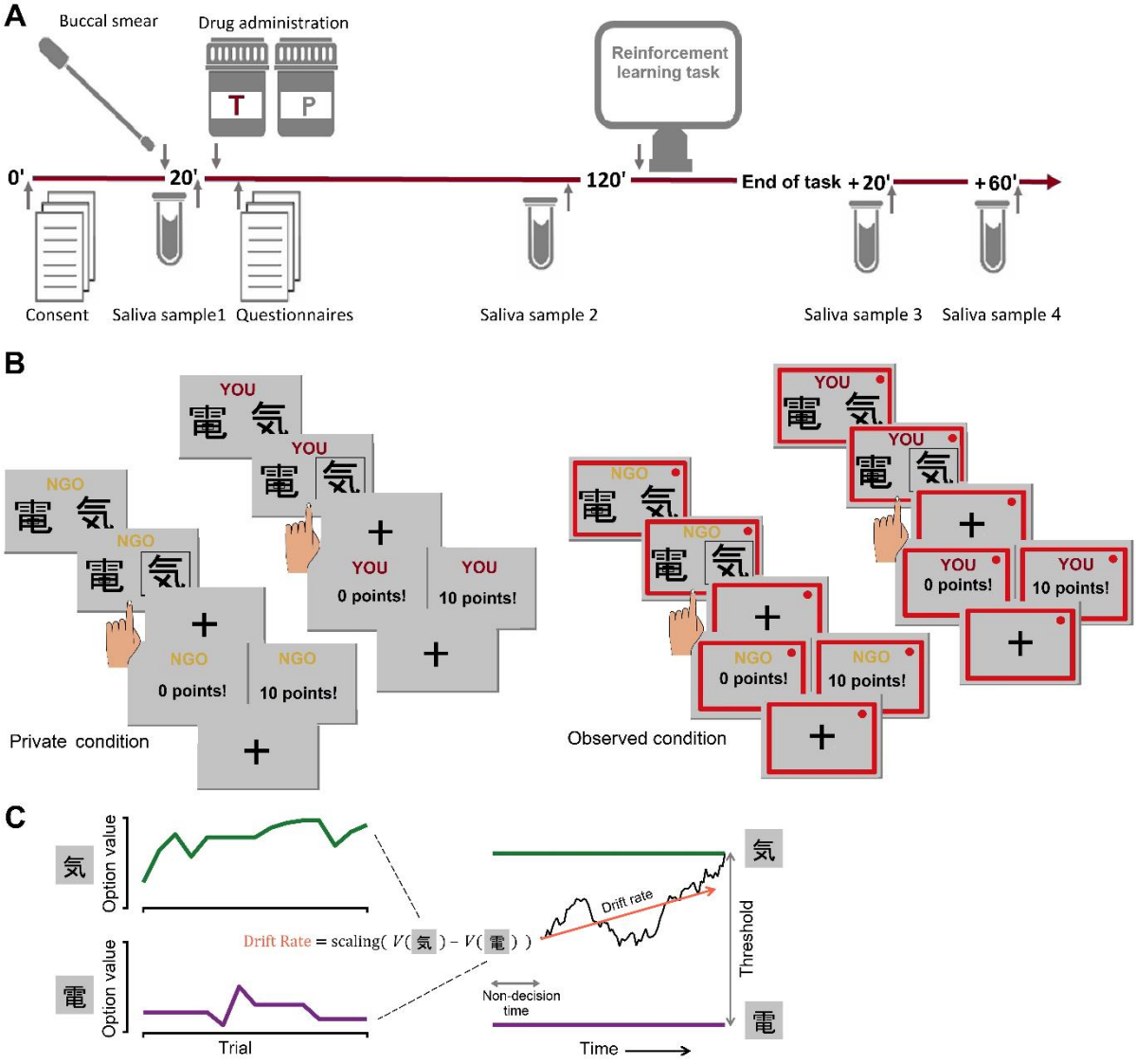


Figure 1. Experimental design and task. *(A)* Timeline of the experimental session. *(B)* Prosocial reinforcement learning task. Participants performed the task either in private or watched by an observer introduced as an NGO association representative. The observation was signaled by a red frame. Each participant completed three blocks of 16 trials for themself and three blocks of 16 trials to benefit an NGO of his choice. *(C)* Schematic of the reinforcement learning drift diffusion model (RLDDM). Left panel: trial-by-trial value updates in RL; right panel: evidence accumulation in DDM. Importantly, the drift rate in DDM is calculated from the value difference between choice options in RL.

Prosocial learning task

Participants performed a probabilistic reinforcement learning task [25], where they could earn rewards either for themselves (self condition) or for an NGO of their choice (other condition). On each trial, participants were presented with two abstract symbols, one associated with a high (75%) and the other with a low (25%) reward probability. These contingencies were not instructed but had to be learned through trial and error. Participants selected a symbol by a button press and then received feedback on whether they obtained points or not. This way participants learned which symbol to choose to maximize the rewards in the long run. The points were converted to monetary rewards at the end of the experiment. Participants completed 6 blocks, 3 blocks in self and 3 blocks in the other condition. Each block started with a new pair of symbols and consisted of 16 trials/choices. In the self condition, the blocks started with "YOU" displayed and had the word "YOU" at the top of each screen. In the other condition, the blocks started with "NGO" displayed and had the word "NGO" at the top of each screen. The order of the blocks was pseudo-randomized so that the same recipient block did not occur twice in a row, and that half of the participants' sample started the task with the *self* condition and the other half with the *other* condition. At the end of the experimental task, participants could choose the recipient of the money they earned in the other condition from a list of 6 different charities.

Immediately after completing the task, participants were asked to fill in a post-task questionnaire to estimate their subjective perception of being watched. The participants were asked the question: "Did you feel that you were being watched while performing the task?" The answers were classified into three categories: 1 (Not at all), 2 (Moderately), and 3 (Strongly).

Statistical analysis of correct choices

Statistical analysis was performed using R statistical language [40]. We analyzed the treatment (testosterone/placebo) x visibility (observed/private) x recipient (self/other) interaction effect on correct choice using generalized linear mixed models (GzLMM) with binomial distribution and logit link function. The correct choice was defined as choosing the symbol with a higher reward probability. The participant's identity was modeled as a random intercept effect and the within-subject factor recipient (self/other) was entered as a random slope.

To examine whether the effects of testosterone on correct choice varied as a function of trait dominance, CAG repeat, DAT1 polymorphism, baseline cortisol, cortisol reactivity, and personal value orientations, we added these variables separately as predictors in interaction with the other factors specified in the above GzLMM (See *SM* for information on the used R packages).

Reinforcement learning drift-diffusion modeling

To uncover the cognitive computational processes underlying our learning task, we performed modeling analysis under the joint reinforcement learning drift diffusion model (RLDDM)

framework [24, 41]. In essence, RLDDM bridges RL, which typically models choices, and DDM, which commonly models response times (RT). This approach has been proven to provide more granularity than using RL or DDM alone [24]. We tested candidate models with a single learning rate (Rescorla-Wagner models) as well as models with dual learning rates. Together, we tested 6 candidate RLDDM models, and the winning model is described below (see *SM: Supplementary information on computational modeling* for full model description, estimation, and comparison procedures). The RL part of the winning RLDDM model was implemented with a dual learning rates reinforcement learning model, where both the learning rate for a positive prediction error and the learning rate for a negative prediction error were employed to update values (i.e., V(A) and V(B) for two-choice options) [42] (Equation (1); see also *SM: Supplementary information on computational modeling).*

The DDM part of the winning RLDDM model was implemented via a non-linear transformation of the accuracy-codded value differences computed from the RL counterpart, to construct the trial-by-trial drift rates [24] (Equation (2); see *also SM: Supplementary information on computational modeling*). The winning model contained 14 parameters: 7 separate parameters for each between-subject condition (i.e., placebo/testosterone, private/observed), and differential parameters for the within-subject condition (i.e., other/self; see *SM: Table S4* for the parameter list and description).

In all models, we simultaneously modeled participants' choice and RT, separately for each between-subject condition (i.e., placebo/testosterone; observed/private). Model estimations of all candidate models were performed with hierarchical Bayesian analysis (HBA). HBA was particularly useful when the number of trials was limited (here 16 trials per block) because in HBA, group-level and individual-level parameters were mutually informing each other during model estimation. All models reached convergence (see *SM: Supplementary information on computational modeling*).

Statistical analysis of model parameters

The drug treatment (testosterone/placebo) x visibility (observed/private) x recipient (other/self) effect on the extracted free parameters was analyzed using GzLMMs analogous to the analysis of the correct choice. Due to the non-normal distribution of residuals, gamma distribution with a log link function was used for the parameter analyses. Finally, we tested whether the RLDDM parameter estimates, which were affected by the interaction of the drug treatment, visibility, and recipient could explain the differences observed in the behavioral prosociality measure. To do so, we conducted multiple linear regressions with the difference in the number of correct choices made for other and self (*prosociality index*) as a dependent variable and the differences in the RLDDM parameter estimates (αneg_{other}- αneg_{self}, τ_{other} – τ_{self}, $threshold_{other}$ -$threshold_{self,}$ drift-$scaling_{other}$-drift-$scaling_{self}$) as separate predictors. Bonferroni correction for multiple comparisons was used.

Results

Manipulation check

In the testosterone, compared to the placebo group, we observed higher salivary testosterone levels 110 minutes after gel administration, and this difference remained stable until the end of the experiment (drug treatment x time: $F(3, 554.82) = 48.00$, $p = .001$, $R^2_{conditional} = .737$), see *Figure S1* and *SM: Supplementary analysis of hormone data* for analysis details). Analysis of the subjective ratings of being watched showed that participants in the observed condition felt watched to a greater extent than in the private condition (X^2 (2, N=190) = 114.49, $p < .001$), and that testosterone administration did not influence the perception of being watched (X^2 (2, N=190) = 0.006, $p = .997$). The degree to which the participants felt watched, was positively associated r (185) = .177, $p = .016$) with cortisol reactivity to the visibility manipulation (*Δ cortisol levels 20 minutes after the end of the task - cortisol levels immediately before the task*).

Testosterone eliminates the audience effect

The three-way interaction of the factors drug treatment (P/T), visibility (private/observed), and type of recipient (self/other) predicted the number of correct choices (i.e., options that have higher reward probability) the participants made ($OR = 0.94$, $CI = [0.89, 1.00]$, $p = .043$; Figure 2A). Follow-up analysis using treatment contrasts showed that participants in the placebo group showed more prosocial behavior, as indicated by relatively more correct prosocial choices when being watched compared to the private setting in which they were not watched (recipient x visibility interaction in the placebo group: $OR = 1.43$, $CI = [1.01, 2.02]$, $p = .042$).

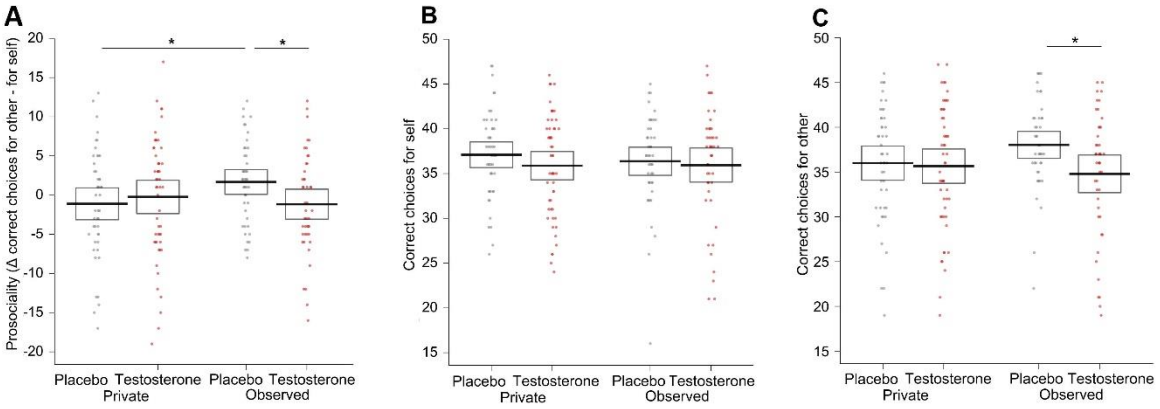


Figure 2. Differences in the number of correct choices. *(A)* Three-way interaction of the factors treatment x recipient x visibility. Participants in the placebo group behaved more prosocially (as captured by the prosociality index = correct choices for other – correct choices for self) when being observed than in privacy. Exogenous testosterone eliminated this audience effect. Note that the analyses were performed with raw data in the 2 x 2 x 2 factorial design; the plotted difference score (other minus self) is to improve readability and interpretability. Breaking down the three-way interaction by using treatment contrasts showed that there was no significant effect of the drug treatment and visibility factors, or their interaction, on the number of correct choices made for oneself *(B)*. On the other hand, testosterone, compared to placebo, decreased the number of correct choices made for the NGO when being observed *(C)*. Dots represent the data of individual participants, lines represent mean values per group, and boxes 95% confidence intervals.

Supporting our prediction based on the social dominance hypothesis, this audience effect was absent in the testosterone group (recipient x visibility interaction in the testosterone group: *OR* = 0.87, *CI* = [0.62, 1.22], *p* = .418). Specifically, when participants were observed, testosterone, compared to placebo, reduced the number of correct choices made for another (*OR* = 0.69, *CI* = [0.50, 0.94], *p* = .019, Figure 2C). The number of correct choices made for self, however, was not influenced by the drug treatment (*OR* = 0.98, *CI* = [0.75, 1.28], *p* = .875), visibility (*OR* = 1.00, *CI* = [0.78, 1.30], *p* = .982, or their interaction (*OR* = 0.88, *CI* = [0.61, 1.28], *p* = .509, Figure 2B).

Behavior is best explained by a reinforcement learning drift diffusion model with dual learning rates

Next, we sought to uncover the computational mechanisms underlying the experiment-condition-specific behavioral differences on a trial-by-trial basis. The winning model (winning over five other candidate models; see *Materials and Methods*, *SM: Model selection and validation, and Table S3*) entailed combined RL and DDM components, and thus simultaneously predicted individuals' choices and RTs (see *SM: Table S4* for a complete list of parameters and their description). The RL component section predicted participants' learning behavior via the value updates through the computation of PEs with separate learning rates for positive and negative PEs (i.e., α^{posPE} and α^{negPE} Equation (1)). In other words, the model that best accounted for the data assumed a differential speed of learning with and without positive feedback:

$$V_{c,t} = \begin{cases} V_{c,t-1} + \alpha^{\text{pos}}\left(O_{t-1} - V_{c,t-1}\right), \text{if } O_{t-1} > 0 \\ V_{c,t-1} + \alpha^{\text{neg}}\left(O_{t-1} - V_{c,t-1}\right), \text{otherwise} \end{cases}. \quad (1)$$

where O_{t-1} denotes the outcome, and $V_{c,t-1}$ the subjective value of choice c at trial $t-1$.

In addition, the DDM component predicted RTs by assuming an evidence accumulation process (as quantified by the drift rate; decisions were made when the evidence reached a certain threshold [41]). Importantly, the marriage between RL and DDM allowed a fine-grained investigation into how the drift rate (v_t) was shaped by the value difference between two symbols at the trial-by-trial level (Equation (2); *S*, a non-linear transformation function; $v_{scaling}$, a weight parameter that maps accuracy-coded value difference into the drift rate [24]).

$$v_t = S\left[v_{\text{scaling}}\left(V_{\text{correct},t} - V_{\text{incorrect},t}\right)\right], \quad (2)$$

We fitted all candidate models (see *Materials and Methods* and *SM: Supplementary information on computational modeling*) under the hierarchical Bayesian estimation scheme [43] to incorporate both group-level commonality and individual differences, according to our task design (effects of drug treatment (P/T), visibility (private/observed), and type of recipient (self/other)).

Testosterone's impact on strategic prosocial behavior is associated with choice consistency

Next, we investigated which RLDDM parameters of our validated winning model are associated with the effects found in the behavioral analysis of the correct choice. As a first step, we tested the parameters for the 3-way interaction effect of drug treatment, visibility, and type of recipient. In the second step, we examined whether the parameters that showed a three-way interaction effect of our experimental manipulation predict behavioral prosociality (the difference between correct choices made for others and self). Out of the five parameters (learning rate for positive PE, learning rate for negative PE, choice consistency, threshold, drift-scaling parameter), only choice consistency showed the requisite three-way interaction of our experimental manipulations (B = 0.98, CI = [0.97, 0.98], $p < .001$), and at the same time significantly predicted behavioral prosociality (Bonferroni correction for multiple comparisons, B = 3.82, CI = [2.64, 5.01], $p < .001$; Figure 3D). Specifically, participants in the placebo group displayed relatively higher consistency in choices made for the other (vs. self) when being observed than in privacy (recipient x visibility interaction in the placebo group: B = 1.09, CI = [1.05, 1.14], $p < .001$). On the contrary, in the testosterone group, observation, compared to privacy, decreased the consistency of choices made for the other (vs. self) (recipient x visibility interaction in testosterone group: B = 0.90, CI = [0.84, 0.98], $p < .001$; Figure 3B). When participants were observed, testosterone, compared to placebo, diminished the relative consistency of prosocial choices (recipient x treatment interaction in observed condition: OR = 0.91, CI = [0.84, 0.99], p = .025; for analysis of all RLDDM parameters, see *SM: Analysis of the RLDDM parameters and their association with prosocial behavior*).

Altogether, these results suggest that testosterone eliminates audience-dependent prosocial behavior by affecting choice consistency.

Interaction of testosterone effects with trait dominance

In further support of the social dominance hypothesis, trait dominance interacted with testosterone's effects on correct choice (recipient x drug treatment x visibility x trait dominance: OR = 1.04, CI = [1.01, 1.09], p = .026). In a follow-up analysis aimed at decoding this interaction, the continuous measure of dominance was replaced by a categorical variable with levels of high and low dominance, based on the median split of dominance scores (Med = 3.949). Decomposition of the four-way interaction revealed that testosterone reduced the number of correct choices made for others during observation specifically among men with high trait dominance (OR = 0.60, CI = [0.42, 0.87], p = .008) and this effect was weaker and non-significant among those with low dominance (OR = 0.77, CI = [0.55, 1.04], p = .132). Trait dominance did not significantly interact with the RLDDM parameters (all ps>.331 see *SM: Interaction of trait dominance with testosterone effects on RLDDM parameters).*

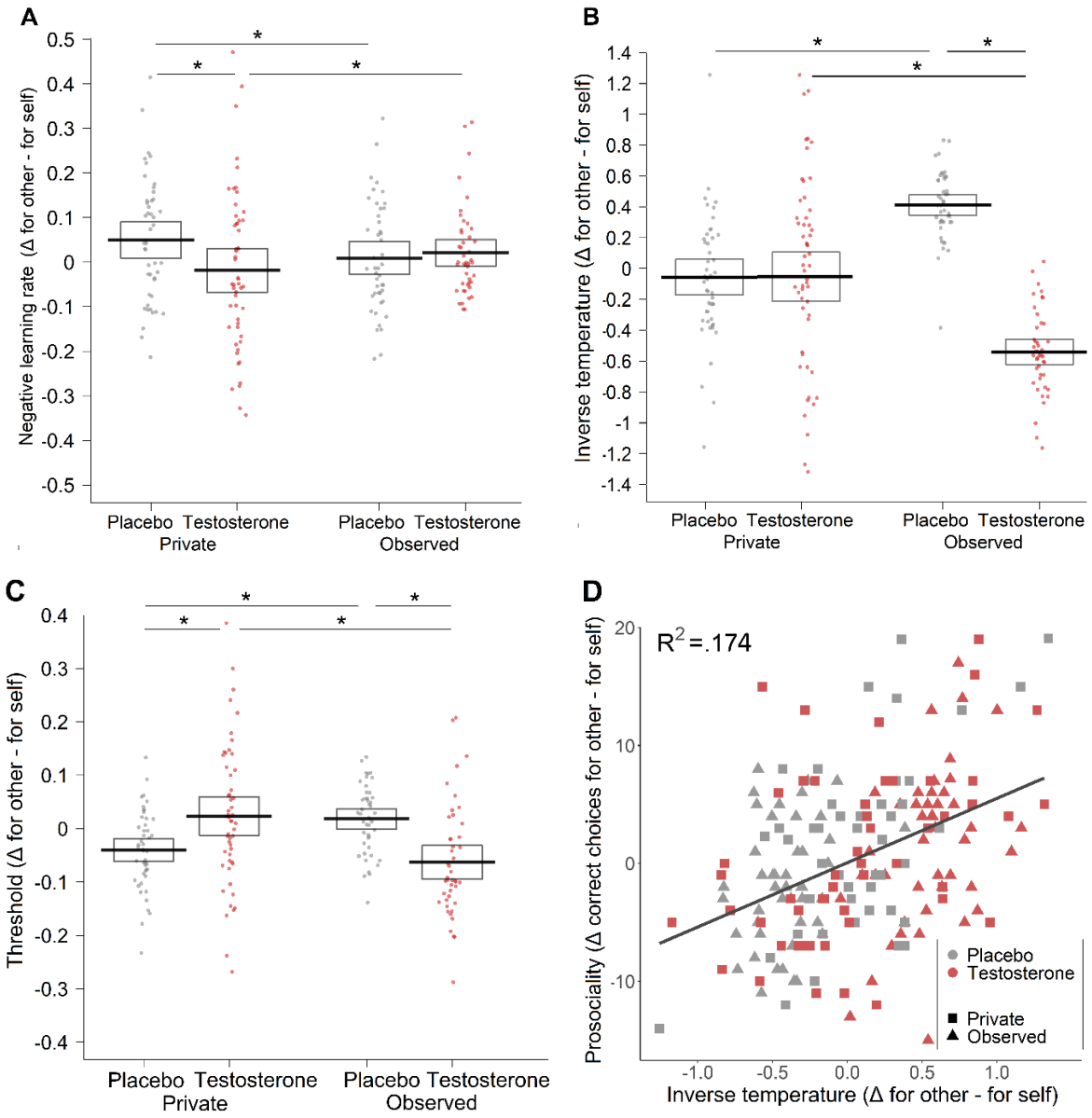


Figure 3. Differences in the parameters estimated by the reinforcement learning drift diffusion model (RLDDM). *(A)* In the placebo group, observation compared to privacy relatively decreased the prosocial learning rate for negative PE (i.e., the difference between α^{negPE} in the other condition and α^{negPE} in the self condition). Testosterone administration reversed the observation effect. The results suggest that for better performance in the task, a lower learning rate from negative PE is more suitable. *(B)* In the placebo group, observation compared to privacy, relatively increased the consistency of the prosocial choices. Testosterone administration reversed this audience effect. *(C)* In the placebo group, observation compared to privacy, relatively increased the DDM threshold for prosocial choices. Testosterone administration reversed the audience effect. *(D)* Inverse temperature parameter tau that captures choice consistency significantly predicted prosociality. Dots represent the data of individual participants, lines represent mean values per group, and boxes 95% confidence intervals.

Interaction of testosterone effects with genetic polymorphisms and cortisol levels

CAG-repeat and DAT1 polymorphisms did not interact with the effects of testosterone on correct choice or RLDDM parameters (all *p*s>.091, see *SM: Supplementary information on the analysis of genetic data*). Furthermore, neither baseline cortisol levels, nor cortisol reactivity to visibility manipulation (Δ cortisol levels 20 minutes after the end of task - cortisol levels immediately before the task) interacted with the effects of testosterone on correct choice or RLDDM parameters (all *p*s >.052, see *SM: Supplementary analysis of hormone data, Figure S2, and Table S2 for details on cortisol levels*).

Interaction of testosterone effects with personal value orientations

We next explored whether four principal value orientations (self-enhancement, self-transcendence, openness, conservation) measured using a self-report questionnaire [35,36] interacted with testosterone's influence on the number of correct choices and choice consistency.
This revealed an interaction of *self-enhancement value orientation* with testosterone's effect on the number of correct choices (recipient x visibility x administration x self-enhancement*: OR* = 0.65, *CI* = [0.48, 0.88], p = .006) and interaction of *conservation value orientation* and testosterone's effects on choice consistency (recipient x visibility x administration x conservation: *B* = 0.60, *CI* = [0.17, 1.02], p = .006). The treatment contrast analysis of the interaction effect with self-enhancement showed that when testosterone participants were watched, a higher score in self-enhancement value was negatively associated with correct prosocial choices (*OR* = 1.29, *CI* = [0.21, 2.36], p = .008). In the placebo group, we did not observe such an association (*OR* = 1.11, *CI* = [0.89, 1.38], p = .349) and this difference between testosterone and placebo group was significant (*OR* = 0.72, *CI* = [0.55, 0.94], p = .018).

The treatment contrast analysis of the interaction effect with conservation value showed that when placebo participants were watched, the prosocial choice consistency was positively associated with conservation value (*B* = 1.29, *CI* = [0.22, 2.35], p = .019). However, after testosterone administration, the link between conservation value and prosocial choice consistency was abolished (*B* = -0.02, *CI* = [-0.94, 0.90, p = .969), but this difference between testosterone and placebo group did not reach significance (*OR* = 1.30, *CI* = [-0.10, 2.71], p = .069). No other interaction between value orientations and testosterone effect on choice behavior or RLDDM parameters was detected (all *p*s >.287 see *SM: Supplementary information on the questionnaire data).*

Learning parameters in relation to optimal learning rates

To gain a deeper understanding of how the learning parameters were related to the task performance in our experimental design, we performed a simulation study to identify optimal learning rates [44] (see *SM: Simulations of optimal learning rates*). In all conditions, both the posterior positive and negative learning rates were smaller with respect to the optimal ones (see

Figure 4A, 4C). Crucially, to validate whether the choice accuracy corresponding to the posterior parameters in our winning model could capture key patterns in our behavior findings (i.e., posterior predictive check), we let our winning model generate synthetic data and analyzed the generated prosocial behavior (i.e., choice accuracy for other minus choice accuracy for self) in the same way as we analyzed the observed data. We found that results from the generated data (Figure 4B, 4D) greatly resembled the behavioral patterns reported in Figure 2A.

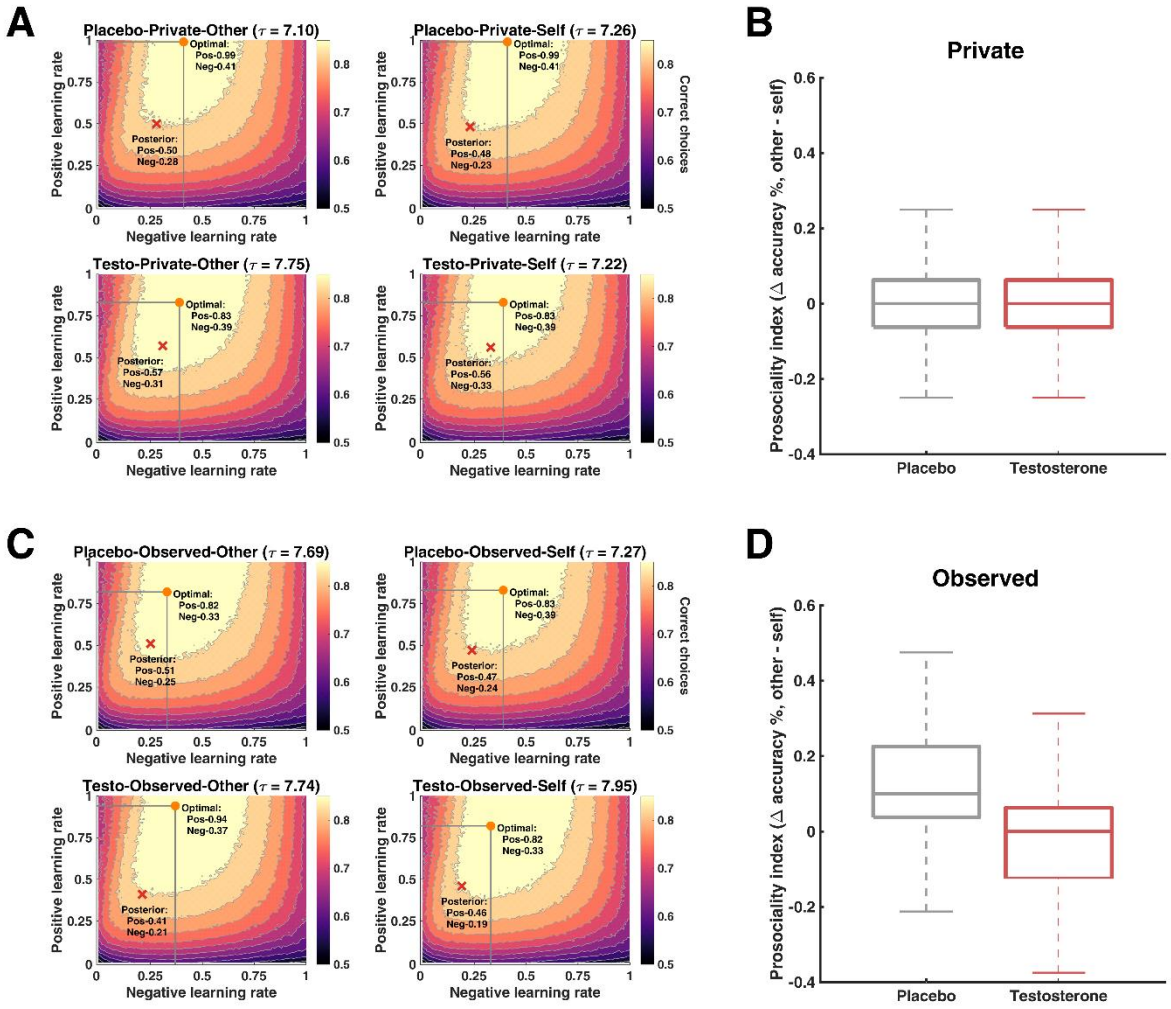


Figure 4. Optimal learning rates and posterior predictive checks. Posterior learning rates in relation to the optimal learning rates in the private *(A)* and observed *(C)* conditions. Orange dots represent the optimal combination between learning rates for positive and negative PE identified via simulation; red crosses indicate the posterior means of learning rates. The posterior learning rates were employed to perform posterior predictive checks for the main behavioral findings for the private *(B)* and observed *(D)* conditions. Simulated data from posteriors were analyzed in a similar fashion as the real data and the model prediction largely matched our main behavioral effect (cf. Figure 2A).

Discussion

Using pharmacological manipulation and a novel computational model integrating reinforcement learning with the drift diffusion modeling framework (RLDDM), we tested and characterized testosterone's role in audience-dependent prosocial behavior. The results show that testosterone diminishes the typical audience effect present in the placebo condition. Computational modeling pinpoints this effect to a reduction in the extent to which the performance of prosocial (vs. selfish) choices is consistent with learned reward values. Moreover, the effects are more pronounced in participants with higher trait dominance. Taken together, these findings are in line with the social dominance hypothesis and are thus consistent with the notion that testosterone decreases submission to audience expectations, rather than promoting the strategic display of socially pleasing behavior [45, 46].

A growing body of evidence suggests that testosterone exerts its behavioral effects through the modulation of reward-related processes [19, 20]. However, to our knowledge, no study investigated the computational mechanisms underlying such effects. Using joint RLDDMs, we found that in the placebo group, observation (vs privacy) increased the relative consistency of prosocial choices. Testosterone administration eliminated this audience effect, making the performance of prosocial (vs. self-benefitting) choices less consistent with value computations. Low choice consistency means that individuals select options with non-maximal expected values, which is often referred to as exploratory behavior [47]. In environments with static reward probabilities, participants can maximize their reward by initially exploring which option tends to be more fruitful. Once learners discover the better option, exploration yields no benefit. One possible explanation of the present effect could therefore be that testosterone impaired individuals' ability to adapt and control the amount of exploration. However, our data do not indicate that testosterone affects exploration in general, as we did not find any testosterone influence on choice consistency in the private setting. Instead, the effects of testosterone appeared only in a situation where social status was at stake. Interestingly, research in monkeys has shown that socially challenging environments (vs socially isolated environments) increased the availability of D_2 receptors [48], which play a role in choice consistency [49]. This effect was present in particular in dominant monkeys and absent in the subordinate ones. Such findings are in line with our results showing enhanced testosterone effects in individuals with high trait dominance. We, therefore, suggest that future studies should examine the potential mediating role of D2 receptors in testosterone's effect on reward learning in social situations.

Alternatively, it could be speculated that the elimination of the audience effect by testosterone stems from the hormone's ability to reduce fear in social situations. Indeed, earlier research shows that exogenous testosterone diminishes the physiological stress response to the presence of an observer [13] and has anxiolytic-like properties in humans and across species [10, 50]. However,

we did not observe any interaction of the testosterone's effect with cortisol levels measured at baseline or with cortisol reactivity, thus our data do not provide support for such an interpretation. To examine this topic further, studies on testosterone and audience effect should include more explicit measures of subjectively perceived stress and anxiety.

The present data also shows that testosterone administration substantially alters the relation between the audience effect and self-reported value orientations. *Self-enhancement* value, as measured here [35], is characterized by power, achievement, and the pursuit of one's own interests, success, and dominance over others. We found that a higher emphasis on self-enhancement was related to a lower number of correct prosocial choices while being watched in the testosterone, but not in the placebo group. This finding extends the evidence that the hormone testosterone interacts with dominant personality traits. In contrast to self-enhancement, conservation value reflects a personal emphasis on conformity, security, tradition, and self-restriction [35]. We showed that in the placebo group, the degree to which one identifies with conservation value is positively associated with the consistency of prosocial choices made while being watched. Testosterone administration abolished this link between conservation value and prosocial choice consistency. In consideration of the conformity aspect of the conservation value, it is of interest that in Western societies, nonconforming people are perceived as having higher status and competence than those who conform to the social expectations [51]. Thus, these findings are suggestive of the interpretation that by inducing a non-confirming attitude, testosterone reaches its principle goal - to be observed as having high status and competence[17,46]. We note though that the analyses of value orientations are exploratory and were performed post-hoc, and thus need independent confirmation.

Variability in dominance, conservation, and cultural differences in social status attaintment, can also account for the results of another recent study, which was conducted among Chinese students and showed that testosterone enhanced audience effects [16]. Indeed, contrary to Western society, in Eastern cultures, high social status is associated with increased self-restriction and other-orientation [52]. Consistently, individuals from Western and Eastern cultures differ in their self-construal, i.e., in the way they define the self in relation to others, with, for example, European individuals construing themselves as being more independent, or less interdependent, than Asian individuals [53]. Interestingly, research has shown that acute testosterone changes in men are positively associated with aggressive behavior for those with more independent self-construals, whereas basal testosterone is negatively associated with aggression when individuals have more interdependent self-construals [54]. Moreover, the cultural differences in independent vs. interdependent social orientations have been linked to polymorphisms in the dopamine D4 receptor gene [53], implying a putative biological mechanism that could explain cultural differences in testosterone effects. Finally, contrasting results may also stem from differences in the applied methods. While Wu et al. [16] used a modified dictator game, where participants were

explicitly asked whether they want to donate a certain monetary amount to charity, in the present task, the donation to charity was determined indirectly by the participant's performance in a reinforcement learning task. Our paradigm thus presents a more implicit measure of prosociality. For these reasons, we suggest future studies of how testosterone affects status-seeking behavior should focus on exploring these cultural differences, specifically by including measures of value orientations, self-construal, implicit behavioral tasks, as well as assessments of dopamine receptor polymorphisms.

Our results are, furthermore, in line with studies showing that testosterone decreases deception [55-57]. Further research is, however, needed to determine whether testosterone reduces lying per se, or only in situations where dishonest behavior may be considered "cheap", dishonorable, and lower the subject's feelings of pride and self-image [55].

There are also some limitations inherent to the methodology of our study. Due to the sex differences in testosterone metabolism and unknown pharmacokinetics following the topical administration of testosterone in women [38], the study included only male participants. Hence, the generalization of these findings to females requires further investigation. Furthermore, the observers in our study were exclusively female. Future research will also be required to more systematically test whether testosterone's influence on the prosocial audience effect is sensitive to the gender, number, and salience of the present observers. Nevertheless, our survey data suggest that the salience of the observers used in our study was representative of a wide range of social contacts and that the subjective feeling of being watched scaled with an established stress biomarker.

In conclusion, we conducted a multifaceted examination of the computational, endocrinological, and genetic mechanisms underlying audience effect and showed that testosterone reduced strategic prosocial learning through impairment of choice consistency. These findings provide evidence that in the Western student sample, testosterone abolishes audience effects, and therefore does not foster the seeking of social leadership by reputational politics. The present study is the first to specify testosterone's role in reward processing by revealing that testosterone impacts status-seeking through modulation of how the learned reward values are expressed in behavior.

Acknowledgments

We thank Felix Dörflinger and Maximilian Kathofer for their dedicated assistance with data collection. We also thank Shawn Geniole for his helpful feedback.

Author Contributions

H.H.K. and L.Z. share the first authorship of this article. H.H.K, C.E., and C.L. designed research; H.H.K. performed research; H.H.K. and L.Z. analyzed data; H.H.K., L.Z., C.L., and J.v.H. wrote the paper.

Funding

This work was supported by the Vienna Science and Technology Fund (WWTF VRG 13-007).

Competing Interest Statement

The authors have nothing to disclose.

References

1. Bradley A, Lawrence C, Ferguson E. Does observability affect prosociality? Proceedings of the Royal Society B: Biological Sciences. 2018;285:20180116.
2. Lacetera N, Macis M. Social image concerns and prosocial behavior: Field evidence from a nonlinear incentive scheme. Journal of Economic Behavior & Organization. 2010;76:225–237.
3. Soetevent AR. Anonymity in giving in a natural context—a field experiment in 30 churches. Journal of Public Economics. 2005;89:2301–2323.
4. Li Y, Météreau E, Obeso I, Butera L, Villeval MC, Dreher J-C. Endogenous testosterone is associated with increased striatal response to audience effects during prosocial choices. Psychoneuroendocrinology. 2020;122:104872.
5. Böckler A, Tusche A, Singer T. The Structure of Human Prosociality: Differentiating Altruistically Motivated, Norm Motivated, Strategically Motivated, and Self-Reported Prosocial Behavior. Social Psychological and Personality Science. 2016;7:530–541.
6. Hamilton AF de C, Lind F. Audience effects: what can they tell us about social neuroscience, theory of mind and autism? Cult Brain. 2016;4:159–177.
7. Gintis H, Smith EA, Bowles S. Costly Signaling and Cooperation. Journal of Theoretical Biology. 2001;213:103–119.
8. Dreher J-C, Dunne S, Pazderska A, Frodl T, Nolan JJ, O'Doherty JP. Testosterone causes both prosocial and antisocial status-enhancing behaviors in human males. PNAS. 2016;113:11633–11638.
9. Ou J, Wu Y, Hu Y, Gao X, Li H, Tobler PN. Testosterone reduces generosity through cortical and subcortical mechanisms. PNAS. 2021;118.
10. Terburg D, Syal S, Rosenberger LA, Heany SJ, Stein DJ, Honk J van. Testosterone abolishes implicit subordination in social anxiety. Psychoneuroendocrinology. 2016;72:205–211.
11. Geniole SN, Proietti V, Bird BM, Ortiz TL, Bonin PL, Goldfarb B, et al. Testosterone reduces the threat premium in competitive resource division. Proc Biol Sci. 2019;286:20190720.
12. Kutlikova HH, Geniole SN, Eisenegger C, Lamm C, Jocham G, Studer B. Not giving up: Testosterone promotes persistence against a stronger opponent. Psychoneuroendocrinology. 2021;128.
13. Kutlikova HH, Durdiaková JB, Wagner B, Vlček M, Eisenegger C, Lamm C, et al. The effects of testosterone on the physiological response to social and somatic stressors. Psychoneuroendocrinology. 2020;117:104693.
14. Cañigueral R, Hamilton AF de C. Being watched: Effects of an audience on eye gaze and prosocial behaviour. Acta Psychol (Amst). 2019;195:50–63.
15. Eisenegger C, Haushofer J, Fehr E. The role of testosterone in social interaction. Trends in Cognitive Sciences. 2011;15:263–271.
16. Wu Y, Zhang Y, Ou J, Hu Y, Zilioli S. Exogenous testosterone increases the audience effect in healthy males: evidence for the social status hypothesis. Proceedings of the Royal Society B: Biological Sciences. 2020;287:20200976.
17. Terburg D, van Honk J. Approach–Avoidance versus Dominance–Submissiveness: A Multilevel Neural Framework on How Testosterone Promotes Social Status. Emotion Review. 2013;5:296–302.
18. de Souza Silva MA, Mattern C, Topic B, Buddenberg TE, Huston JP. Dopaminergic and serotonergic activity in neostriatum and nucleus accumbens enhanced by intranasal administration of testosterone. European Neuropsychopharmacology. 2009;19:53–63.
19. Hermans EJ, Bos PA, Ossewaarde L, Ramsey NF, Fernández G, van Honk J. Effects of exogenous testosterone on the ventral striatal BOLD response during reward anticipation in healthy women. Neuroimage. 2010;52:277–283.
20. Op de Macks ZA, Moor BG, Overgaauw S, Güroğlu B, Dahl RE, Crone EA. Testosterone levels correspond with increased ventral striatum activation in response to monetary rewards in adolescents. Developmental Cognitive Neuroscience. 2011;1:506–516.
21. Sutton RS, Barto AG. 2018. Reinforcement Learning, second edition: An Introduction. MIT Press.

22. Cohen JY, Haesler S, Vong L, Lowell BB, Uchida N. Neuron-type-specific signals for reward and punishment in the ventral tegmental area. Nature. 2012;482:85–88.
23. Diederen KMJ, Spencer T, Vestergaard MD, Fletcher PC, Schultz W. Adaptive Prediction Error Coding in the Human Midbrain and Striatum Facilitates Behavioral Adaptation and Learning Efficiency. Neuron. 2016;90:1127–1138.
24. Fontanesi L, Gluth S, Spektor MS, Rieskamp J. A reinforcement learning diffusion decision model for value-based decisions. Psychon Bull Rev. 2019;26:1099–1121.
25. Lockwood PL, Apps MAJ, Valton V, Viding E, Roiser JP. Neurocomputational mechanisms of prosocial learning and links to empathy. PNAS. 2016;113:9763–9768.
26. Lengersdorff LL, Wagner IC, Lockwood PL, Lamm C. When Implicit Prosociality Trumps Selfishness: The Neural Valuation System Underpins More Optimal Choices When Learning to Avoid Harm to Others Than to Oneself. J Neurosci. 2020;40:7286–7299.
27. Geniole SN, Procyshyn TL, Marley N, Ortiz TL, Bird BM, Marcellus AL, et al. Using a Psychopharmacogenetic Approach To Identify the Pathways Through Which—and the People for Whom—Testosterone Promotes Aggression. Psychol Sci. 2019;30:481–494.
28. Losecaat Vermeer AB, Krol I, Gausterer C, Wagner B, Eisenegger C, Lamm C. Exogenous testosterone increases status-seeking motivation in men with unstable low social status. Psychoneuroendocrinology. 2020;113:104552.
29. Knight EL, Sarkar A, Prasad S, Mehta PH. Beyond the challenge hypothesis: The emergence of the dual-hormone hypothesis and recommendations for future research. Hormones and Behavior. 2020;123:104657.
30. Prasad S, Knight EL, Mehta PH. Basal testosterone's relationship with dictator game decision-making depends on cortisol reactivity to acute stress: A dual-hormone perspective on dominant behavior during resource allocation. Psychoneuroendocrinology. 2019;101:150–159.
31. Qu C, Ligneul R, Van der Henst J-B, Dreher J-C. An Integrative Interdisciplinary Perspective on Social Dominance Hierarchies. Trends in Cognitive Sciences. 2017;21:893–908.
32. Carré JM, Geniole SN, Ortiz TL, Bird BM, Videto A, Bonin PL. Exogenous Testosterone Rapidly Increases Aggressive Behavior in Dominant and Impulsive Men. Biological Psychiatry. 2017;82:249–256.
33. Cheng JT, Tracy JL, Henrich J. Pride, personality, and the evolutionary foundations of human social status. Evolution and Human Behavior. 2010;31:334–347.
34. Schultheiss OC, Rohde W. Implicit Power Motivation Predicts Men's Testosterone Changes and Implicit Learning in a Contest Situation. Hormones and Behavior. 2002;41:195–202.
35. Schwartz SH. Chapter 7 A Proposal for Measuring Value Orientations across Nations 2007.
36. Schwartz, SH, Breyer, B, & Danner, D. Human Values Scale (ESS). Zusammenstellung sozialwissenschaftlicher Items und Skalen (ZIS) 2015.
37. Green P, MacLeod CJ. SIMR: an R package for power analysis of generalized linear mixed models by simulation. Methods in Ecology and Evolution. 2016;7:493–498.
38. Eisenegger C, von Eckardstein A, Fehr E, von Eckardstein S. Pharmacokinetics of testosterone and estradiol gel preparations in healthy young men. Psychoneuroendocrinology. 2013;38:171–178.
39. WMA - The World Medical Association-WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/. Accessed 29 June 2021.
40. R Core Team. R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing; 2020.
41. Ratcliff R, McKoon G. The Diffusion Decision Model: Theory and Data for Two-Choice Decision Tasks. Neural Comput. 2008;20:873–922.
42. den Ouden HEM, Daw ND, Fernandez G, Elshout JA, Rijpkema M, Hoogman M, et al. Dissociable effects of dopamine and serotonin on reversal learning. Neuron. 2013;80:1090–1100.

43. Ahn W-Y, Haines N, Zhang L. Revealing Neurocomputational Mechanisms of Reinforcement Learning and Decision-Making With the hBayesDM Package. Comput Psychiatr. 2017;1:24–57.
44. Zhang L, Lengersdorff L, Mikus N, Gläscher J, Lamm C. Using reinforcement learning models in social neuroscience: frameworks, pitfalls and suggestions of best practices. Social Cognitive and Affective Neuroscience. 2020;15:695–707.
45. Dabbs JM. Testosterone and the concept of dominance. Behavioral and Brain Sciences. 1998;21:370–371.
46. Mazur A, Booth A. Testosterone and dominance in men. Behav Brain Sci. 1998;21:353–363; discussion 363-397.
47. Daw ND, O'Doherty JP, Dayan P, Seymour B, Dolan RJ. Cortical substrates for exploratory decisions in humans. Nature. 2006;441:876–879.
48. Morgan D, Grant KA, Gage HD, Mach RH, Kaplan JR, Prioleau O, et al. Social dominance in monkeys: dopamine D2 receptors and cocaine self-administration. Nat Neurosci. 2002;5:169–174.
49. Eisenegger C, Naef M, Linssen A, Clark L, Gandamaneni PK, Müller U, et al. Role of Dopamine D2 Receptors in Human Reinforcement Learning. Neuropsychopharmacology. 2014;39:2366–2375.
50. Fernández-Guasti A, Martínez-Mota L. Anxiolytic-like actions of testosterone in the burying behavior test: role of androgen and GABA-benzodiazepine receptors. Psychoneuroendocrinology. 2005;30:762–770.
51. Bellezza S, Gino F, Keinan A. The red sneakers effect: Inferring status and competence from signals of nonconformity. Journal of Consumer Research. 2014;41:35–54.
52. Miyamoto Y, Yoo J, Levine CS, Park J, Boylan JM, Sims T, et al. Culture and Social Hierarchy: Self- and Other-Oriented Correlates of Socioeconomic Status across Cultures. J Pers Soc Psychol. 2018;115:427–445.
53. Kitayama S, King A, Yoon C, Tompson S, Huff S, Liberzon I. The dopamine D4 receptor gene (DRD4) moderates cultural difference in independent versus interdependent social orientation. Psychol Sci. 2014;25:1169–1177.
54. Welker KM, Norman RE, Goetz S, Moreau BJP, Kitayama S, Carré JM. Preliminary evidence that testosterone's association with aggression depends on self-construal. Horm Behav. 2017;92:117–127.
55. Wibral M, Dohmen T, Klingmüller D, Weber B, Falk A. Testosterone Administration Reduces Lying in Men. PLOS ONE. 2012;7:e46774.
56. van Honk J, Will G-J, Terburg D, Raub W, Eisenegger C, Buskens V. Effects of Testosterone Administration on Strategic Gambling in Poker Play. Sci Rep. 2016;6:18096.
57. Henderson A, Thoelen G, Nadler A, Barraza J, Nave G. Testing the influence of testosterone administration on men's honesty in a large laboratory experiment. Sci Rep. 2018;8:11556.

Supplementary Materials for:

Testosterone eliminates strategic prosocial behavior through impacting choice consistency in healthy males

Hana H. Kutlikova, Lei Zhang, Christoph Eisenegger, Jack van Honk, Claus Lamm

Data and codes can be accessed at: https://osf.io/qr4ve/

Supplementary information on the use of statistical software and functions

Statistical analysis was performed using the R statistical language [1] and the packages: lme4 [2] for construction of general linear mixed models (GLMM) and generalized linear mixed model (GzLMM); car package [3] for construction of general linear models and computation of *p*-values based on Type III Wald chi-square tests; sjPlot package [4] for post-hoc tests of significant three-way interactions including odds ratios (ORs) and 95% confidence intervals (95%CIs); yarrr [5] and ggplot2 [6] packages for construction of plots. Computational modeling was performed using Markov chain Monte Carlo with the statistical computing language Stan [7] while following the hBayesDM package [8]. Model comparison and evaluation were performed using the LOO package [9].

Supplementary analysis of hormone data

The effect of drug treatment on hormone levels

After data collection was complete, saliva samples were shipped on dry ice to Dresden LabService GmbH led by Clemens Kirschbaum, Germany. Liquid chromatography-tandem mass spectrometry was used to determine the hormonal levels. To examine the change of the hormonal levels throughout the experimental session, testosterone, cortisol, and estradiol levels were analyzed using GLMMs with the fixed factors drug treatment (testosterone/placebo), visibility (observed/private), time (baseline/1 h 50 min after drug treatment/20 min after the end of the task/60 min after the end of the task), and participant's identity as a random intercept. Due to the non-normal distribution of residuals, hormonal data were log-transformed. Baseline hormonal levels did not significantly differ across experimental groups (all *p*s > .336, see Table S1). As expected, 1h 50 min after gel administration, we observed higher testosterone levels in the testosterone group ($M_{Sample2}$ = 5014.10 pg/mL, 95%CI [3866.10, 6502.88]) compared to the placebo group ($M_{Sample2}$ = 134.30, 95%CI [103.54, 175.92]; drug treatment x time: $F(3,554.82) = 48.00$, $p < .001$, $R^2_{conditional} = .737$), a difference that remained stable until the end of the experiment (see Figure S1).

There were no effects of drug treatment on cortisol (drug treatment x time: $F(3,520.6) = 1.246$, $p = .292$) or estradiol levels (drug treatment x time: $F(3,550.79) = 1.497$, $p = .214$).

The observation condition did not significantly influence any hormonal levels (testosterone: visibility x time: $F(3,554.82) = 2.447$, $p = .063$; cortisol: visibility x time: $F(3,520.6) = 0.900$, $p = 441$; estradiol: visibility x time: $F(3,550.79) = 0.796$, $p = .496$).

Contamination of salivary samples

Out of a total of 192 baseline samples, we noted that 34 contained above-normal testosterone levels, atypical for normal young men (> 2000 pg/mL). All other baseline values were hormonally

typical. The samples with abnormally high testosterone values appeared only in the participants, who later received testosterone treatment, not in the placebo group. Previous research [10, 11] described similar abnormally high testosterone levels and attributed it to the testosterone contamination of the common surfaces (e.g., doorknobs, keyboards), excluding the option of physiological contamination. Based on their recommendation, we implemented a cleaning protocol that included the wearing of disposable sterile gloves, and cleaning of keyboards, computer mice, tables, and doorknobs with an alcohol-based solution after each session. Although these precautions successfully prevented between-session contamination, we suspect that they still did not reliably impede within-session contamination of the saliva containers. For future studies, we, therefore, recommend even stricter sanitizing protocols and more careful handling of the saliva collection tubes and boxes, before, during, and also after sample collection.

In our sample, the abnormally high values were present only in the sessions where testosterone was administered, and this notwithstanding, the testosterone group showed a reliable testosterone increase after the drug administration in comparison to the placebo group. We, therefore, decided to retain the participants with contaminated baseline samples for the behavioral analyses, except for the analysis that includes baseline testosterone levels.

The effect of salivary testosterone levels on the correct choice

To examine whether salivary testosterone levels measured in the saliva samples taken before the start of the experimental task (i.e., 2 hours after the drug administration) predicted participants' behavior, we included the mean-centered log-transformed testosterone levels as a predictor in interaction with the factors recipient and visibility to the GzLMM of the correct choice. The analysis did not reveal a main effect of testosterone levels (OR = 0.99, CI = [0.96, 1.03], p = .624) or a significant interaction effect on correct choice (recipient x drug treatment x testosterone levels : OR = 1.02, CI = [0.99, 1.05], p = .162). The absence of a significant association between salivary testosterone concentrations and behavior is in line with studies that point out that although salivary testosterone measurements are correlated with the hormone concentration in serum, they do not precisely track the availability of free serum testosterone after transdermal application [11, 12]. Thus, although the between-groups comparison of saliva testosterone provides a manipulation check of topical drug administration, for the analysis of the relationship between behavior and post-administration hormonal levels on the individual level, salivary testosterone measures may presently lack sensitivity**.**

Interaction of salivary cortisol levels with testosterone effects on the correct choice and RLDDM parameters

To examine whether cortisol levels interacted with testosterone's effect on correct choice and reinforcement learning drift diffusion model (RLDDM) parameters, we separately added baseline cortisol levels and cortisol reactivity as predictors to our main analysis. The cortisol reactivity was defined as a difference between cortisol levels detected in the saliva sample taken 20 minutes after the end of visibility manipulation and cortisol levels from the sample taken immediately before the start of the paradigm. The values were mean-centered and entered as a predictor in interaction with the other factors (recipient, drug treatment, visibility) to the GzLMM of correct choice and the GzLMMs of the RLDDM parameters with log link function (see *Materials and Methods* in the main manuscript text). The analysis revealed no significant interaction of baseline cortisol levels with testosterone effect on correct choice (recipient x drug treatment x visibility baseline cortisol: OR = 1.02, CI = [0.97, 1.07], p = .385), α^{posPE} (recipient x drug treatment x visibility baseline cortisol: B = 1.01, CI = [0.98, 1.04], p = .549), α^{negPE} (recipient x drug treatment x visibility baseline cortisol: B = 0.97, CI = [0.94, 1.00], p = .052), choice consistency (recipient x drug

treatment x visibility baseline cortisol: B = 1.00, CI = [0.99, 1.01], p = .583) or decision threshold (recipient x drug treatment x visibility baseline cortisol: OR = 1.00, CI = [1.00, 1.0], p = .902).

Similarly, the analysis revealed no significant interaction of cortisol reactivity with testosterone effect on correct choice (recipient x drug treatment x visibility x post-task cortisol: OR = 1.04, CI = [0.99, 1.09], p = .133), α^{posPE} (recipient x drug treatment x visibility x post-task cortisol: B = 1.01, CI = [0.99, 1.03], p = .454), α^{negPE} (recipient x drug treatment x visibility x post-task cortisol: B = 1.01, CI = [0.99, 1.01], p = .078), choice consistency (recipient x drug treatment x visibility x post-task cortisol: B = 1.00, CI = [1.00, 1.01], p = .249) or decision threshold (recipient x drug treatment x visibility x post-task cortisol: B = 1.00, CI = [1.00, 1.00], p = .996).

Supplementary information on computational modeling

Rescorla-Wagner (RW) model

We started with the simple Rescorla-Wagner [13] model as our baseline model. On each trial, the value ($V_{c,t}$) of the chosen option was updated with the reward prediction error (RPE):

$$V_{c,t} = V_{c,t-1} + \alpha\left(O_{t-1} - V_{c,t-1}\right), \quad (1)$$

where O_{t-1} was the received outcome, and α ($0 < \alpha < 1$) denoted the learning rate.

Dual learning rates (DLR) model.

Previous studies have reported differences in learning following positive and negative PEs [14, 15] and these differences have been linked to the distinctive roles of striatal D1 and D2 dopamine receptors in segregated cortico-striatal pathways [16]. Furthermore, analyses of genetic polymorphisms of DARPP-32 that predict choice behavior associated with a positive outcome, and the DRD2 gene predicting avoidance of choices associated with negative outcomes, support the notion that independent dopaminergic mechanisms contribute to learning from positive and negative feedback [17]. RL models with dual learning rates have been successful in capturing this asymmetric learning effect [18,19], including studies in social neuroscience examining prosocial behavior [20]. Hence, we tested a dual learning rates model on top of the RW model:

$$V_{c,t} = \begin{cases} V_{c,t-1} + \alpha^{\text{pos}}\left(O_{t-1} - V_{c,t-1}\right), \text{if } O_{t-1} > 0 \\ V_{c,t-1} + \alpha^{\text{neg}}\left(O_{t-1} - V_{c,t-1}\right), \text{otherwise} \end{cases}, \quad (2)$$

where α^{posPE} and α^{negPE} were the learning rates for positive and negative RPEs, respectively.

In both RW and DLR models, action values were converted to action probabilities using the softmax function. Let A and B be the choice symbols per trial, the probability of choosing A was computed via the difference between V(A) and V(B):

$$p(\text{A}) = \frac{1}{1 + e^{\beta(-(V_{\text{A}} - V_{\text{B}}))}},\ p(\text{B}) = 1 - p(\text{A}), \quad (3)$$

where β ($\beta > 0$) was the inverse temperature that represented choice consistency. Higher β indicated that individuals' choices were more consistent with their value computation, where lower β indicated that individuals behaved more randomly. The action probability was then used to model participants' choice data with a categorical distribution:

$$\text{choice}_t \sim categorical([p_t(\text{A}), p_t(\text{B})]) \quad (4)$$

It is worth noting that our winning model with differential learning rates for positive and negative PEs is in line with previous studies on learning and decision-making that report asymmetric learning effect [14, 15, 18, 19]. The theoretical interpretation of these differences, however, is mixed in the literature. While some studies reported enhanced learning after positive PE compared to negative and related this feature to optimism bias [21], others report a higher learning rate for negative than for positive PEs, interpreted as possibly reflecting risk aversion [14]. Our findings in this regard may contribute to this debate such that learning update is much quicker after receiving positive feedback, especially when the feedback is associated with appetitive stimuli (e.g., monetary reward). This is likely to be generalized to situations with relatively positive feedback, rather than the actual positive feedback *per se*. For instance, in aversive learning, receiving no feedback (e.g., a neutral outcome) is, on a relative scale, more positive than actual negative feedback (e.g., an electric shock). Learning rates for such no-feedback events have been shown to be higher than those for stimuli with negative feedback, including learning under social contexts [20].

Drift diffusion model (DDM)

The drift diffusion model (a.k.a., diffusion decision model [22]) was a widely used computational framework to model individuals' response times (RTs). In its canonical expression, DDM contained four parameters, namely, the drift rate (v; $v > 0$), the initial bias (z; $z > 0$), non-decision time (T; $0 < T < \min(RT)$), as well as the decision threshold (a). For simplicity in learning tasks with abstract symbols, the initial bias z was fixed at 0.5. Trial-by-trial RTs were distributed according to the Wiener first passage time (WFPT [23]):

$$RT_t \sim wfpt(a, T, z, v) \quad (5)$$

Reinforcement learning drift diffusion model (RLDDM)

In value-based decision-making, individuals' RTs may vary as the function of trial-by-trial valuation, such that the larger the value difference between choice alternatives, the faster the RT. Therefore, a joint reinforcement learning drift diffusion model (RLDDM) framework has been proposed [15,24], bridging RL and DDM. This approach provides more granularity than using RL or DDM alone [24]. In essence, the drift rate in DDM was characterized by the accuracy-coded value differences computed from the RL counterpart. This way, the drift rate was no more a constant parameter throughout the entire experiment, instead, it varied across trials (i.e., v_t, instead of v) according to the values computed from RL updates (in the present study, RW or RP). In the simplest RLDDM, trial-by-trial drift rates were constructed via a linear function of value difference:

$$v_t = v_{\text{scaling}} \left(V_{\text{correct},t} - V_{\text{incorrect},t} \right), \quad (6)$$

where v_{scaling} ($v_{\text{scaling}} > 0$) was the scaling parameter that quantified the impact of value difference. Note that we employed stimulus coding in our RLDDM, so that in Equation (6), the drift rate was always a function of the value difference between the correct (i.e., more rewarding, 75% reward probability) and the incorrect options (i.e., less rewarding, 25% reward probability), rather than between the chosen and unchosen options.

Reinforcement learning drift diffusion model with non-linear transformation (RLDDM-nonlin)

There is evidence that a non-linear mapping between value difference and the drift rate could better capture individuals' RTs as opposed to a linear transformation [24]. This is likely because

non-linear functions may provide more sensitivity, akin to the softmax function in choice models. We thus implemented an RLDDM-nonlin following:

$$v_t = S\left[v_{\text{scaling}}\left(V_{\text{correct},t} - V_{\text{incorrect},t}\right)\right], \quad (7)$$

with

$$S(x) = 2 \cdot \frac{v_{\max}}{1 + e^{-x}} - v_{\max}, \quad (8)$$

where $S(x)$ was a non-linear sigmoid function centered at 0, that convert x to lie between $-v_{\max}$ and $v_{\max}$ ($v_{\max} > 0$). It is worth noting that $v_{\max}$ only affected the maximum value of the drift rate, whereas v_{scaling}, as in Equation 6, established the trial-by-trial mapping between the value difference and the drift rate.

In both RLDDM and RLDDM-nonlin, all other DDM parameters (i.e., *a*, *T*, *z*) were identical to the canonical DDM model, and RTs were distributed with *wfpt* using trial-by-trial drift rate (v_t):

$$RT_t \sim wfpt\left(a, T, z, v_t\right). \quad (9)$$

Note that, in all candidate models (Table S3), we introduced differential parameters for the within-subject condition of our experiment, namely, all parameters were separately modeled for the "self" and the "other" conditions.

Model estimation

The model estimation and model selection procedures were largely similar to [25]. Hence, below we echoed these procedures from [25] to enhance reproducibility, with modifications that were specific to the current study.

In all models, we simultaneously modeled participants' choice and RT, separately for each between-subject condition (i.e., placebo vs. testosterone; observed vs. private). Model estimations of all candidate models were performed with hierarchical Bayesian analysis (HBA) [26] using the statistical computing language Stan [7] in R. Stan utilizes a Hamiltonian Monte Carlo (HMC; an efficient Markov Chain Monte Carlo, MCMC) sampling scheme to perform full Bayesian inference and obtain the actual posterior distribution. We performed HBA rather than maximum likelihood estimation (MLE) because HBA provides much more stable and accurate estimates than MLE [24]. Following the approach in the "hBayesDM" package [8] for using Stan in the field of reinforcement learning, we assumed, for instance, that a generic individual-level parameter φ was drawn from a group-level normal distribution, namely, $\varphi \sim$ Normal (μ_φ, σ_φ), with μ_φ and σ_φ. being the group-level mean and standard deviation, respectively. Both these group-level parameters were specified with weakly-informative priors [26]: $\mu_\varphi \sim$ Normal (0, 1) and $\sigma_\varphi \sim$ half-Cauchy (0, 1). This was to ensure that the MCMC sampler traveled over a sufficiently wide range to sample the entire parameter space. Appropriate parameter transformations were applied to double-bounded parameters (e.g., learning rate, [0, 1]) with the inverse probit function (i.e., the cumulative distribution function of the standard normal distribution), and single-bounded parameters (e.g., drift rate, (0, +∞)) with the soft-plus function (i.e., ln(1 + e^x)), respectively.

In HBA, all group-level parameters and individual-level parameters were simultaneously estimated through the Bayes' rule by incorporating behavioral data. We fit each candidate model with four independent MCMC chains using 1,000 iterations after 1,000 iterations for the initial algorithm warmup per chain, which resulted in 4,000 valid posterior samples. The convergence of MCMC chains was assessed both visually (from the trace plot) and through the Gelman-Rubin $\hat{R}$

Statistics [27]. $\hat{R}$ values of all parameters were smaller than 1.05 in the current study), which indicated adequate convergence.

Model selection and validation

For model comparison and model selection, we computed the Leave-One-Out information criterion (LOOIC) score per candidate model [28]. The LOOIC score provides the point-wise estimate (using the entire posterior distribution) of out-of-sample predictive accuracy in a fully Bayesian way, which is more reliable compared to information criteria using point-estimate (e.g., Akaike information criterion, AIC; deviance information criterion, DIC). By convention, a lower LOOIC score indicates better out-of-sample prediction accuracy of the candidate model. We selected the model with the lowest LOOIC as the winning model. We additionally performed Bayesian model averaging (BMA) with Bayesian bootstrap [29]to compute the probability of each candidate model being the best model. Conventionally, the BMA probability of 0.8 (or higher) is a decisive indication.

Moreover, given that model comparison provided merely relative performance among candidate models [28], we then tested how well our winning model's posterior prediction was able to replicate the key features of the observed data (a.k.a., posterior predictive checks, PPCs). Since we only found an effect in choice data, we performed PPCs only for choices (excluding RTs). To this end, we applied a one-step-ahead PPC [25, 30] that factored in participants' actual action and outcome sequences to generate predictions with the entire posterior MCMC samples. Specifically, we let the winning model generate choices as many times as the number of MCMC samples (i.e., 4,000 times) per trial per participant, and we analyzed the generated data the same way as we did for the observed data. We then assessed whether these analyses could reproduce the behavioral pattern in our behavioral analyses (Figure 4B, 4D in the main text).

Simulations of optimal learning rates

To better understand and interpret the magnitude of the posterior learning rates, we performed simulations with grid approximation to obtain "optimal learning rates", and then compared the estimated posterior learning rates in relation to these optimal parameters (Figure 4A, 4C in the main text). Because there were two learning rates (α^{posPE} and α^{negPE}), to reduce complexity, we fixed the inverse temperature parameter to be the corresponding group-level posterior mean in each condition. For each simulation, we took a small grid per parameter (0:0.01:1) and computed the choice accuracy across 16 trials (identical to the main experiment) for each combination of the parameters. Each simulation was repeated 1000 times to obtain stable results. We then considered the parameters that gave the highest choice accuracy as the optimal learning rates.

Analysis of the RLDDM parameters and their association with prosocial behavior

Next, we examined whether the behavioral pattern found in the analysis of the correct choice would be associated with differences in the individual model parameters.

As a first step, we tested the parameters of our validated winning model for the 3-way interaction effect of drug treatment, visibility, and type of recipient. There was no significant 3-way interaction in the learning rate for positive PE (B = 1.03, CI = [1.00, 1.06], p = .063). The analysis of the learning rate for negative PE revealed a three-way interaction of drug treatment, visibility, and type of recipient (B = 0.94, CI = [0.90, 0.98], p = .003) so that the participants in the placebo group had a relatively lower negative learning rate for prosocial choices when being watched than in privacy (recipient x visibility interaction in the placebo group: B = 0.68, CI = [0.40, 0.96], p = .023). Conversely, in the testosterone group, observation (vs privacy) relatively increased the negative learning rate for prosocial choices (recipient x visibility interaction in testosterone group: B = 1.21, CI = [1.00, 1.40], p = .048; Figure 2A). Moreover, the analysis of the choice consistency

(inverse temperature parameter tau, described also in the main text) likewise showed a three-way interaction (B = 0.98, CI = [0.97, 0.98], p < .001). Placebo group participants had relatively higher consistency in choices made for the other (vs. self) when being observed than in privacy (recipient x visibility interaction in the placebo group: B = 1.09, CI = [1.05, 1.14], p < .001). On the contrary, in the testosterone group, observation, compared to privacy, decreased the consistency of choices made for the other (vs. self) (recipient x visibility interaction in testosterone group: B = 0.90, CI = [0.84, 0.98], p < .001). When participants were observed, testosterone, compared to placebo, diminished the relative consistency of prosocial choices (recipient x treatment interaction in observed condition: OR = 0.91, CI = [0.84, 0.99], p =.025). In the private condition, there was no evidence for such an effect (recipient x treatment interaction in private condition: OR = 0.99, CI = [0.97, 1.02], p = .605).
The analysis of the DDM threshold parameter revealed a three-way interaction as well (B= 1.01, CI = [1.00, 1.02], p < .001; Figure 2C). Placebo group participants had a relatively higher threshold for choices made for another (vs. self) when being observed than in privacy (recipient x visibility interaction in the placebo group: B = 1.03, CI = [1.01, 1.05], p < .001). Conversely, in the testosterone group, observation, compared to privacy, decreased the amount of information required for choices made for another (vs. self) (recipient x visibility interaction in testosterone group: B = 0.95, CI = [0.93, 0.97], p < .001). When participants were observed, testosterone, compared to placebo, decreased the relative threshold of prosocial choices (recipient x treatment interaction in observed condition: B = 0.95, CI = [0.93, 0.97], p < . 001). The analysis of the DDM drift-scaling parameter revealed a three-way interaction (B = 1.01, CI = [1.00, 1.02], p < .001). Participants in both placebo (recipient x visibility interaction in placebo group B = 0.93, CI = [0.91, 0.95], p < .001) and testosterone group (recipient x visibility interaction in placebo group B = 0.73, CI = [0.51, 0.95], p < .001) showed relatively lower drift scaling for choices made for another (vs. self) when being observed than in privacy. When participants were observed, testosterone, compared to placebo, decreased the relative drift scaling of prosocial choices (recipient x treatment interaction in the observed group: B = 0.91, CI = [0.90, 0.92], p < .001).

As a second step, we examined whether the RLDDM parameters that were impacted by testosterone administration predict behavioral prosociality, measured by the difference between correct choices made for other and self across the whole sample. Out of the five parameters, choice consistency (B = 3.82, CI = [2.64, 5.01], p < .001), and DDM threshold (B = 10.67, CI = [1.57, 19.76], p = .022) predicted prosociality, however, only choice consistency survived the Bonferroni correction for multiple comparisons (p <.01). Altogether, as reported in the main text, these results suggest that testosterone's impact on strategic prosocial behavior (i.e., audience effect) is strongly linked to testosterone's effect on choice consistency (inverse temperature parameter tau).

Analysis of the drift-scaling parameter and response times

As specified in equation (7), on each trial t, the drift rate v_t was defined with a drift-scaling parameter, v_{scaling} that scales the value difference between the correct and incorrect symbol. Drift-scaling parameter affects the curvature of the function: smaller values lead to a more linear mapping between the value difference and the drift rate, and therefore less sensitivity to value differences.
Drift scaling is conceptually linked to the speed of integration and response times [22], we, therefore, tested whether drift-scaling parameter predicted response times and found a significant association (B = 0.97, CI = [0.95, 0.98], p < .001). However, contrary to correct choices, response times did not differ across experimental groups (drug treatment: B = 1.01, CI = [0.97, 1.05], p = .737; visibility: B = 0.98, CI = [0.94, 1.02], p < .265; recipient: B = 0.99, CI = [0.99, 1.00], p < .106; drug treatment x visibility x recipient: B = 1.00, CI = [0.99, 1.01], p < .806).

Supplementary information on the analysis of genetic data

Previous research suggested that testosterone may influence behavior through dopaminergic pathway [31]. In humans, testosterone administration enhanced activation of the ventral striatum to monetary rewards [32] and the enhancing effects of exogenous testosterone on competitive status-seeking were more pronounced among individuals with a 9/10R compared to 10/10R genotype of the dopamine transporter (DAT) [33]. The expression of DAT, which regulates striatal dopamine, is linked to a 40 base-pair variable number tandem repeat polymorphism of the DAT1 gene [34]. Homozygous 10/10-repeat carriers of this polymorphism have higher DAT expression (i.e., lower striatal dopamine) than heterozygous, 9-repeat variant, individuals [34].

Testosterone's effects on status-seeking behavior have likewise been shown to be enhanced among individuals with fewer CAG repeats in exon 1 of the androgen-receptor gene [33,36]. In-vitro experimental work suggests that increasing the number of CAG repeats within the androgen receptor (AR) gene reduces the receptor's transcriptional potential [37]. In other words, the efficiency of the androgen receptors is negatively related to the CAG repeat [38].
We, therefore, tested whether testosterone's effects on strategic prosociality depended on individual differences in striatal dopamine, assessed by DAT1 polymorphism, and the efficiency of ARs, assessed by the CAG repeat polymorphism.

Genotyping of AR CAG repeat and DAT1 polymorphisms
DNA was extracted from buccal swabs and isolated using a resin-based method with Chelex®100 (Sigma Aldrich, USA). For amplification of the CAG repeat polymorphism in exon 1 of the AR gene primers forward - 5' GCGCGAAGTGATCCAGAAC 3' tagged with 6–carboxyfluorescein and reverse - 5' CTCATCCAGGACCAGGTAGC 3', and for amplification of the DAT1-3'UTR VNTR polymorphism primers forward - 5' GTCCTTGTGGTGTAGGGAAC 3' tagged with 6–carboxyfluorescein and reverse - 5' CTGGAGGTCACGGCTCAAG 3' were used in PCR with 20 µL reaction using 250 nmol/L final primer molarity. As PCR masterrmix 5x Hot FIREPol Blend Mastermix with 7.5 mM MgCl2 (Solis Biodyne, Tartu, Estonia) was used in all amplifications.

The following PCR program was used: initial denaturation step at 95°C for 15 min, followed by 30 cycles each consisting of denaturation at 95°C for 30 s, annealing at 60°C for 30 s and polymerization at 72°C for 1 min. The number of repeats of AR CAG STR and DAT1-3'UTR VNTR was analyzed by fragment analysis using Sanger sequencing on ABI 3500 Genetic Analyzer (Applied Biosystems, USA).

Interaction of DAT1 polymorphism with testosterone effects on the correct choice and RLDDM parameters
There were no significant differences in the distribution of the genotype among our experimental groups (χ^2 (6, N = 190) = 5.76 p = .451). The 9/10R and the 10/10R genotypes accounted for most of the observed DAT1 genotypes in our sample (36% (N=68) and 56% (N=105), respectively), and we thus used these two genotypes in the analyses by adding DAT1 polymorphisms as a predictor in interaction with the other factors (recipient, drug treatment, visibility) to the GzLMM of correct choice and the GzLMMs of the RLDDM parameters (see *Materials and Methods* in the main manuscript text). The analysis revealed no significant interaction of DAT1 polymorphism with testosterone effect on correct choice (recipient x drug treatment x visibility x DAT1: OR = 1.08, CI = [0.95, 1.23], p = .258), α^{posPE} (recipient x drug treatment x visibility x DAT1: B = 0.98, CI = [0.92, 1.05], p = .578), α^{negPE} (recipient x drug treatment x visibility x DAT1: B = 1.07, CI = [0.98, 1.17], p = .141), choice consistency (recipient x drug treatment x visibility x DAT1: B = 1.01, CI = [1.00, 1.02], p = .091) or decision threshold (recipient x drug treatment x visibility x DAT1: B = 1.00, CI = [1.00, 1.00], p = .986).

Interaction of AR CAG repeat polymorphism with testosterone effects on the correct choice and RLDDM parameters

Mean-centered CAG repeat lengths of the AR gene in exon 1 were included as a predictor in interaction with the other factors (recipient, drug treatment, visibility) to the GzLMM of correct choice and the GzLMMs of the RLDDM parameters (see *Materials and Methods* in the main text). The analysis revealed no significant interaction of CAG repeat polymorphism with testosterone effect on correct choice (recipient x drug treatment x visibility x CAG: *OR* = 1.00, *CI* = [0.99, 1.02], *p* = .599), α^{posPE} (recipient x drug treatment x visibility x CAG: *B* = 1.00, *CI* = [1.00, 1.01], *p* = .363), αneg^{PE} (recipient x drug treatment x visibility x CAG: *B* = 1.01, *CI* = [0.99, 1.01], *p* = .243), choice consistency (recipient x drug treatment x visibility x CAG: *B* = 1.00, *CI* = [0.99, 1.01], *p* = .576) or decision threshold (recipient x drug treatment x visibility x CAG: *B* = 1.00, *CI* = [1.00, 1.00], *p* = .103).

Interaction of trait dominance with testosterone effects on RLDDM parameters

Mean-centered dominance scores [39] were included as a predictor in interaction with the other factors (recipient, drug treatment, visibility) to the GzLMM of correct choice (reported in the main text) and the GzLMMs of the RLDDM parameters. Contrary to the former, the latter analysis revealed no significant interaction of dominance scores with testosterone effect RLDDM parameters: learning rate for positive PE (recipient x drug treatment x visibility x dominance: *B* = 1.01, *CI* = [0.97, 1.04], *p* = .743), learning rate for negative PE (recipient x drug treatment x visibility x dominance: *B* = 1.02, *CI* = [0.98, 1.07], *p* = .331), choice consistency (recipient x drug treatment x visibility x dominance: *B* = 1.00, *CI* = [0.99, 1.02], *p* = .644), or decision threshold (recipient x drug treatment x visibility x dominance: *B* = 1.00, *CI* = [1.00, 1.00], *p* = .578).

Supplementary information on the questionnaire data

Post-task questionnaire

To estimate the subjective perception of being watched, a post-task questionnaire was administered immediately after the end of the reinforcement-learning paradigm. The participants were asked the question: “Did you feel that you were being watched while performing the task?” The answers were classified into three categories: 1 (Not at all), 2 (Moderately), and 3 (Strongly). First, we investigated whether the subjective feelings of being watched were related to the cortisol reactivity to visibility manipulation (see *Manipulation check* in the manuscript's main text). We next examined whether the subjective feelings of being watched interact with the testosterone administration effect on prosocial choice and RLDDM parameters. As the factors *visibility* and *subjective feeling of being watched* are not orthogonal, we did not add the subjective feelings of being watched as a fourth factor to the analysis. Instead, we replaced the factor *visibility* with the factors *subjective feeling of being watched* and compared whether such a model explains more variance than the original one. We did not find a significant interaction of the factors administration x recipient x subjective feeling of being watched (*OR* = 0.89, *CI* = [0.79, 1.01], *p* = .133). This model did not explain more variance (*Conditional R2*=.102) than the original administration x recipient x visibility model (*Conditional R2*=.103).

Portrait Values Questionnaire

We conducted exploratory analyses to examine what motivational constructs may have interacted with testosterone’s effects. To this end, we analyzed data from the Portrait Values Questionnaire [40, 41] which had been administered as part of the study’s extensive questionnaire battery. Note that these are exploratory analyses and that this specific questionnaire was originally intended to be used for analyses related to other tasks that were part of the overall study. They should therefore be considered with caution, and we have clearly labeled them as exploratory and post-

hoc. In brief, the Portrait Values Questionnaire is designed to capture the structure of human values explaining the motivational bases of our attitudes and behavior. The questionnaire allowed us to distinguish four principal value orientations: self-transcendence, self-enhancement, conservation, and openness. The four value subscales were separately added to our analysis of recipient x administration x visibility interaction as mean-centered interaction terms. This revealed a significant interaction of *self-enhancement value orientation* with testosterone's effect on the number of correct choices (recipient x visibility x administration x self-enhancement*: OR* = 0.65, *CI* = [0.48, 0.88], *p* = .006) and interaction of *conservation value orientation* and testosterone's effects on choice consistency (recipient x visibility x administration x conservation: *B* = 0.60, *CI* = [0.17, 1.02], *p* = .006). The follow-up analyses of these significant interactions are reported in the main manuscript text.

Self-enhancement value did not significantly interact with testosterone effects on choice consistency (recipient x drug treatment x visibility x self-enhancement: *B* = -0.01, *CI* = [-0.06, 0.04], *p* = .633).

Conservation did not significantly interact with testosterone effects on correct choice (recipient x drug treatment x visibility x conservation: *OR* = 0.98, *CI* = [0.94, 1.02], *p* = .287). Self-transcendence did not significantly interact with testosterone effects on correct choice (recipient x drug treatment x visibility x self-transcendence: *OR* = 0.97, *CI* = [0.91, 1.03], *p* = .319) or choice consistency (recipient x drug treatment x visibility x self-transcendence: *B* = 0.33, *CI* = [-0.34, 1.00], *p* = .337). Lastly, openness value did not significantly interact with testosterone effects on correct choice (recipient x drug treatment x visibility x openness: *OR* = 1.02, *CI* = [0.98, 1.07], *p* = .328) or choice consistency (recipient x drug treatment x visibility x openness: *B* =-0.01, *CI* = [-0.07, 0.04], *p* = .646).

Observers' salience survey

To estimate the salience of the observers introduced as NGO representatives in our paradigm, we conducted an additional online survey. Using Amazon Mechanical Turk (MTruk) we interviewed N = 73 volunteers (sample size determined by G*Power [42] to achieve 95 % power to detect a small effect size *f* = .20) aged *M* = 34.55 (*SD* = 9.12) years. Participants were asked to perform the task alone and rate how much they agree with the statements regarding different types of observers. Together they rated 7 statements with the following wording, and each statement concerned a different type of observer:

> "As I perform this task on my computer/mobile device alone, I anticipate I would feel differently if …… would watch me perform this task."

The observer's types were: an unknown other, a friend, a parent, a shop assistant, an NGO representative, a colleague from work, and a technical support worker. A repeated-measures ANOVA comparing the ratings of the respective observers showed that there was a difference across the levels of the within-subject factor *F*(6, 396) = 2.69, *p* = .014, *f* =.204. A follow-up analysis using treatment contrasts and the NGO as a reference level showed a significant difference between the levels of NGO representative and parent (*B* = -0.57, *p* < 0.001), meaning that participants would feel different to a greater extent if they were watched by an NGO representative than a parent. Crucially, no other pairwise comparisons were significant, all *p*s >.169).

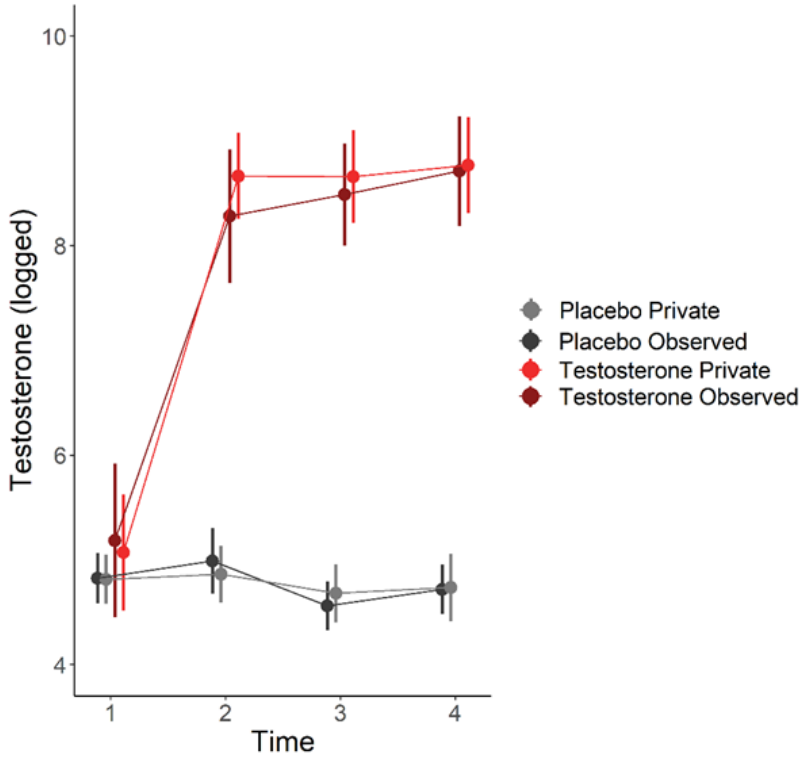


Figure S1. Testosterone levels during the experimental session. Error bars = Mean ± 95%CI.

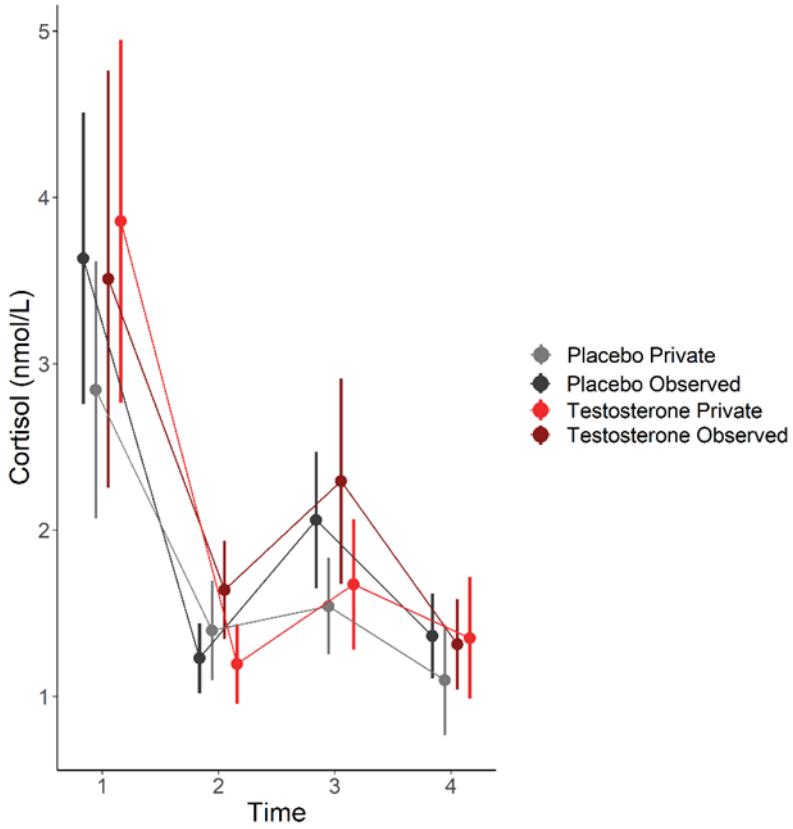


Figure S2. Cortisol levels during the experimental session. Error bars = Mean ± 95%CI.

Table S1. Summary statistics across experimental groups: Mean (95%CI), ANOVA.

Drug treatment	**Placebo**		**Testosterone**			
Visibility	**Private**	**Observed**	**Private**	**Observed**	**F**	**p**
N	47	45	53	45		
Age	25.4 (24.5, 26.3)	24.5 (23.3, 25.7)	24.0 (23.1, 24.9)	25.1 (24.0, 26.2)	1.140	.239
Baseline testosterone [pg/mL]	143 (76.7, 209)	142 (74.9, 209)	225 (153.5, 296)	268 (180.9, 354)		
log	4.75 (4.52, 4.98)	4.76 (4.53, 5.00)	4.94 (4.69, 5.19)	4.99 (4.69, 5.30)	0.024	.877
Baseline cortisol [nmol/L]	2.84 (1.81, 3.87)	3.67 (2.64, 4.71)	3.89 (2.93, 4.86)	3.56 (2.52, 4.61)		
log	0.77 (0.52, 1.02)	0.98 (0.73, 1.24)	0.90 (0.65, 1.12)	0.86 (0.60, 1.11)	0.930	.336
Baseline estradiol [pg/mL]	3.68 (3.12, 4.23)	3.76 (3.20, 4.31)	3.71 (3.19, 4.22)	3.75 (3.19, 4.31)		
log	1.23 (1.09, 1.36)	1.20 (1.06, 1.33)	1.19 (1.07, 1.32)	1.23 (1.09, 1.36)	0.194	.660
CAG-repeat polymorphism	19.7 (18.7, 20.7)	19.8 (18.8, 20.8)	19.3 (18.4, 20.3)	19.3 (18.4, 20.5)	0.001	.999
Dominance	3.90 (3.63, 4.17)	4.02 (3.74, 4.30)	4.04 (3.78, 4.30)	3.82 (3.55, 4.10)	1.526	.218

Table S2. Descriptive statistics of cortisol levels during the experiment.

Drug treatment	**Placebo**						**Testosterone**					
Visibility	**Private**			**Observed**			**Private**			**Observed**		
	Mean (CI)	**Min**	**Max**	**Mean (CI)**	**Min**	**Max**	**Mean (CI)**	**Min**	**Max**	**Mean (CI)**	**Min**	**Max**
Time 1	2.84 (1.81, 3.87)	0.64	15.34	3.67 (2.64, 4.71)	0.37	12.87	3.89 (2.93, 4.86)	0.23	18.59	3.56 (2.52, 4.61)	0.44	23.80
Time 2	1.39 (1.13, 1.66)	0.34	5.14	1.22 (0.96, 1.49)	0.22	3.55	1.19 (0.95, 1.45)	0.17	4.40	1.63 (1.33, 1.93)	0.29	3.98
Time 3	1.54 (1.11, 1.98)	0.38	3.94	2.05 (1.62, 2.50)	0.51	6.49	1.67 (1.27, 2.08)	0.28	9.12	2.29 (1.85, 2.74)	0.30	11.62
Time 4	1.09 (0.78, 1.42)	0.21	5.73	1.36 (1.05, 1.67)	0.47	4.86	1.31 (1.06, 1.64)	0.15	6.57	1.35 (0.99, 1.63)	0.15	3.77

Table S3. Model space and model evidence.

RW, Rescorla-Wagner model; DLR dual learning rates model; DDM, drift diffusion model; RLDDM, reinforcement learning drift diffusion model; RLDDM-nonlinear, RLDDM with a non-linear transformation function; LOOIC leave-one-out information criterion (lower LOOIC value indicates better out-of-sample predictive accuracy); weight, model weight calculated with Bayesian model averaging using Bayesian bootstrap (higher model weight value indicates a higher probability of the candidate model to have generated the observed data). The winning model is highlighted in bold. Because LOOIC provides relative quantifications of model performance, and the data to be modeled varied across conditions, the absolute magnitude of LOOIC should not be interpreted.

Model space		Placebo Observed		Placebo Private		Testosterone observed		Testosterone Private	
		LOOIC	Weight	LOOIC	Weight	LOOIC	Weight	LOOIC	Weight
RW	DDM	9688	0	10939	0	10202	0	12716	0
	RLDDM	8365	0	9747	0	9135	0	11450	0
	RLDDM-nonlinear	8235	0	9611	0	8984	0	11184	0
DLR	DDM	9538	0	10709	0	10018	0	12487	0
	RLDDM	7877	0.004	9081	0.3	8643	0.002	10688	0
	RLDDM-nonlinear	**7832**	**0.996**	**9040**	**0.97**	**8352**	**0.998**	**10516**	**1**

Table S4. Summary of parameters in the winning model.

Note that all parameters were further separated for "self" versus "other", hence for each between-subject condition, the winning model contained 14 parameters. The initial bias *z* in DDM was fixed at 0.5. min (RT), lowest response time from observed data.

Component	Parameter	Meaning	Interpretation
RL	$0 < \alpha^{posPE} < 1$	learning rate for updating from positive reward prediction error	the learning rate weighs the effect of the reward prediction error in the value update; a higher (lower) learning rate means a faster (slower) value update from the most recent outcome
	$0 < \alpha^{negPE} < 1$	learning rate for updating from negative reward prediction error	
	$\beta > 0$	inverse temperature in softmax action selection function	choice consistency parameter, captures how much choices rely on the value updates
DDM	$v_{max} > 0$	maximum value of the drift rate in the non-linear function	defines the upper/lower boundaries in the sigmoid non-linear function
	$v_{scaling} > 0$	drift scaling that maps value difference into the drift rate	scales the effect of value difference between the choice options on the drift rate
	$a > 0$	decision threshold, i.e., the distance between choice alternatives	"the endpoint" of the evidence accumulation process, captures the amount of information necessary to make a decision
	$0 < T <$ min(RT)	non-decision time	considered to capture sensory delay and/or movement initiation

SM References

1. R Core Team. R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing; 2020.
2. Bates D, Mächler M, Bolker B, Walker S. Fitting Linear Mixed-Effects Models Using lme4. Journal of Statistical Software. 2015;67:1–48.
3. Fox J, Weisberg S. An R Companion to Applied Regression. Third. Thousand Oaks CA: Sage; 2019.
4. Lüdecke D. sjPlot: Data Visualization for Statistics in Social Science. 2020.
5. Phillips N. yarrr: A Companion to the e-Book 'YaRrr!: The Pirate's Guide to R'. 2017.
6. Wickham H. ggplot2: Elegant Graphics for Data Analysis. Springer-Verlag New York; 2016.
7. Carpenter B, Gelman A, Hoffman MD, Lee D, Goodrich B, Betancourt M, et al. Stan: A Probabilistic Programming Language. Journal of Statistical Software. 2017;76:1–32.
8. Ahn W-Y, Haines N, Zhang L. Revealing Neurocomputational Mechanisms of Reinforcement Learning and Decision-Making With the hBayesDM Package. Comput Psychiatr. 2017;1:24–57.
9. Vehtari A, Gelman A, Gabry J. Practical Bayesian model evaluation using leave-one-out cross-validation and WAIC. ArXiv:150704544 [Stat]. 2016. 12 September 2016. https://doi.org/10.1007/s11222-016-9696-4.
10. Knight EL, McShane BB, Kutlikova HH, Morales PJ, Christian CB, Harbaugh WT, et al. Weak and Variable Effects of Exogenous Testosterone on Cognitive Reflection Test Performance in Three Experiments: Commentary on Nave, Nadler, Zava, and Camerer (2017). Psychol Sci. 2020;31:890–897.
11. Nave G, Nadler A, Zava D, Camerer C. Single-Dose Testosterone Administration Impairs Cognitive Reflection in Men. Psychol Sci. 2017;28:1398–1407.
12. Wang C, Plymate S, Nieschlag E, Paulsen CA. Salivary testosterone in men: further evidence of a direct correlation with free serum testosterone. J Clin Endocrinol Metab. 1981;53:1021–1024.
13. R. A. Rescorla, A. R. Wagner, "A theory of Pavlovian conditioning: Variations in the effectiveness of reinforcement and nonreinforcement" in *Classical Conditioning II: Current Research and Theory*, (Appleton-Century-Crofts, 1972), pp. 64–99.
14. Gershman SJ. Do learning rates adapt to the distribution of rewards? Psychon Bull Rev. 2015;22:1320–1327.
15. Pedersen ML, Frank MJ, Biele G. The drift diffusion model as the choice rule in reinforcement learning. Psychon Bull Rev. 2017;24:1234–1251.
16. Cox SML, Frank MJ, Larcher K, Fellows LK, Clark CA, Leyton M, et al. Striatal D1 and D2 signaling differentially predict learning from positive and negative outcomes. Neuroimage. 2015;109:95–101.
17. Frank MJ, Moustafa AA, Haughey HM, Curran T, Hutchison KE. Genetic triple dissociation reveals multiple roles for dopamine in reinforcement learning. Proc Natl Acad Sci U S A. 2007;104:16311–16316.
18. den Ouden HEM, Daw ND, Fernandez G, Elshout JA, Rijpkema M, Hoogman M, et al. Dissociable effects of dopamine and serotonin on reversal learning. Neuron. 2013;80:1090–1100.
19. Crawley D, Zhang L, Jones EJH, Ahmad J, Oakley B, Cáceres ASJ, et al. Modeling flexible behavior in childhood to adulthood shows age-dependent learning mechanisms and less optimal learning in autism in each age group. PLOS Biology. 2020;18:e3000908.
20. Lengersdorff LL, Wagner IC, Lockwood PL, Lamm C. When Implicit Prosociality Trumps Selfishness: The Neural Valuation System Underpins More Optimal Choices When Learning to Avoid Harm to Others Than to Oneself. J Neurosci. 2020;40:7286–7299.
21. Lefebvre G, Lebreton M, Meyniel F, Bourgeois-Gironde S, Palminteri S. Behavioural and neural characterization of optimistic reinforcement learning. Nat Hum Behav. 2017;1:1–9.
22. Ratcliff R, McKoon G. The Diffusion Decision Model: Theory and Data for Two-Choice Decision Tasks. Neural Comput. 2008;20:873–922.

23. Navarro DJ, Fuss IG. Fast and accurate calculations for first-passage times in Wiener diffusion models. Journal of Mathematical Psychology. 2009;53:222–230.
24. Fontanesi L, Gluth S, Spektor MS, Rieskamp J. A reinforcement learning diffusion decision model for value-based decisions. Psychon Bull Rev. 2019;26:1099–1121.
25. Zhang L, Gläscher J. A brain network supporting social influences in human decision-making. Science Advances. 2020;6:eabb4159.
26. Gelman A, Carlin JB, Stern HS, Dunson DB, Vehtari A, Rubin DB. Bayesian Data Analysis. 3rd ed. New York: Chapman and Hall/CRC; 2015.
27. Gelman A, Rubin DB. Inference from Iterative Simulation Using Multiple Sequences. Statistical Science. 1992;7:457–472.
28. Vehtari A, Gelman A, Gabry J. Practical Bayesian model evaluation using leave-one-out cross-validation and WAIC. ArXiv:150704544 [Stat]. 2016. 12 September 2016. https://doi.org/10.1007/s11222-016-9696-4.
29. Yao Y, Vehtari A, Simpson D, Gelman A. Using Stacking to Average Bayesian Predictive Distributions (with Discussion). Bayesian Analysis. 2018;13:917–1007.
30. Zhang L, Lengersdorff L, Mikus N, Gläscher J, Lamm C. Using reinforcement learning models in social neuroscience: frameworks, pitfalls and suggestions of best practices. Social Cognitive and Affective Neuroscience. 2020;15:695–707.
31. Purves-Tyson TD, Owens SJ, Double KL, Desai R, Handelsman DJ, Weickert CS. Testosterone Induces Molecular Changes in Dopamine Signaling Pathway Molecules in the Adolescent Male Rat Nigrostriatal Pathway. PLoS One. 2014;9:e91151.
32. Hermans EJ, Bos PA, Ossewaarde L, Ramsey NF, Fernández G, van Honk J. Effects of exogenous testosterone on the ventral striatal BOLD response during reward anticipation in healthy women. Neuroimage. 2010;52:277–283.
33. Losecaat Vermeer AB, Krol I, Gausterer C, Wagner B, Eisenegger C, Lamm C. Exogenous testosterone increases status-seeking motivation in men with unstable low social status. Psychoneuroendocrinology. 2020;113:104552.
34. Vandenbergh DJ, Persico AM, Hawkins AL, Griffin CA, Li X, Jabs EW, et al. Human dopamine transporter gene (DAT1) maps to chromosome 5p15.3 and displays a VNTR. Genomics. 1992;14:1104–1106.
35. Heinz A, Goldman D, Jones DW, Palmour R, Hommer D, Gorey JG, et al. Genotype Influences In Vivo Dopamine Transporter Availability in Human Striatum. Neuropsychopharmacol. 2000;22:133–139.
36. Geniole SN, Procyshyn TL, Marley N, Ortiz TL, Bird BM, Marcellus AL, et al. Using a Psychopharmacogenetic Approach To Identify the Pathways Through Which—and the People for Whom—Testosterone Promotes Aggression. Psychol Sci. 2019;30:481–494.
37. Chamberlain NL, Driver ED, Miesfeld RL. The length and location of CAG trinucleotide repeats in the androgen receptor N-terminal domain affect transactivation function. Nucleic Acids Res. 1994;22:3181–3186.
38. Zitzmann M, Nieschlag E. The CAG repeat polymorphism within the androgen receptor gene and maleness. Int J Androl. 2003;26:76–83.
39. Cheng JT, Tracy JL, Henrich J. Pride, personality, and the evolutionary foundations of human social status. Evolution and Human Behavior. 2010;31:334–347.
40. Schwartz SH. Chapter 7 A Proposal for Measuring Value Orientations across Nations 2007.
41. Schwartz, SH, Breyer, B, & Danner, D. Human Values Scale (ESS). Zusammenstellung sozialwissenschaftlicher Items und Skalen (ZIS) 2015.
42. Faul F, Erdfelder E, Lang A-G, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods. 2007;39:175–191.

Exploratory analysis of estradiol levels

The post-hoc exploratory analyses reported here were conducted after the publication of the above article, in order to examine whether the salivary levels of the hormone estradiol explained more variance than the drug administration factor (see also General Discussion).

The analysis of the change in the estradiol levels across the duration od the experiment did not show a significant interaction between the factors drug administration and time ($F(3,534.96) = 0.70$, $p = .551$).

Contrary to the drug administration factor (original model, see Methods), including the difference in estradiol levels (before task - baseline) in the GzLMM of correct choice did not reveal a significant interaction with the recipient and visibility condition *(OR* = 0.89, CI = [0.77 – 1.03], $p = .598$), nor main effects of estradiol on correct choice (*OR* = 0.99, CI = [0.89 – 1.11], $p = .901$). The original model had lower AIC and BIC values, and log-likelihood value closer to 0. A chi-squared test for model comparison yielded a non-significant result ($\chi 2(1) = 2.739$, $p > .05$), indicating that there was no significant difference in model fit between the original model and the model including the predictor estradiol levels instead of drug administration group.

Chapter 4

STUDY 3:
NOT GIVING UP: TESTOSTERONE PROMOTES PERSISTENCE AGAINST A STRONGER OPPONENT

Original manuscript as published in Psychoneuroendocrinology, doi: 10.1016/j.psyneuen.2021.105214

Hana H. Kutlikova[a,b*], Shawn N. Geniole[a,c], Christoph Eisenegger[a,†], Claus Lamm[a,d] , Gerhard Jocham[e], Bettina Studer[f,g]

[a] Neuropsychopharmacology and Biopsychology Unit, Department of Cognition, Emotion, and Methods in Psychology, Faculty of Psychology, University of Vienna, Liebiggasse 5, 1010 Vienna, Austria

[b] Department of Behavioural Neuroscience, Institute of Normal and Pathological Physiology, Centre of Experimental Medicine, Slovak Academy of Sciences, Sienkiewiczova 1, 813 71 Bratislava, Slovakia

[c] Department of Psychology, University of the Fraser Valley, 33844 King Road, Abbotsford, Canada, V2S 7M8

[d] Vienna Cognitive Science Hub, University of Vienna, Liebiggasse 5, 1010 Vienna, Austria

[e] Biological Psychology of Decision Making, Institute of Experimental Psychology, Heinrich Heine University Düsseldorf, Düsseldorf, Germany

[f] Institute of Clinical Neuroscience and Medical Psychology, Medical Faculty, University of Düsseldorf, Universitätsstraße 1, 140225, Düsseldorf, Germany

[g] Mauritius Hospital Meerbusch, Strümper Straße 111, 40670 Meerbusch, Germany

[†] deceased on the 27th of February 2017

*Corresponding author: Hana H. Kutlikova, Liebiggasse 5, University of Vienna, Vienna 1010, Austria, hana.kutlikova@univie.ac.at.

Abstract

Recent research suggests that when we lack a sense of control, we are prone to motivational failures and early quitting in competitions. Testosterone, on the other hand, is thought to boost competitiveness. Here we investigate the interaction between these factors, testing the testosterone's potential to enhance persistence in a competition against a stronger opponent, depending on experimentally manipulated perceived control. Healthy participants were administered a single dose of testosterone or placebo. They first underwent a task designed to either induce low or high perceived control and then entered a costly competition against a progressively stronger opponent that they could quit at any time. In the placebo group, men with low perceived control quitted twice as early as those with high perceived control. Testosterone countered this effect, making individuals with low control persist in the competition for as long as those with high perceived control, and did so also despite raising participants' explicit awareness of the opponents' advantage. This psychoendocrinological effect was not modulated by basal cortisol levels, CAG repeat polymorphism of the androgen receptor gene, or trait dominance. Our results provide the first causal evidence that testosterone promotes competitive persistence in humans and demonstrate that this effect depends on the psychological state elicited prior to the competition, broadening our understanding of the complex relationships between testosterone and social behaviors.

Keywords: testosterone, persistence, illusory control, motivation, competence

Introduction

Competition is an important feature of society and beating a competitor is a powerful motivator (e.g., Le Bouc and Pessiglione, 2013; Studer et al., 2016; Vansteenkiste and Deci, 2003). But what makes us persist when opponents outperform us? Theoretical and empirical research identifies perceived personal control as one deciding factor of motivation in challenging situations (Ryan and Deci, 2000). Perceived personal control is defined as the belief in the ability to influence one's environment (Rotter, 1966; Tobias-Webb, et al., 2017), and is thought to enhance motivation by increasing our perceived competence (Deci and Ryan, 2000), expectations of performing well (Wulf et al., 2014) and of achieving a wanted outcome (Bandura and Locke, 2003; Eccles and Wigfield, 2002; Lawler and Porter, 1967; Thompson et al., 2007). Consistent with this, high control- and competence-related beliefs have been linked to enhanced competitive behavior, such as participation in sports, math tournaments (Niederle and Vesterlund, 2007), or gambling (Lim et al., 2014). Importantly, perceived control is not a mere reflection of objective control. Previous empirical research has shown that it is possible to induce a high level of perceived control — even when objective control is null — by manipulating factors such as choice, frequency of reinforcement, outcome sequences, the need to avoid aversive outcomes, and involvement (Langer, 1975; see meta-analysis by Stefan and David, 2013). In the context of gambling, where odds are against the player, such induced "illusory control" enhances wish to continue gambling (Clark et al., 2014) as well as actual playing (Côté, et al., 2003). Moreover, recent laboratory research revealed that experimentally induced illusory control influences subsequent neural responses to self-generated stimuli (Seidel et al., 2021), and boosts persistence under diminishing returns (Studer et al., 2020). These findings indicate that perceptions of high control could make us persist in competitions, even against stronger opponents.

A separate line of research suggests a critical role of the hormone testosterone in driving competition behavior. In nonhuman animals, testosterone injections increase persistence with food searching and social investigation (Thor, 1980). In men, basal testosterone levels were linked to a preference for entering a competition (Eisenegger et al., 2013, but see Apicella et al., 2011; Carré and McCormick, 2008). Furthermore, competition-induced changes in testosterone concentrations have been found to correlate with physical competitive performance (Casto et al., 2020), as well as one-time willingness to compete again, particularly when the first competition had resulted in a loss (Mehta and Josephs, 2006) or an ambiguous outcome (Carré and McCormick, 2008). Together, these correlational studies suggest that basal levels and competition-induced release of testosterone may promote efforts to regain or solidify social status (Geniole and Carré, 2018; see also Losecaat Vermeer et al., 2020). No studies to date, however, have examined the hormone's causal effects on persistence in an ongoing

competition over more than one round and — most relevant — whether and how such effects interact with those of perceived control.

We investigated the effect of testosterone administration (single dose, 150 mg) on persistence in a rigged social competition in which the opponent became progressively stronger than the participant. To test whether testosterone's impact on competition persistence is dependent on an individual's perceived personal control, we experimentally manipulated participants' perceived control prior to them entering the competition. In each round of the competition, both the participant and their opponent tried to illuminate a light bulb presented on their screen by pressing one of two response buttons. Participants had to pay a non-recoverable entry fee for each competition round and, critically, could quit the competition whenever they wanted (and keep any remaining funds). Unbeknownst to participants, neither light bulb illumination nor competition outcomes were contingent on their selected responses; instead, the light bulb illuminations were rigged in such a way that the opponent became progressively stronger. We hypothesized that, compared to placebo, testosterone administration would enhance persistence in this rigged, disadvantageous competition.

Method

Participants

The sample consisted of 88 healthy men aged between 18 and 40 years (M = 25.2, SD = 3.7). Participants were recruited via flyers placed around university campuses and online advertisements and screened by an online questionnaire and a telephone interview. The exclusion criteria comprised a history of neurological or psychiatric disorders, endocrine, cardiovascular, or other internal diseases, obesity, substance dependence, and the use of steroids. Only male participants were included because testosterone metabolism is subject to sex differences and because the pharmacokinetics of topical administration of testosterone are unknown in women (Eisenegger et al., 2013).

The sample size was determined based on previous testosterone administration studies available at the time of designing the experiment (Buskens et al., 2016; Mehta et al., 2015b; van Honk et al., 2016) and our own prior work on persistence-enhancing effects of illusory control (Studer et al., 2020). We inferred that for relevance in clinical and nonclinical applications, between-condition differences in persistence would have to be of moderate to large size. Our sample size and design allow detecting effects of size $f^2 \geq .14$.

Procedure and double-blind testosterone administration

Testing took place in groups of four to six participants who were seated individually in small cubicles within the same testing room. Experimental sessions started at 14:00h or 14:30h. First, a buccal smear sample for the analysis of AR CAG polymorphism was taken, followed by a baseline saliva sample

collected 20 minutes after arrival. Participants were asked to drool 2 mL of saliva directly into a polyethylene collection tube. All samples were frozen on-site and stored at -30 °C until analysis. Participants were then administered topical testosterone or placebo gel in a double-blind between-subjects design with random group allocation. Those allocated to the testosterone group received a single dose of testosterone gel, containing 150 mg testosterone [Androgel®]; participants in the placebo group received an equivalent amount of placebo gel. The *only* difference between the testosterone and placebo gel was that the placebo gel did not contain testosterone, and both the investigator and participants were fully blinded to whether the placebo or testosterone was administered at any given testing session and to any given individual. Participants rubbed the gel onto their upper arms and shoulders in small increments using disposable latex gloves until the full sample was rubbed into their skin. Gel administration was followed by a 2-hour waiting period, during which participants remained in the laboratory premises, completed the Dominance-Prestige Scale (Cheng et al., 2010) and demographic questionnaires, and were offered leisure-time reading materials. One hour and 50 minutes after the gel application, participants provided a second saliva sample and subsequently began the experimental task (see Figure 1A). The experimental task consisted of two parts: (1) illusion of control (IoC) induction and (2) competition (main task phase). In the IoC induction phase, participants were randomly assigned to one of two between-subject conditions aimed to induce either *high* or *low* levels of perceived personal control (see section 2.3. for details). Participants were thus divided into four experimental groups: testosterone high IoC group (N = 22), testosterone low IoC group (N = 22), placebo high IoC group (N = 20), placebo low IoC group (N = 24). The IoC induction phase comprised 160 trials and lasted on average 8 minutes.

Immediately following this first task phase, the competition phase began. The length of this task was determined by each individual's persistence and therefore varied across participants. On average, it lasted 7.5 minutes [Min =1.35 min, Max = 27.5 min]. Twenty minutes after the individual end of the competition, participants provided a third saliva sample. Participants were debriefed and received a flat participation fee plus a bonus payment based on their real performance in competition.

All participants provided written consent. All procedures were approved by the local research ethics board and conducted following the latest revision of the Declaration of Helsinki (World Medical Association, 2013).

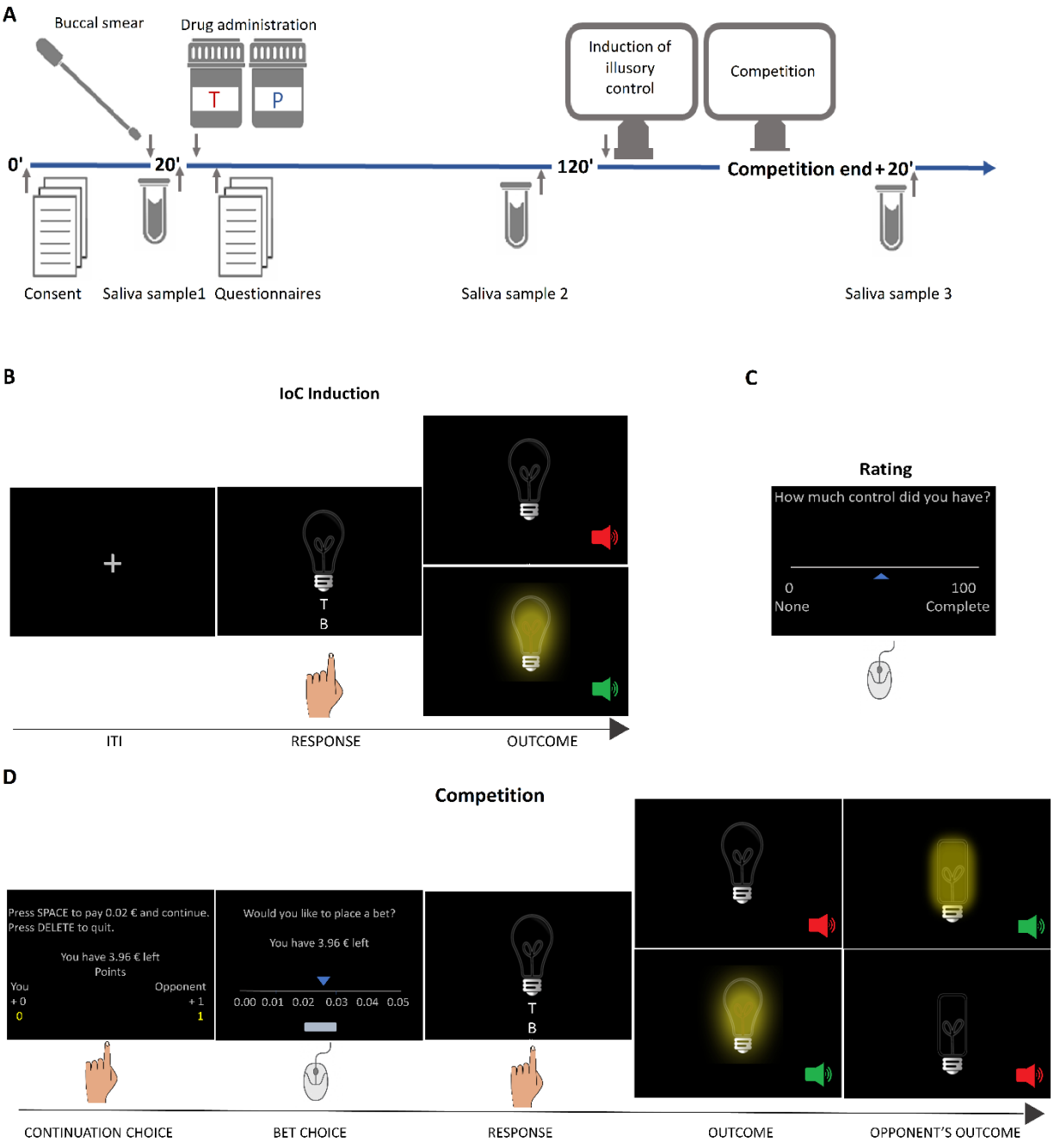


Figure 1. Experimental procedure and task. **A**: Time course of the experiment. **B:** Illusion of Control (IoC) induction phase. On each trial, participants selected between two possible actions and then observed either the positive or the negative outcome accompanied by a corresponding sound. No money could be won or lost. For complete instructions, see Supplementary Material B. **C:** Control rating. After every 20 trials of the IoC induction, participants were asked to rate their perceived personal control. In the competition phase, participants were asked to rate both their and their opponent's perceived control. **D:** Competition (main task phase). On each trial, participants decided whether to play on or leave the competition. If they decided to remain in the competition, they next chose a bet (0−5 cents) and afterward attempted to illuminate their light bulb. Once they observed their own outcome (normal light bulb on or off), the opponent's outcome (square light bulb on or off) was displayed and the competition score was updated. Original texts were in German.

Experimental Task

Participants completed a competitive persistence task, programmed in PsychoPy2 (Peirce et al., 2019), inspired by our prior research on the effects of illusory control upon persistence (Studer et al., 2020). The task started with an IoC induction based on the manipulation of the (non-contingent) density of the positive outcome (see Alloy and Abramson, 1979; Gillan et al., 2014; Studer et al., 2020), during which participants played the task alone (Figure 1B). Participants were instructed that their goal was to illuminate a lightbulb on their screen as often as possible, by pressing one of two response keys (self-paced). They were informed that the relationship between the keys and the light bulb illumination can be different in each block, therefore it was recommended to try both keys. Following a keypress, the lightbulb either illuminated (positive outcome) or remained off (negative outcome). In truth, light bulb illumination was non-contingent on the selected key; instead, the probability of a positive outcome varied based on a predefined schedule involving three within-subject conditions: a *low-density* condition, in which the light bulb illuminated in 25% of trials, a *medium-density* condition, in which the light bulb illuminated in 50% of trials, and a *high-density* condition, in which the light bulb illuminated in 75% of trials. To ascertain that this outcome density manipulation successfully modulated participants' perceived personal control, they were asked - after every 20 trials - to rate their own control over the light bulb illumination on a visual analog scale (Figure 1C) ranging from 0% (= "NO CONTROL, the lighting of the bulb had nothing to do with my button choices and was thus entirely random") to 100% (= "COMPLETE control, the lighting of the bulb was completely determined by my button choices"). In order to evoke different levels of perceived personal control immediately before the start of the competition, two different sequences of the outcome density conditions were used across participants. Participants assigned to the '*high IoC induction group*' underwent the density conditions in ascending order, finishing with the *high-density* condition before starting the competition. Participants assigned to the '*low IoC induction group*' underwent the density conditions in descending order, finishing with the *low-density* condition before starting the competition. This mixed design allowed us to test the effects of the pre-competition level of illusory control on subsequent competition persistence (comparison between induction groups) while also checking for potentially confounding effects of testosterone administration on the IoC induction itself (i.e., comparison of the personal control ratings in the high- vs low-density condition). Afterward, the main task phase (competition) started (Figure 1D). Participants were told that they would compete against an opponent present either in the same or neighboring testing room, in truth, opponents were computer-controlled. In each round of the competition, both the participant and their opponent tried to illuminate a light bulb presented on their screen, by pressing one of two response buttons (self-paced). Next, they saw their own outcome - that is, their lightbulb either illuminated or not. This was followed by a presentation of the opponent's outcome, i.e., participants saw whether the opponent's lightbulb

was illuminated or not. Participants won the round if their lightbulb illuminated but the opponent's did not, tied if both light bulbs illuminated or did not, and lost the trial if their bulb remained off but the opponent's light bulb illuminated. Each participant was endowed four euros at the beginning of the competition and had to pay a non-recoverable two-cent entry fee for each competition round that they decided to enter. In addition, participants could bet up to 5 cents on each competition round. If they won, they received double the wager back, if there was a draw, the original wager was returned, if they lost, the wager was lost. Unbeknownst to participants, the illumination of their light bulb was again independent of which key they selected. Instead, the light bulb illumination probability of the participant was fixed to 50% (non-contingent on their selected response), whereas that of the opponent steadily increase from 50% to 80% over the first 30 trials and then stayed at 80% for the remaining competition. The opponent thus became progressively stronger and persistence in the competition became increasingly disadvantageous and costly.

Crucially, participants were instructed that they could quit the competition at any time, receive their current monetary reward, and instead play a non-competitive version of the task (in which no money could be won or lost) until the end of the session. The number of completed competition trials served as the main outcome measure. Bets placed (trial-by-trial) and overall monetary loss (determined when the participant quit the competition) served as secondary outcome measures.

At the beginning of the competition, every 20 competition trials, and at the time of quitting the competition, participants were again asked to rate their own control over the light bulb illumination and that of the opponent on the same 0% - 100% visual analog scale as in the first task phase.

Data processing and statistical analyses

The statistical analyses were performed in the R statistical software (version, 4.0.3, R Core Team, 2020). We analyzed normally distributed, homoscedastic outcome data using general linear models or, in the case of nested observations, general linear mixed models (GLMM) (nlme package, Pinheiro et al., 2020). Outcome data with non-gaussian distribution were analyzed with generalized linear models (GzLM) using gamma distribution with log link function or with generalized linear mixed models (GzLMM) in case of nested observations (lme4 package, Bates et al., 2015). The respective models are specified below. All coefficients and 95% confidence intervals (CIs) are reported on the log scale, reported mean values are exponentiated. For interactions, we calculated the Type 3 sum of squares and used orthogonal contrasts. Follow-up p*ost-hoc* comparisons were computed with the *emmeans* (Lenth, 2020) and the *sjPlot* (Lüdecke, 2020) packages. All reported p-values are based on Wald tests from the car package (Fox and Weisberg, 2019). Plots were created using the ggplot2 (Wickham, 2016) and ggpubr (Kassambara, 2020) package.

Verification of the testosterone manipulation

After data collection was complete, saliva samples were shipped on dry ice to Dresden LabService GmbH lead by Clemens Kirschbaum's, Germany. Liquid chromatography-tandem mass spectrometry was used to measure the levels of testosterone and cortisol. Due to high kurtosis, testosterone data were winsorized to a score of 3 SD above or below the mean for each time point. To verify the effectiveness of the gel administration, testosterone levels at baseline, 1 h 50 min after administration, and 20 min after the end of the competition phase were compared across the between-subject factors drug treatment (*testosterone/placebo*) and IoC induction group (*high/low*) using a GzLMM with a random intercept. Cortisol levels were analyzed in the same manner.

Verification of pre-competition induction of illusory control

To verify the successful manipulation of perceived personal control before the start of the competition, we conducted an ANOVA with the factors drug treatment (*testosterone/placebo*) and IoC induction group (*high/low*), and the dependent variable pre-competition control rating.

Statistical analyses of competition data

Our primary analyses aimed to investigate the effects of testosterone and perceived personal control on our primary outcome measure, competition persistence. First, we examined whether the potential influence of personal control on competition persistence is fully captured by the individual pre-competition control ratings (*continuous*), or whether the fixed dichotomous factor of the IoC induction group (*high/low*) makes a significant contribution to the predictive accuracy of the persistence model. We, therefore, compared a series of increasingly complex, hierarchically related GzLMs with the predictors drug treatment (*testosterone/placebo*), individual's pre-competition ratings of personal control (mean-centered), IoC induction group (*high/low*), and their interactions, using Bayesian information criterion (see SM A for details). The strongest model (which included the predictors drug treatment, pre-competition ratings of personal control, and their interaction) was then used also for the analysis of our secondary outcome - monetary loss (in euro cents). Our other secondary outcome measure, bets placed trial-by-trial during the competition, was analyzed with a GLMM with the same predictors as used in the strongest model from the primary analyses, plus the additional predictor outcome of the previous trial (*win/loss/draw*) and all resulting interactions. Outcome of the previous trial was entered as a random slope, and an autoregressive first-order model of covariance structure AR(1) was used.

In addition, control ratings during the *competition phase* were analyzed, to examine the potential changes in the perception of own and opponent's control. The ratings of participants who completed at least one competition block of 20 trials (N = 58; $N_{Placebo}$ = 28), were entered into a GLMM with a between-subject factor drug treatment (*testosterone/placebo*), continuous predictor individual pre-

competition rating of personal control, and within-subject predictors agent (*self/opponent*) and time (*beginning/end of the competition*). The within-subject factors time and agent were included as random slopes in the model.Seven participants ($N_{placebo}$ = 3, $N_{testosterone}$ = 4), who quit the task before playing a single competitive round, were not included in the analyses.[1]

Control analyses

In addition to the aforementioned main analyses, we explored two alternative pathways through which drug treatment could in theory influence competition persistence. First, we tested whether testosterone administration had a systematic effect upon the effectiveness of the IoC induction, by conducting an ANOVA on pre-competition control ratings with the between-subject factors drug treatment and IoC group. Such an effect would allow us to test whether testosterone boosted illusory control before the competition, which could potentially account for any differences in persistence during the subsequent competition phase. Second, we assessed if testosterone administration systematically influenced participants' sensitivity to positive and negative outcomes during the IoC induction phase, by fitting a reinforcement learning model to their choice data (Jocham et al., 2011; Sutton and Barto, 1998). Again, such an effect could also covertly affect behavior in the competition phase. The reinforcement learning model estimated the expected value of each action (top or bottom button press) in every trial. At the beginning of each condition, the expected values were set to zero, and then the value of the chosen option was updated after each trial according to the following rule:

$$V(a)_{t+1} = V(a)_t + \alpha_O(r_t - V(a)_t)$$

where $V(a)_t$ is the value of action a (top or bottom) selected on trial t, r_t is the reward (0 or 1) obtained on trial t, and α_O is the outcome-specific learning rate that scales how strongly each outcome is used to update value estimates. We used separate learning rates, $\alpha_{positive}$ and $\alpha_{negative}$ for positive (light bulb on) and negative (lightbulb off) outcome trials.

The probability of choosing a particular action (here, top) on a given trial was computed using a softmax rule:

$$P(top) = \frac{1}{1+e^{-\Delta V/\tau}}$$

where ΔV is the value difference (here: top minus bottom) and τ is the softmax temperature. The free parameters $\alpha_{positive,}$ $\alpha_{negative,}$ and τ were estimated by maximum likelihood (Burnham & Anderson, 2002) and then separately compared between the drug treatment and IoC induction groups by means of a GzLM.

[1] A complimentary analysis where these participants were included with a persistence value of 0 provided qualitatively equivalent results.

Supplementary analyses on modulating biological mechanisms

A series of supplementary analyses explored potential biological mechanisms that might elucidate the pathways through which testosterone exerts its effect. One such potential pathway is via androgen receptors expressed in multiple brain regions (Rubinow and Schmidt, 1996). The efficiency of the androgen receptors substantially varies between individuals and was reported to be negatively related to the CAG repeat length (Zitzmann and Nieschlag, 2003). Testosterone's effects have previously been shown to be enhanced among individuals with fewer CAG repeats (Geniole et al., 2019a). Interactive effects between exogenous testosterone and endogenous cortisol levels have also been found, with testosterone influencing status-seeking behaviors more strongly when cortisol levels are low (Knight et al., 2020; Mehta and Prasad, 2015). Finally, one recent study found that testosterone administration *increased* competitive decisions only among high-dominant individuals (Mehta, van Son, et al., 2015). We, therefore, explored whether persistence-enhancing effects of testosterone also varied as a function of CAG repeat polymorphism, baseline cortisol, and trait dominance by adding these factors as covariates/moderators to the GzLM of competition persistence (see Supplementary Material SM A for more details).

Results

Verification of testosterone manipulation

Baseline testosterone and cortisol levels did not significantly differ across experimental groups (all *p*s > .140, see Table S2). Two hours after gel administration, we observed higher testosterone levels in the testosterone group (M = 6.25 ngmL, SE = 1.53) compared to the placebo group (M = 0.104 ngmL, SE = 0.01, drug treatment x time: $F(2,165) = 90.06$, $p < .001$), a difference that remained stable until the end of the experiment (see SM A, Figure S1). Testosterone levels were not influenced by the IoC induction group (main effect: $F(1,165) = .894$, $p = .089$; IoC group x time: $F(2,165) = 1.664$, $p = .102$). Testosterone administration did not affect cortisol levels (drug treatment x time: $F(2,165) = 0.716$, $p = .490$). Cortisol levels decreased during the experiment (time: $F(2,165) = 91.62$, $p < .001$), but were not systematically influenced by the IoC induction group either (main effect: $F(2,165) = 0.04$, $p = .843$; IoC x time: $F(2,165) = 0.082$, $p = .907$).

Verification of pre-competition induction of illusory control

Ratings of perceived personal control at the end of the IoC induction phase were significantly higher in the *high* IoC induction group compared to the *low* IoC induction group (M_{high} = 71.88, SE_{high} = 2.94; M_{low} = 11.22, SE_{low} = 2.81; IoC group main effect: $F(1,84) = 220.06$, $p < .001$, $\eta 2 = .722$, Figure 2A), confirming an effective manipulation of perceived personal control immediately prior to the start of the competition.

Competition behavior

Competition persistence was best explained by a model including predictors drug treatment, pre-competition ratings of perceived personal control (i.e., the individual's perceived control as induced by our manipulation), and their interaction; the IoC induction group per se did not improve model fit over and above the ratings of perceived control, which is why it was removed from the final model (see Table S1). The results from this best fitting model showed that the effect of testosterone (versus placebo) administration upon competition persistence varied as a function of perceived personal control (interaction effect: $B = 0.009$, $CI = [0.003, 0.015]$, $p = .003$, control rating: $B = 0.004$, $CI = [-0.003, 0.010]$, $p = .218$, drug treatment: $B = -0.108$, $CI = [-0.309, 0.094]$, $p = .297$).
Simple slope analysis (Aiken & West, 1991) of this interaction revealed that pre-competition levels of personal control positively predicted competition persistence in the placebo group ($B = 0.013$, $CI = [0.005, 0.021]$, $t(79) = 3.15$, $p = .003$), such that higher levels of control were associated with higher persistence. However, this was not the case in the testosterone group ($B = -0.005$, $CI = [-0.014, 0.003]$, $t(79) = -1.266$, $p = .213$. That is to say, testosterone administration disrupted the relationship between perceived personal control and persistence (see Figure 2B). Follow-up pairwise comparisons conducted separately in participants with high perceived personal control (control rating > group median of 28) and with low perceived personal control (control rating ≤ 28) showed that testosterone administration significantly and selectively increased persistence in participants with low pre-competition levels of perceived personal control, such that these participants on testosterone persisted twice as long as those on placebo ($M_{placebo} = 28.65$, $SE = 2.69$; $M_{testosterone} = 56.19$, $SE = 4.36$, $z(77) = 2.305$, $p = .021$).

In contrast, testosterone (compared to placebo) did not significantly influence persistence in participants with high perceived personal control ($z(77) = -0.949$, $p = .343$, see Figure 2C). Increased persistence in the competition resulted in a higher monetary loss, and as such monetary loss also varied as a function of drug treatment and pre-competition control rating (interaction effect: $B = -0.011$, $CI = [-0.017, -0.005]$, $p = .001$, control rating: $B = 0.004$, $CI = [-0.002, 0.010]$, $p = .189$, drug treatment: $B = 0.15$, $CI = [-0.054, 0.359]$, $p = .151$, see Figure 2D). Participants with low pre-competition personal control who were administered testosterone lost more money than those administered placebo ($M_{placebo} = 140.2$, $SE_{placebo} = 22.8$; $M_{testosterone} = 60.8$, $SE_{testosterone} = 22.2$; $z = -2.782$, $p = .005$), in line with the increased persistence of this testosterone subgroup. Meanwhile, the monetary loss of participants with high pre-competition levels of personal control did not vary as a function of drug treatment ($z = 0.921$, $p = .357$), again mirroring the comparable levels of competition persistence observed in these subgroups.

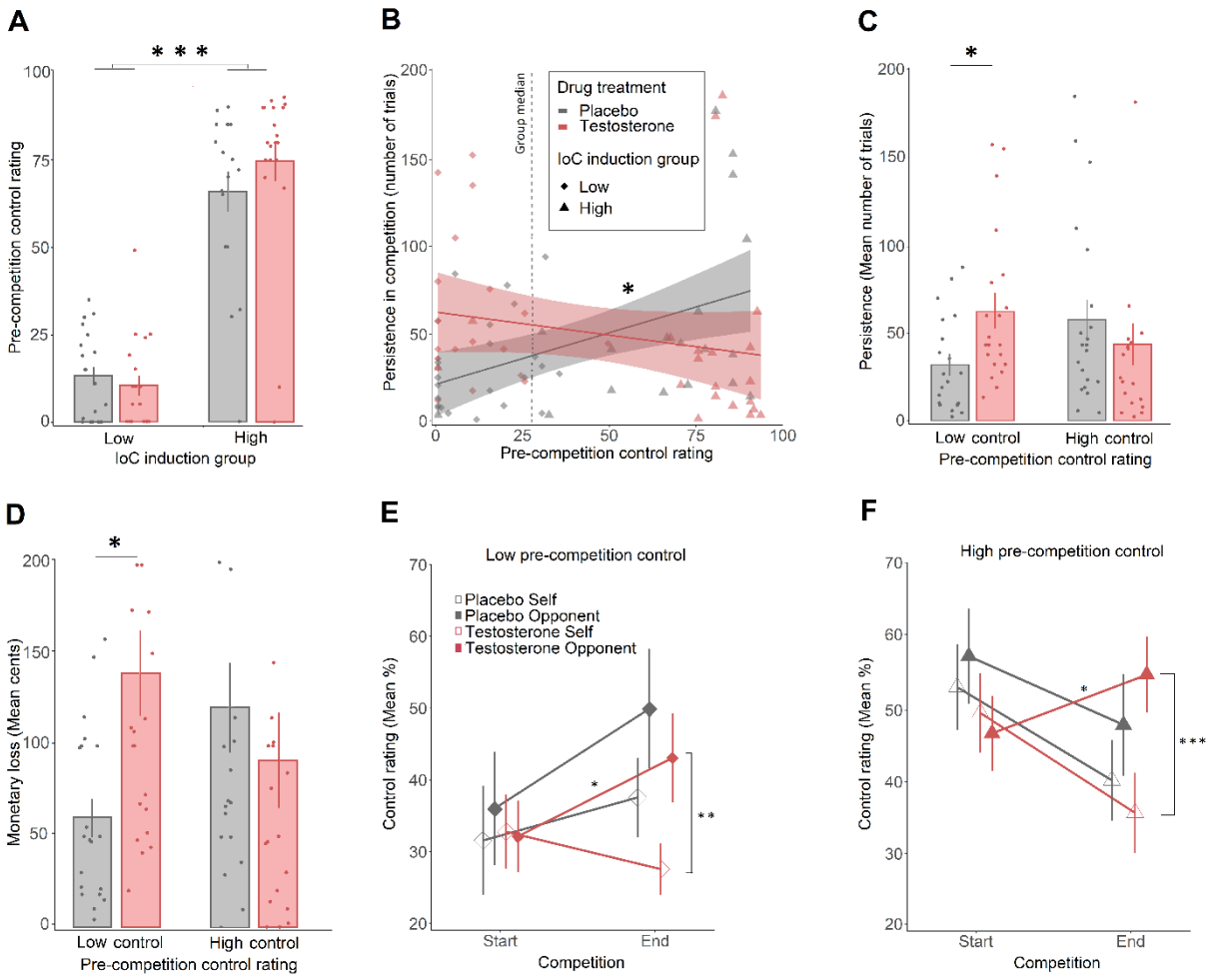


Figure 2. Induction of illusory control (IoC) and competition. **A** Perceived personal control at the end of the IoC induction phase (i.e., immediately before the competition) was rated significantly higher by participants in the *high* IoC induction compared to those in the *low* IoC induction group. **B** The interaction effect of drug treatment and perceived personal control on competition persistence. Testosterone administration disrupts the positive relationship between the pre-competition ratings of perceived personal control and subsequent persistence in the disadvantageous competition. **C** Testosterone administration increases competition persistence uniquely among participants with low levels of perceived personal control (groups plotted based on a median split of individual pre-competition control ratings). **D** Testosterone administration increased the amount of lost money among participants with low levels of perceived personal control (groups plotted based on a median split of individual pre-competition control ratings). **E, F** The interaction effect of the drug treatment, agent, and time on the ratings of perceived control during the competition (plots divided based on a median split of individual pre-competition control ratings). Participants in the testosterone group rated the control of the opponent as higher at the end of the competition than at the start of the competition. Participants in the testosterone group after competition also rated the opponent's control as higher in comparison to their own control.
Shaded area and error bars: Mean ± SE.

In contrast to competition persistence, betting behavior was not significantly affected by drug treatment (B = -0.13, CI = [-0.43, 0.17], p = .408), pre-competition levels of personal control (B = 0.00, CI = [-0.01, 0.01], p = .952), or their interaction (B = 0.00, CI = [-0.01, 0.01], p = .539). Rather, bets placed varied as a function of the outcome on the previous trial, such that significantly lower bets

were placed immediately following a loss (M = 3.36, SE = 0.15) compared to a draw (M = 3.50, SE = 0.15; B = 0.13, CI = [0.04, 0.19], p = .003) or win (M = 3.61, SE = 0.16, B = 0.24, CI = [0.11, 0.37], p < .001).

Finally, the analysis of the control ratings during the competition phase revealed a significant three-way interaction of the factors drug treatment, time, and agent (B = 1.68, CI = [0.01, 3.34], p = .048, see Figure 2E, F). At the time of quitting the competition, participants that were administered testosterone rated the opponent's control as higher (M = 48.7, SE = 4.58) than at the beginning of the competition (M = 39.0, SE = 4.11 B = 9.78, CI = [0.28, 19.27], p = .044) and as higher than their own control (M = 31.4, SE = 3.36; B = 17.27, CI = [8.14, 26.41], p < .001). That is to say, the control ratings of the testosterone group during the competition reflected the objective advantage of the opponent. Meanwhile, in the placebo group, no significant differences were found in either of these contrasts (B = 0.96, CI = [-9.10, 11.01], p = .851; B = 9.67, CI = [0.00, 19.34], p = .050, respectively). We also observed a main effect of the pre-competition rating (B = 0.25, CI = [0.12, 0.38], p < .001) indicating that higher (vs lower) pre-competition ratings predicted higher ratings at the end of the competition. No significant interaction effects between pre-competition ratings and drug treatment (B = 0.01, CI = [-0.12, 0.14], p = .891), time (B = -0.07, CI = [-0.15, 0.08], p = .701) or agent (B = 0.01, CI = [-0.05, 0.08], p = .701), or any higher-order interactions (all ps >.379), were found.

Control analyses

Testosterone treatment did not affect pre-competition control ratings (F(1,84) = 0.123, p = .727) and it did not interact with the IoC induction group (F(1,84) = 1.242, p = .268; see SM A 3.1 for further details). Model-estimates of participants' sensitivity to the outcomes during the IoC induction phase ($\alpha_{positive}$, $\alpha_{negative}$, τ) likewise showed no systematic effect of testosterone administration (drug treatment: F(1,83) = 1.460, p = .230; F(1,83) = 0.040, p = .843; F(1,83) = 1.723, p = .397; drug treatment x IoC group interaction: F(1,83) = 1.055, p = .307; F(1,83) = 0.174, p = .678; F(1,83) = 0.007, p = .932, respectively; see SM A 3.2 for further details) suggesting that effects of testosterone among low control participants cannot be explained by differential sensitivity to positive or negative outcomes.

Supplementary analyses

CAG-repeat length, basal cortisol, and trait dominance did not interact with the control-dependent effects of testosterone on competition persistence (B = -0.003, CI = [-0.007, 0.002], p = .162; B = 0.015, CI = [-0.008, 0.037], p = .179; B = 0.00, CI = [-0.001, 0.002], p = .653, respectively).

Discussion

The present study investigated testosterone's effects on competition persistence and the psychological and biological mechanisms that may underlie such effects. Our results show that the causal effect of testosterone on men's persistence in a disadvantageous social competition depends on their subjective control beliefs. A single dose of exogenous testosterone boosted persistence against an increasingly stronger opponent uniquely among participants who entered the competition with low perceived personal control over task outcomes. To the best of our knowledge, this work provides the first causal evidence that testosterone modulates competitive persistence and that it does so dependent on one's psychological state prior to the competition. This result critically extends previous research reporting that testosterone's effect on the willingness to compete again is dependent on the outcome of the previous contests (Losecaat Vermeer et al., 2020; Mehta et al., 2015a) and indicates that testosterone‘s impact upon competitive drive is moderated by a broader situational context exceeding the competition setting.

In the placebo group, perceptions of low (vs high) personal control - induced immediately before the competition - promoted earlier quitting in the disadvantageous competition. This finding aligns with previous experimental and theoretical work (Bandura and Locke, 2003; Eccles and Wigfield, 2002; Studer et al., 2020). In contrast, in the testosterone group, such reductions in control did not translate into earlier quitting. Rather, testosterone made such individuals with low perceived control act as if they entered the competition with high perceived control, boosting persistence despite the opponent becoming increasingly stronger.

One explanation for these findings could be that testosterone rendered participants insensitive to the opponent's superior performance. However, ratings collected during the competition suggested that participants who had received testosterone appeared even more aware of the opponent's advantage than those who had received a placebo. Thus, after testosterone administration, participants maintained, and even slightly gained, sensitivity to the superior performance of the opponent, yet still engaged in monetarily disadvantageous competitive behavior. These effects are consistent with a recent testosterone administration study (Geniole et al., 2019b) in which the hormone reduced submissive resource-ceding to high- (but not low-) threat competitors, but did not diminish participants‘ sensitivity to this threat information. Together, these findings suggest that rather than modulating explicit assessment of social threat/competitiveness, testosterone appears to act by modifying behavioral responses to such information. Not all studies demonstrate such effects though: for example, Panagiotidis et al. (2017) found that testosterone administration increased self-reported but not behavioral aggressive responses to non-social provocation. These differences across studies

further highlight the idea that testosterone effects are crucially dependent on the social context (Kutlikova et al., 2020).

When we have the opportunity to pursue a relevant goal, but goal attainment is costly, our decision to persist or discontinue is thought to be contingent on the outcomes experienced during previous, similar attempts (Sturgeon and Zautra, 2016). Given that testosterone has been observed to shift the motivational balance by lowering sensitivity to punishment (van Honk et al., 2004), it could also be speculated that testosterone decreased sensitivity to negative outcomes more generally (e.g., failed bulb illuminations), regardless of other features related to the competition. However, the results of our reinforcement learning model argue against such an outcome-insensitivity effect. Neither learning from negative nor from positive outcomes was systematically altered by exogenous testosterone (i.e., testosterone did not alter button-press choices in response to successful or unsuccessful bulb illuminations in the induction phase, preceding the competition).

A second potential explanation could be that testosterone increased the rewarding effect of competition per se (Hermans, et al., 2010, Purves-Tyson, 2014). However, such an effect would arguably be expected to manifest independently of perceived control, rather than selectively in participants entering the competition with low perceived control. Instead, we posit that a likely mechanism driving the observed persistence-enhancing effect of testosterone in those with low (induced) perceived control is that these participants appraised persistence in the competition as a means for social-status enhancement (Losecaat Vermeer et al., 2020; Mazur and Booth, 1998) and were consequently motivated to persist regardless of the outcome and monetary value. Convergent with this proposition, previous research has shown that testosterone can affect the appraisal of competitive environments (Salvador, 2005) and that higher testosterone levels prior, during, and after a competition are associated with increased satisfaction with personal performance even in the case of a loss (Casto et al., 2017).

Contrary to persistence, we did not find an effect of testosterone or induced levels of control on the bets placed during the competition. Instead, betting was modulated only by the outcome of the preceding competition round, with betting decreasing after a loss compared to a draw or win. This aligns with previous studies reporting that betting behavior is insensitive to perceived control (Studer et al., 2020) and does not always follow decision confidence (Studer et al., 2015).

Our supplementary analyses found no significant modulation of testosterone's persistence enhancing effects by CAG repeat length (a genetic determinant of androgen receptor sensitivity to testosterone), basal cortisol levels, or trait dominance. In contrast, prior studies observed an influence of CAG repeated length on testosterone's effects upon status-seeking behaviors (Geniole et al., 2019; Losecaat

Vermeer et al., 2020), and increased testosterone effects on status-seeking behaviors among individuals with low basal cortisol (Knight et al., 2020; Mehta and Prasad, 2015) and high dominance (Geniole et al., 2019; Mehta, et al., 2015). One speculative reason could be that the current psychological state (in our case induced perceived personal control) overrides the effects of such trait(-like) predictors. In any case, one limitation of our study lies in the relatively small sample size, which led to reduced statistical power, especially when analyzing some of these three-way interactions. The null findings (e.g., of CAG repeat length and trait dominance) should therefore be interpreted with caution. Another limitation, shared by most other psychoneuroendocrinological research using testosterone, was that due to the sex differences in testosterone metabolism and unknown pharmacokinetics following the topical administration of testosterone in women (Eisenegger et al., 2013), the study included only male participants. Hence, the validity of these findings and generalizability to biological females and those identifying as women will require further investigation.

Our results also raise questions for future research. For instance, neuroimaging studies might elucidate the mechanisms through which testosterone disrupts the link between perceived control and behavioral persistence. Even in the absence of an identified mechanism, however, evidence that testosterone boosts persistence especially in individuals who do not feel in control might provide helpful information for settings that require extensive repetitive training, such as neurorehabilitation (Studer et al., 2016). To expand this application potential, it would also be useful to test the transferability of these effects to different tasks and environments, for instance, disadvantageous persistence versus persistence that leads to success (McFarlin et al., 1984).

In conclusion, the present study demonstrates that testosterone's effects on competitive behavior depend on one's psychological state, with the hormone specifically making individuals with low perceived control persist longer against a stronger opponent. This experimental evidence of context-dependent testosterone effects highlights the importance of studying the intersection of biological and psychosocial factors that shape testosterone functioning.

Acknowledgments

We wish to thank Alexander Kudrna for his help with data collection. This work was supported by the Vienna Science and Technology Fund (WWTF VRG 13-007), University of Vienna uni:docs Fellowship, Aktion Österreich – Slowakei fellowship of Federal Ministry of Education, Science and Research of Austria and Ministry of Education, Science, Research and Sport of the Slovak Republic and a Banting Postdoctoral Fellowship from the Social Sciences and Humanities Research Council of Canada.

References

Alloy, L.B., Abramson, L.Y., 1979. Judgment of contingency in depressed and nondepressed students: Sadder but wiser? J. Exp. Psychol. Gen. 108, 441–485. https://doi.org/10.1037/0096-3445.108.4.441

Apicella, C.L., Dreber, A., Gray, P.B., Hoffman, M., Little, A.C., Campbell, B.C., 2011. Androgens and competitiveness in men. J. Neurosci. Psychol. Econ. 4, 54–62. https://doi.org/10.1037/a0021979

Bandura, A., Locke, E.A., 2003. Negative self-efficacy and goal effects revisited. J. Appl. Psychol. 88, 87–99. https://doi.org/10.1037/0021-9010.88.1.87

Bates, D.,Maechler, M., Bolker, B., & Walker, S., 2015. Fitting Linear Mixed-Effects Models Using lme4. Journal of Statistical Software, 67(1), 1-48. doi:10.18637/jss.v067.i01.

Buskens, V., Raub, W., Van Miltenburg, N., Montoya, E.R., van Honk, J., 2016. Testosterone Administration Moderates Effect of Social Environment on Trust in Women Depending on Second-to-Fourth Digit Ratio. Sci. Rep. 6, 1–8. https://doi.org/10.1038/srep27655

Carré, J.M., McCormick, C.M., 2008. Aggressive behavior and change in salivary testosterone concentrations predict willingness to engage in a competitive task. Horm. Behav. 54, 403–409. https://doi.org/10.1016/j.yhbeh.2008.04.008

Casto, K. V., Edwards, D.A., Akinola, M., Davis, C., Mehta, P.H., 2020. Testosterone reactivity to competition and competitive endurance in men and women. Horm. Behav. 104665. https://doi.org/10.1016/j.yhbeh.2019.104665

Casto, K. V., Rivell, A., Edwards, D.A., 2017. Competition-related testosterone, cortisol, and perceived personal success in recreational women athletes. Horm. Behav. 92, 29–36. https://doi.org/10.1016/j.yhbeh.2017.05.006

Cheng, J.T., Tracy, J.L., Henrich, J., 2010. Pride, personality, and the evolutionary foundations of human social status. Evol. Hum. Behav. 31, 334–347. https://doi.org/10.1016/j.evolhumbehav.2010.02.004

Clark, L., Studer, B., Bruss, J., Tranel, D., Bechara, A., 2014. Damage to insula abolishes cognitive distortions during simulated gambling. PNAS 111, 6098–6103. https://doi.org/10.1073/pnas.1322295111

Côté, D., Caron, A., Aubert, J., Desrochers, V., Ladouceur, R., 2003. Near Wins Prolong Gambling on a Video Lottery Terminal. J Gambl Stud 19, 433–438. https://doi.org/10.1023/A:1026384011003

Deci, E.L., Ryan, R.M., 2000. The "what" and "why" of goal pursuits: Human needs and the self-determination of behavior. Psychol. Inq. 11, 227–268. https://doi.org/10.1207/S15327965PLI1104_01

Eccles, J.S., Wigfield, A., 2002. Motivational Beliefs, Values, and Goals. Annu. Rev. Psychol. 53, 109–132. https://doi.org/10.1146/annurev.psych.53.100901.135153

Eisenegger, C., von Eckardstein, A., Fehr, E., von Eckardstein, S., 2013. Pharmacokinetics of testosterone and estradiol gel preparations in healthy young men. Psychoneuroendocrinology 38, 171–178. https://doi.org/10.1016/j.psyneuen.2012.05.018

Fox, J., Weisberg, S., 2019. An {R} Companion to Applied Regression, Third Edition. Thousand Oaks CA: Sage. URL: https://socialsciences.mcmaster.ca/jfox/Books/Companion/

Geniole, S.N., Carré, J.M., 2018. Human social neuroendocrinology: Review of the rapid effects of testosterone. Horm. Behav. https://doi.org/10.1016/j.yhbeh.2018.06.001

Geniole, S.N., Procyshyn, T.L., Marley, N., Ortiz, T.L., Bird, B.M., Marcellus, A.L., Welker, K.M., Bonin, P.L., Goldfarb, B., Watson, N. V., Carré, J.M., 2019a. Using a Psychopharmacogenetic Approach To Identify the Pathways Through Which—and the People for Whom—Testosterone Promotes Aggression. Psychol. Sci. 30, 481–494. https://doi.org/10.1177/0956797619826970

Geniole, S.N., Proietti, V., Bird, B.M., Ortiz, T.L., Bonin, P.L., Goldfarb, B., Watson, N. V., Carré, J.M., 2019b. Testosterone reduces the threat premium in competitive resource division. Proc. R. Soc. B Biol. Sci. 286, 20190720. https://doi.org/10.1098/rspb.2019.0720

Gillan, C.M., Morein-Zamir, S., Durieux, A.M.S., Fineberg, N.A., Sahakian, B.J., Robbins, T.W.,

2014. Obsessive and compulsive disorder patients have a reduced sense of control on the illusion of control task. Front. Psychol. 5, 204. https://doi.org/10.3389/fpsyg.2014.00204
Hermans, E.J., Bos, P.A., Ossewaarde, L., Ramsey, N.F., Fernández, G., van Honk, J., 2010. Effects of exogenous testosterone on the ventral striatal BOLD response during reward anticipation in healthy women. Neuroimage 52, 277–283. https://doi.org/10.1016/j.neuroimage.2010.04.019
Jocham, G., Klein, T.A., Ullsperger, M., 2011. Dopamine-Mediated Reinforcement Learning Signals in the Striatum and Ventromedial Prefrontal Cortex Underlie Value-Based Choices. Journal of Neuroscience 31, 1606–1613. https://doi.org/10.1523/JNEUROSCI.3904-10.2011
Kassambara, A., 2020. ggpubr: 'ggplot2' Based Publication Ready Plots. R package version 0.4.0. https://CRAN.R-project.org/package=ggpubr
Knight, E.L., Sarkar, A., Prasad, S., Mehta, P.H., 2020. Beyond the challenge hypothesis: The emergence of the dual-hormone hypothesis and recommendations for future research. Horm. Behav. 104657. https://doi.org/10.1016/j.yhbeh.2019.104657
Kutlikova, H.H., Durdiaková, J.B., Wagner, B., Vlček, M., Eisenegger, C., Lamm, C., Riečanský, I., 2020b. The effects of testosterone on the physiological response to social and somatic stressors. Psychoneuroendocrinology 117, 104693. https://doi.org/10.1016/j.psyneuen.2020.104693
Langer, E.J., 1975. The illusion of control. Journal of Personality and Social Psychology 32, 311–328. https://doi.org/10.1037/0022-3514.32.2.311
Lawler, E.E., Porter, L.W., 1967. Antecedent attitudes of effective managerial performance. Organ. Behav. Hum. Perform. 2, 122–142. https://doi.org/10.1016/0030-5073(67)90026-8
Le Bouc, R., Pessiglione, M., 2013. Imaging social motivation: Distinct brain mechanisms drive effort production during collaboration versus competition. J. Neurosci. 33, 15894–15902. https://doi.org/10.1523/JNEUROSCI.0143-13.2013
Lenth, R., 2020. emmeans: Estimated Marginal Means, aka Least-Squares Means. R package version 1.5.2-1. https://CRAN.R-project.org/package=emmeans
Lim, M.S.M., Bowden-Jones, H., Rogers, R.D., 2014. Expressing Gambling-Related Cognitive Biases in Motor Behaviour: Rolling Dice to Win Prizes. J. Gambl. Stud. 30, 625–637. https://doi.org/10.1007/s10899-013-9381-x
Losecaat Vermeer, A.B., Krol, I., Gausterer, C., Wagner, B., Eisenegger, C., Lamm, C., 2020. Exogenous testosterone increases status-seeking motivation in men with unstable low social status. Psychoneuroendocrinology 113, 104552. https://doi.org/10.1016/j.psyneuen.2019.104552
Lüdecke, D. 2020. _sjPlot: Data Visualization for Statistics in Social Science_. R package version 2.8.5, <URL: https://CRAN.R-project.org/package=sjPlot>.
Mazur, A., Booth, A., 1998. Testosterone and dominance in men. Behav. Brain Sci. https://doi.org/10.1017/S0140525X98001228
McFarlin, D.B., Baumeister, R.F., Blascovich, J., 1984. On knowing when to quit: Task failure, self-esteem, advice, and nonproductive persistence. J. Pers. 52, 138–155. https://doi.org/10.1111/j.1467-6494.1984.tb00349.x
Mehta, P.H., Josephs, R.A., 2006. Testosterone change after losing predicts the decision to compete again. Horm. Behav. 50, 684–692. https://doi.org/10.1016/j.yhbeh.2006.07.001
Mehta, P.H., Prasad, S., 2015. The dual-hormone hypothesis: A brief review and future research agenda. Curr. Opin. Behav. Sci. https://doi.org/10.1016/j.cobeha.2015.04.008
Mehta, P.H., Snyder, N.A., Knight, E.L., Lassetter, B., 2015a. Close Versus Decisive Victory Moderates the Effect of Testosterone Change on Competitive Decisions and Task Enjoyment. Adapt. Hum. Behav. Physiol. 1, 291–311. https://doi.org/10.1007/s40750-014-0014-0
Mehta, P.H., van Son, V., Welker, K.M., Prasad, S., Sanfey, A.G., Smidts, A., Roelofs, K., 2015b. Exogenous testosterone in women enhances and inhibits competitive decision-making depending on victory-defeat experience and trait dominance. Psychoneuroendocrinology 60, 224–236. https://doi.org/10.1016/j.psyneuen.2015.07.004
Niederle, M., Vesterlund, L., 2007. Do Women Shy Away From Competition? Do Men Compete Too Much? Q. J. Econ. 122, 1067–1101. https://doi.org/10.1162/qjec.122.3.1067
Panagiotidis, D., Clemens, B., Habel, U., Schneider, F., Schneider, I., Wagels, L., Votinov, M., 2017.

Exogenous testosterone in a non-social provocation paradigm potentiates anger but not behavioral aggression. Eur Neuropsychopharmacol 27, 1172–1184. https://doi.org/10.1016/j.euroneuro.2017.07.006
Peirce, J., Gray, J.R., Simpson, S., MacAskill, M., Höchenberger, R., Sogo, H., Kastman, E., Lindeløv, J.K., 2019. PsychoPy2: Experiments in behavior made easy. Behav. Res. Methods 51, 195–203. https://doi.org/10.3758/s13428-018-01193-y
Pinheiro, J., Bates, D., DebRoy, S., Sarkar, D., R Core Team, 2020. _nlme: Linear and Nonlinear Mixed Effects Models_. R package version 3.1-149, <URL: https://CRAN.R-project.org/package=nlme>.
Purves-Tyson, T.D., Handelsman, D.J., Double, K.L., Owens, S.J., Bustamante, S., Weickert, C., 2012. Testosterone regulation of sex steroid-related mRNAs and dopamine-related mRNAs in adolescent male rat substantia nigra. BMC Neurosci 13, 95. https://doi.org/10.1186/1471-2202-13-95
R Core Team, 2020. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/
Rotter, J.B., 1966. Generalized expectancies for internal versus external control of reinforcement. Psychological Monographs: General and Applied 80, 1–28. https://doi.org/10.1037/h0092976
Rubinow, D. R., Schmidt, P. J., 1996. Androgens, brain, and behavior. *The American Journal of Psychiatry, 153*(8), 974–984. https://doi-orgR/10.1176/ajp.153.8.974
Ryan, R.M., Deci, E.L., 2000. Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being. Am. Psychol. 55, 68–78. https://doi.org/10.1037/0003-066X.55.1.68
Salvador, A., 2005. Coping with competitive situations in humans. Neurosci. Biobehav. Rev. https://doi.org/10.1016/j.neubiorev.2004.07.004
Seidel, A., Ghio, M., Studer, B., Bellebaum, C., 2021. Illusion of control affects ERP amplitude reductions for auditory outcomes of self-generated actions. Psychophysiology. https://doi.org/10.1111/psyp.13792
Stefan, S., David, D., 2013. Recent developments in the experimental investigation of the illusion of control. A meta-analytic review: A meta-analysis of the illusion of control. J Appl Soc Psychol 43, 377–386. https://doi.org/10.1111/j.1559-1816.2013.01007.x
Studer, B., Geniole, S.N., Becker, M.L., Eisenegger, C., Knecht, S., 2020. Inducing illusory control ensures persistence when rewards fade and when others outperform us. Psychon. Bull. Rev. 1–10. https://doi.org/10.3758/s13423-020-01745-4
Studer, B., Limbrick-Oldfield, E.H., Clark, L., 2015. 'Put Your Money Where Your Mouth Is!': Effects of Streaks on Confidence and Betting in a Binary Choice Task. J. Behav. Decis. Mak. 28, 239–249. https://doi.org/10.1002/bdm.1844
Studer, B., Van Dijk, H., Handermann, R., Knecht, S., 2016. Increasing self-directed training in neurorehabilitation patients through competition, in: Progress in Brain Research. Elsevier B.V., pp. 367–388. https://doi.org/10.1016/bs.pbr.2016.06.012
Sturgeon, J.A., Zautra, A.J., 2016. Resilience to Chronic Arthritis Pain Is Not About Stopping Pain That Will Not Stop: Development of a Dynamic Model of Effective Pain Adaptation, in: Psychosocial Factors in Arthritis. Springer International Publishing, pp. 133–149. https://doi.org/10.1007/978-3-319-22858-7_8
Sutton, R.S., Barto, A.G., 1998. Reinforcement learning: an introduction, Adaptive computation and machine learning. MIT Press, Cambridge, Mass.
Thompson, S.C., Nierman, A., Schlehofer, M.M., Carter, E., Bovin, M.J., Wurzman, L., Tauber, P., Trifskin, S., Marks, P., Sumner, J., Jackson, A., Vonasch, A., 2007. How Do We Judge Personal Control? Unconfounding Contingency and Reinforcement in Control Judgments. Basic and Applied Social Psychology 29, 75–84. https://doi.org/10.1080/01973530701331189
Thor, D.H., 1980. Testosterone and persistence of social investigation in laboratory rats. J. Comp. Physiol. Psychol. 94, 970–976. https://doi.org/10.1037/h0077831
Tobias-Webb, J., Limbrick-Oldfield, E.H., Gillan, C.M., Moore, J.W., Aitken, M.R.F., Clark, L.,

2017. Let me Take the Wheel: Illusory Control and Sense of Agency. Quarterly Journal of Experimental Psychology 70, 1732–1746. https://doi.org/10.1080/17470218.2016.1206128
van Honk, J., Schutter, D.J.L.G., Hermans, E.J., Putman, P., Tuiten, A., Koppeschaar, H., 2004. Testosterone shifts the balance between sensitivity for punishment and reward in healthy young women. Psychoneuroendocrinology 29, 937–943. https://doi.org/10.1016/j.psyneuen.2003.08.007
van Honk, J., Will, G.J., Terburg, D., Raub, W., Eisenegger, C., Buskens, V., 2016. Effects of Testosterone Administration on Strategic Gambling in Poker Play. Sci. Rep. 6, 1–10. https://doi.org/10.1038/srep18096
Vansteenkiste, M., Deci, E.L., 2003. Competitively Contingent Rewards and Intrinsic Motivation: Can Losers Remain Motivated? Motiv. Emot. https://doi.org/10.1023/A:1026259005264
Wickham, H, 2016. ggplot2: Elegant Graphics for Data Analysis. Springer-Verlag New York, 2016.
Wulf, G., Chiviacowsky, S., Cardozo, P.L., 2014. Additive benefits of autonomy support and enhanced expectancies for motor learning. Hum. Mov. Sci. 37, 12–20. https://doi.org/10.1016/j.humov.2014.06.004
Zitzmann, M., Nieschlag, E., 2003. The CAG repeat polymorphism within the androgen receptor gene and maleness. Int. J. Androl. https://doi.org/10.1046/j.1365-2605.2003.00393.x

Supplementary Materials A for:

Not giving up: testosterone promotes persistence against a stronger opponent

Hana H. Kutlikova, Shawn N. Geniole, Christoph Eisenegger, Claus Lamm, Gerhard Jocham, Bettina Studer

Data and main statistical analysis scripts can be found at the project's Open Science Framework websi te: https://osf.io/43wjp/

Table S1. Model comparison showed that the model 3 (highlighted in yellow), which included the factors of drug treatment, pre-competition rating of personal control (mean-centered), and their interaction is the most suitable model to predict persistence in competition. CI = 95% confidence interval.

	Persistence in competition: number of trials														
	model 1			model 2			model 3			model 4			model 5		
Predictors	*B*	*CI*	*p*	*B*	*CI*	*p*	*B*	*CI*	*p*	*B*	*CI*	*p*	*B*	*CI*	*p*
(Intercept)	3.789	3.591 – 4.001	**<.001**	3.784	3.592 – 3.990	**<.001**	3.764	3.570 – 3.972	**<.001**	3.740	3.545 – 3.949	**<.001**	3.595	3.206 – 4.504	**<.001**
Drug treatment	-0.085	0.291 – 0.120	. 418	-0.107	-0.3109 – 0.097	.296	-0.108	-0.309 – 0.094	.297	-0.117	-0.319 – 0.085	.257	-0.174	-0.613 – 0.240	.385
Control rating				0.003	-0.003 – 0.009	.322	0.004	-0.003 – 0.010	.218	0.010	-0.002 – 0.021	.056	0.003	-0.004 – 0.010	.404
Drug treatment* Control rating							0.009	0.003 – 0.015	**.003**	0.009	0.004 – 0.015	**.002**	0.008	0.002 – 0.015	.008
IoC induction group										-0.270	-0.642 – 0.148	.154			
Control rating* Drug treatment (P)*IoC Induction group													0.008	-0.011 – 0.026	.306
Control rating* Drug treatment (T)*IoC Induction group													0.003	-0.016 – 0.019	.696
Observations	81			81			81			81			81		
R^2 Nagelkerke	0.012			0.029			0.182			0.208			0.197		
BIC	786.8			790.2			783.8			786.2			791.5		

Analysis of inter-individual difference variables

Summary statistics of hormone levels and interindividual-difference variables

Table S2. Summary statistics across experimental groups: mean (SD), ANOVA.

Drug treatment	**Placebo**		**Testosterone**			
IoC Induction	**High**	**Low**	**High**	**Low**	**F**	***p***
Sample size	20	24	22	22		
Baseline testosterone [pg/ml] (SD)	92.42 (67.32)	28.51 (90.70)	106.99 (84.92)	94.73 (34.55)		
log (SD)	4.39 (0.48)	4.69 (0.53)	4.49 (0.55)	4.48 (0.36)	2.221	.140
Baseline cortisol [nmol/L] (SD)	5.59 (7.40)	5.42 (2.79)	5.44 (3.99)	5.20 (3.37)		
log (SD)	1.37 (0.72)	1.55 (0.57)	1.42 (0.78)	1.46 (0.62)	0.238	.627
CAG repeat length	18.21(2.70)	19.68(2.97)	18.78 (3.55)	19.54 (4.33)	0.223	.638
Dominance trait	33.79(5.73)	32.21(8.62)	32.23 (6.21)	33.95(9.05)	1.016	.317
2D4D ratio	0.96(0.03)	0.95 (0.03)	0.95 (0.02)	0.95 (0.04)	1.197	.277

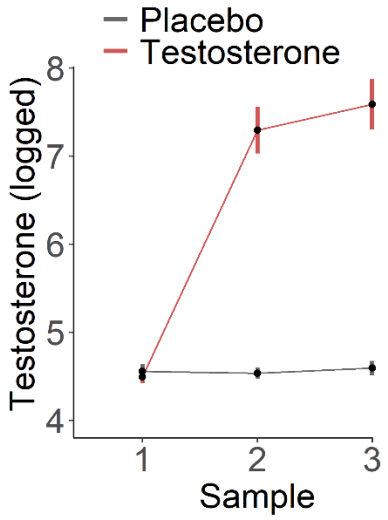


Figure S1. Testosterone levels during the experimental session. Error bars = Mean ± SE

Table S3. The interaction of inter-individual differences with the effect of drug treatment and perceived personal control on competition persistence. CI = 95% confidence interval.

	Persistence in competition: number of trials								
	Dominance model			CAG model			Cortisol model		
Predictors	*B*	*CI*	*p*	*B*	*CI*	*p*	*B*	*CI*	*p*
(Intercept)	3.739	3.553 - 3.937	**<.001**	3.767	3.581 - 3.966	**<.001**	3.71	3.514 - 3.920	**<.001**
Drug treatment	-0.089	-0.280 - 0.104	.372	-0.087	-0.279 - 0.106	.378	-0.156	-0.359 - 0.048	.136
Control rating	0.004	-0.002 - 0.009	.190	0.003	-0.003 - 0.009	.308	0.005	-0.001 - 0.011	.083
Dominance	0.021	-0.006 - 0.050	.136						
Drug treatment x Control rating	0.009	0.003 - 0.014	**.003**	0.010	0.004 - 0.015	**.002**	0.011	0.005 - 0.017	**<.001**
Drug treatment x Dominance	-0.015	-0.043 - 0.013	.292						
Control rating x Dominacne	0.00	-0.001 - 0.001	.500						
Drug treatment x Control rating x Dominance	-0.00	-0.001 - 0.001	.653						
CAG				-0.021	-0.091 - 0.047	.481			
Drug treatment x CAG				0.019	-0.049 - 0.089	.515			
Control rating x CAG				0.000	-0.002 - 0.002	.995			
Drug treatment x Control rating x CAG				0.001	-0.001 - 0.004	.162			
Cortisol							0.092	-0.291 - 0.480	.586
Drug treatment x Cortisol							0.305	-0.079 - 0.691	.075
Control rating x Cortisol							-0.005	-0.016 - 0.006	.344
Drug treatment x Control rating x Cortisol							-0.007	-0.0183 - 0.004	.179
Observations	81			78			81		
R^2 Nagelkerke	0.241			0.236			0.263		

Genotyping

Buccal mucosa samples were collected by sterile cotton swabs (Sarstedt AG, Germany), the DNA was extracted and isolated using a resin-based method with Chelex®100 (Sigma Aldrich, USA). For amplification of the CAG repeat polymorphism in exon 1 of the AR gene primers forward - 5' GCGCGAAGTGATCCAGAAC 3' tagged with 6–carboxyfluorescein and reverse - 5' CTCATCCAGGACCAGGTAGC 3' were used in PCR with 20 µL reaction using 250 nmol/L final primer molarity. As PCR masterrmix 5x Hot FIREPol Blend Mastermix with 7.5 mM MgCl2 (Solis Biodyne, Tartu, Estonia) was used in the amplifications. The following PCR program was used: initial denaturation step at 95°C for 15 min, followed by 30 cycles each consisting of denaturation at 95°C for 30 s, annealing at 60°C for 30 s and polymerization at 72°C for 1 min. The lengths of the final fragments were 214-277 bp, the number of repeats of AR CAG STR was analyzed by fragment analysis. The analysis was not completed in three participants due to a lack of the provided sample material.

Supplementary control analysis

Testosterone effects on control ratings during IoC induction

Besides the main between-subject manipulation of the positive outcome density during IoC induction, we have also experimentally manipulated the outcome density in a within-subject manner (for details, see Methods in the main manuscript). In addition, participants underwent the IoC induction twice - on two separate days with difference of two weeks. This with-subject manipulation allowed as to test intraindividually whether the potential differences in persistence are related to testosterone effects on control perception when the positive outcome denisty is high or low, and whether testsosterone affects the intraindividual difference between perceived control in high- vs low-density coniditions.

To analyze the control ratings, we implemented Generalized linear mixed model (GzLMM) with the predictors treatment group (testosterone/placebo), IoC Induction group (high/low), day (1/2), outcome density (high/medium/low), and their interactions. Outcome density and day were enterd as random slopes. We did not observe any effects of testosterone treatment on control ratings, or testosterone treatment interaction with other predictors (all ps> .138). The analysis confirmed the expectation that the control ratings were overall higher when the density of the positive outcomes was high (M_{high} = 68.6, SD_{high} =12.59) compared to medium (M_{medium} = 37.3, SD_{medium} = 10.71, B = 31.4, p <.001) and low (M_{low} = 14.7, SD_{low} = 10.3, B = 54.1, p <.001).

To assess the differences in control perception across experimental groups, independent of the outcome density condition, we inspected the ratings from the middle of the IoC induction phase, where probability of the light bulb illumination was fixed to 50% for all participants. We performed the GzLMM analysis using treatment contrasts and set the reference level of the outcome density factor to medium level. There was no interaction of the drug treatment and IoC Induction group (B = -0.28, CI = [-2.96, 2.40], p =.838), thus no difference across experimental group were detected.

Reinforcement learning model: sensitivity to win and loss during IoC induction

In the supplementary analysis, we investigated the learning rates $\alpha_{positive}$ and $\alpha_{negative}$ as indicators for participants' sensitivity to positive and negative outcomes during IoC induction, as well as softmax temperature τ as an indication of choice stochasticity. Parameters were entered into a GLMM with a within-subject factor day (*1/2*) and between-subject factors treatment (*placebo/testosterone*), IoC induction group (*high/low*), and a random intercept. The analysis of $\alpha_{positive}$ showed no effect of the testosterone treatment (F(1, 83.89) = 0.038, p = .845), and no effects or interactions of other predictors (all p > .05). The analysis of $\alpha_{negative}$ revealed that the participants weighted less the update of the negative value (F(1,86) = 5.266 , p = .024, ηp^2 =.033), when they played the task on the day 2 (M =.492, SD = 0.396) compared to the day 1 (M =.631, SD = 0.392). The analysis of the noise parameter (softmax temperature) τ showed a significant interaction of the testosterone treatment and testing day (F(1,83.3) = 4.23, p = .043, ηp^2 =.030), such that the choices of the participants in the

testosterone group were noisier on day 2 - after the testosterone administration (M = 7.30, SD = 13.45) than on day 1 – before the testosterone administration (M = 2.87, SD = 13.45).
In addition, CAG-repeat polymorphism interacted with the effect of testosterone treatment on choice noisiness τ (F(1, 80.21) = 4.236, p = .043, ηp^2 =.034), so that testosterone administration on day 2 increased the noisinees τ only among participants with the shorter repeat length (M_{day1} = 2.59, SD $_{day1}$ = 2.83; M_{day2} = 11.61, SD $_{day2}$ = 2.83), whereas the choice noisiness did not change among individual with longer repeat length (M_{day1} = 2.49, SD $_{day1}$ = 2.91; M_{day2} = 2.96, SD $_{day2}$ = 2.91).

Analysis of potential confounding factors and supplementary variables

A supplementary analysis explored whether the number of participants tested simultaneously in the same room influenced testosterone's effect on persistence in competition. The results of a generalized linear model with the factors drug treatment, control rating, and number of the participants showed neither a significant main effect of the number of the participants (B = 0.029, CI = [-0.203, 0.259], p = .804) nor significant interaction with the effects of drug treatment and control rating (B = 0.003, CI = [-0.003, 0.010], p = .349).

After the experimental task was over, the participants were asked, in a written form, to describe their impression of their opponent. Two participants expressed doubts over the existence of the opponent and suspected that their opponent was, in fact, a computer. Excluding these two participants from the analysis of competition persistence did not cause a qualitative change in the results (drug treatment x control rating interaction: B = 0.009, CI = [0.003, 0.015], p = .003).

Participants were also asked to report on a 7-point Likert scale to what extent they found the task frustrating, provoking, or fun. We analyzed these variables using cumulative link models for ordinal regression (Christensen, 2019) with the factors drug treatment and control rating. We found no effect of drug treatment, control rating, or their interaction (all ps > .083, see Table S3).

Repeated Grubbs's test detected three outliers with an exceptionally high number of competition trials: two in the testosterone high IoC and one in the placebo high IoC group. The exclusion of these three participants did not cause a qualitative change in our main finding (drug treatment x control rating interaction: B = 0.438, CI = [0.232, 0.644], p > .001).

Table S 3. The analysis of the self-reported emotions did not show any significant effects of the experimental manipulations.
CI = 95% confidence interval.

	Fun	**Frustrating**		**Provoking**					
Predictors	*Odds Ratios*	*CI*	*p*	*Odds Ratios*	*CI*	*p*	*Odds Ratios*	*CI*	*p*
Control rating	1.00	0.99 – 1.01	0.687	1.01	0.99 – 1.02	0.339	1.01	1.00 – 1.02	0.097
Drug treatment	0.96	0.67 – 1.39	0.847	1.24	0.85 – 1.80	0.266	1.26	0.86 – 1.83	0.229
Control rating*Drug treatment	1.00	0.99 – 1.01	0.433	0.99	0.98 – 1.00	0.083	1.00	0.99 – 1.01	0.803
Observations	88			87			88		
R^2 Nagelkerke	0.009			0.057			0.045		

SM references

Christensen, R. H. B. (2019). ordinal - Regression Models for Ordinal Data. R package version 2019.12-10. https://CRAN.R-project.org/package=ordinal.

Supplementary Materials B for:

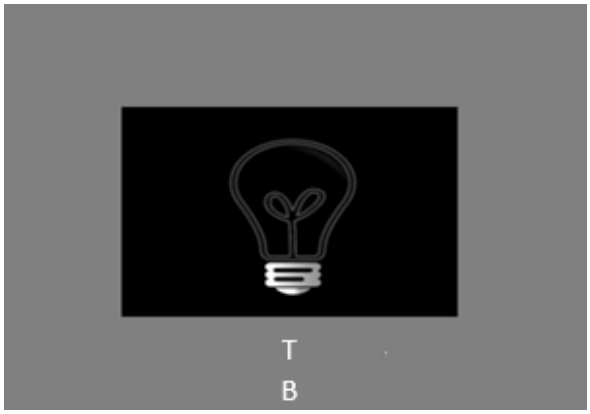
Not giving up: testosterone promotes persistence against a stronger opponent

Hana H. Kutlikova, Shawn N. Geniole, Christoph Eisenegger, Claus Lamm,
Gerhard Jocham, Bettina Studer

Task instructions (original German version)

Aufgabenanweisung

Sie werden gleich ein Spiel am Computer spielen.
Ihre Aufgabe wird es sein, eine abgebildete Glühbirne möglichst häufig zum Erleuchten zu bringen.
In jeder Runde werden Ihnen eine Glühbirne und zwei mögliche Antworttasten „T“ und „B“ gezeigt.



Sie sollen sich in jeder Runde für eine der Tasten entscheiden und diese auf der Tastatur drücken. Sie sehen dann, ob Sie die Glühbirne zum Erleuchten gebracht haben.

Sie erhalten keine Information darüber, wie die beiden Tasten mit dem Erleuchten der Glühbirne zusammenhängen. Es empfiehlt sich also beide Tasten auszuprobieren. D.h. in manchen Runden ist die Taste „T“ und in anderen die Taste „B“ zu wählen.

Das Spiel beinhaltet drei Runden, welche jeweils mehrere Blöcke von Durchgängen beinhalten. Jede Runde hat eine eigene Rahmenfarbe zur Erkennung.

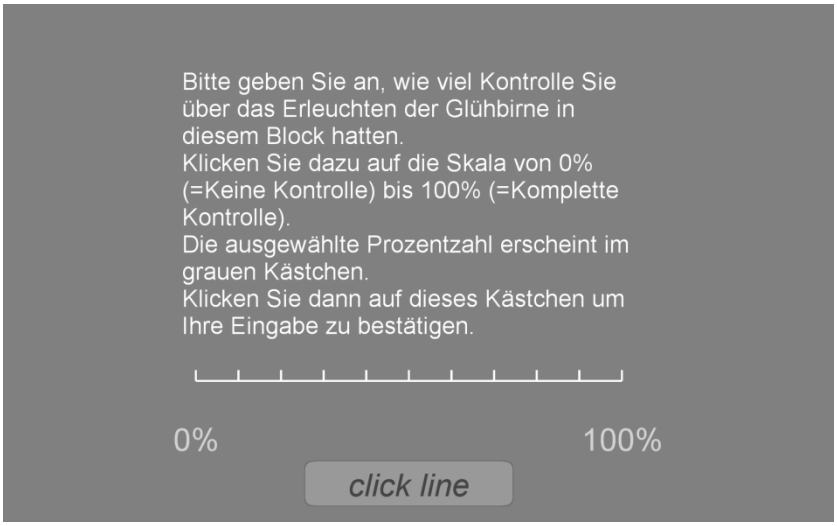
Die Zusammenhänge zwischen den Tasten und dem Erleuchten der Glühbirne können sich in jeder Runde ändern. Sie müssen diese also jedes Mal neu herausfinden.

Jeweils nach einem Block von Durchgängen sollen Sie angeben, wie viel Kontrolle Sie über das Erleuchten der Glühbirne in diesem Block hatten. Dazu benutzen Sie eine Skala von 0% bis 100 %.

0% bedeutet **KEINE Kontrolle**. Das bedeutet, das Erleuchten oder Nicht-Erleuchten der Glühbirne hatte GAR NICHTS mit Ihren Antworten zu tun. Das Erleuchten der Glühbirne war also vollständig durch Zufall bestimmt.

Eine **MITTLERE Kontrolle** bedeutet, dass Ihre Antworten einen Einfluss auf das Erleuchten der Glühbirne hatten, aber Sie dieses nicht vollständig bestimmt haben.

100% bedeutet **KOMPLETTE Kontrolle**. Das bedeutet, das Erleuchten der Glühbirne war komplett durch Ihre Antwort bestimmt.



Nutzen Sie bitte die Maus um die Prozentzahl anzuklicken, für die Sie sich entschieden haben. Sie können Ihre Eingabe ändern, indem Sie erneut eine Zahl auf der Skala anklicken. Wenn Sie die gewünschte Prozentzahl sehen, so klicken Sie auf das Feld mit der Prozentzahlanzeige um fortzufahren.

Wichtiges zum Schluss:

- Denken Sie daran, Ihr Ziel ist es die Glühbirne möglichst oft zum Erleuchten zu bringen!
- Der Zusammenhang zwischen Tasten und Erleuchten der Glühbirne kann in jeder Runde anders sein. Eine neue Runde fängt dann an, wenn die Farbe des Rahmens um die Glühbirne wechselt. Solange die Farbe gleich bleibt, befinden Sie sich noch in der gleichen Runde, auch dann wenn ein neuer Block von Durchgängen anfängt.
- Drücken Sie bitte KEINE ANDEREN Tasten als die, die in den Anweisungen erwähnt werden, da dies Probleme mit dem Programm verursachen könnte.

English translation of task instructions

You are about to play a computer game.

Your task will be to try to illuminate the displayed light bulb as often as possible. In each round, you will see the light bulb and two possible response keys "T" and "B". Please select and press one of these two response keys in each round.

Next, you will see if the light bulb illuminates.

You will not receive any information about the relationship between pressing either key and the illumination of the light bulb. Therefore, it is in your interest to try out both keys, that is to say to choose the "T" key in some trials, and the “B” key in some others.

The game consists of three stages, each of which contains several blocks of rounds. Each stage is signalled by a unique coloured frame. The relationship between the keys and the light bulb illumination can change between stages. Therefore, you must figure this relationship out anew in each new stage.

After a block of rounds, you will be asked to rate the degree of control you think you have had over the illumination of the light bulb on a scale from 0% to 100%.

0% means NO control. Whether or not the light bulb illuminated had NOTHING to do with your button choices, but was entirely determined randomly or by chance.

An INTERMEDIATE level of control means that your button choices influenced the illumination of the light bulb to some extent, but did not completely determine whether or not it illuminated.

100% means COMPLETE control. Having complete control means that the illumination of the light bulb was completely determined by your button choices.

Please use the mouse to click select your answer on the scale indicated on the screen. The selected control percentage will be indicated in the box in the bottom of the screen. You can change your answer by clicking on the scale again. Once you are satisfied with your selection, click on the box showing your answer to submit it.

Important pointers:

- Remember, your goal is to illuminate the light bulb as often as possible!

- The relationship between the response keys and the bulb illumination can be different in each of the three stages of the game. A new stage starts when the color of the frame around the light bulb changes. As long as the color remains the same, you are still in the same stage.

- Please DO NOT press any other keys than those mentioned in the instructions, as this may interfere with the program.

Exploratory analysis of estradiol levels

The post-hoc exploratory analyses reported here were conducted after the publication of the above article, in order to examine whether the salivary levels of the hormone estradiol explained more variance than the drug administration factor (see also General Discussion).

The analysis of the change in the estradiol levels across the duration od the experiment did not show a significant interaction between the factors drug administration and time ($F(4,343) = 0.664$, $p = .617$). Contrary to the drug administration factor (original model, see Methods), including the difference in estradiol levels as a predictor in the linear regression model of persistence did not reveal a significant interaction with the illusory control ($F(1,77) = 0.02$ $p = .889$), nor a main effect of estradiol ($F(1,77) = 0.002$, $p = .962$). The model comparison showed that the original model had a lower RSS value than the model including estradiol levels, indicating that the original model had a better fit ($F(1, 77) = 21.95$, $p < .001$).

Chapter 5

STUDY 4:

WEAK AND VARIABLE EFFECTS OF EXOGENOUS TESTOSTERONE ON COGNITIVE REFLECTION TEST PERFORMANCE IN THREE EXPERIMENTS: COMMENTARY ON NAVE, NADLER, ZAVA, AND CAMERER (2017)

Original manuscript as published in Psychological Science, doi: 10.1177/0956797619885607

Erik L. Knight [a,b,1]*, Blakeley B. McShane[c,1], Hana H. Kutlikova [0]*, Pablo J. Morales [a], Colton B. Christian [a], William T. Harbaugh [e], Ulrich Mayr [a], Triana L. Ortiz [a], Kimberly Gilbert [a], Christine Ma-Kellams[g], Igor Riečanský[0,e], Neil V. Watson [d], Christoph Eisenegger [0,2], Claus Lamm[0], Pranjal H. Mehta [a,e], & Justin M. Carré[a*]

a. Department of Psychology, University of Oregon
b. Center for Healthy Aging, Pennsylvania State University
c. Kellogg School of Management, Northwestern University
d. Department of Basic Psychological Research and Research Methods, University of Vienna
e. Department of Economics, University of Oregon
f. Department of Psychology, Nipissing University
g. Department of Psychology, University of LaVerne
h. Centre of Experimental Medicine, Slovak Academy of Sciences
i. Department of Psychology, Simon Fraser University
j. Department of Experimental Psychology, University College London

*****Correspondence to:
Erik L. Knight: elk24@psu.edu

Hana H. Kutlikova: hana.kutlikova@univie.ac.at

Justin M. Carré: justinca@nipissingu.ca

Notes:
1. Shared first co-authorship
2. Deceased February 27, 2017

Abstract

Nave and colleagues (2017) presented a single experiment (*n*=243) finding that exogenous testosterone caused a decrease in performance on the Cognitive Reflection Test (CRT) by increasing intuitive-but-incorrect responses. We report three new experiments (total *n*=628) that also examine the effect of exogenous testosterone on CRT performance. When pooling the data across experiments, we find (i) substantial variation in CRT performance across experiments, treatment groups, and participants and (ii) variable treatment effects of testosterone on CRT performance across experiments with any average effect being weak relative to this underlying variability – regardless of whether we considered the three new experiments or all four. Given our modeling assumptions, an average treatment effect of a 7% decrease in the odds of correctly responding to a CRT item is the value most compatible with the data from the three new experiments; however, anything from a 53% decrease to a 99% increase is also reasonably compatible. Similarly, a 27% decrease is the value most compatible with the data from all four experiments; however, anything from a 62% decrease to a 58% increase is also reasonably compatible. We explore potential explanations for the pattern of results observed across the four experiments.

Keywords: exogenous testosterone; cognitive reflection; replication; meta-analysis

Introduction

Testosterone is associated with behaviors such as aggression, sensation seeking, and impulse control disorders, including drug addiction and eating disorders, but if and how testosterone affects cognition and decision-making remains unclear. Given the role of testosterone in mating and reproduction, Nave, Nadler, Zava, and Camerer (2017; hereafter NNZC) suggested the "facilitation of rapid intuitive responses by testosterone could be biologically adaptive in contexts in which reproductive success depends on instincts (e.g., during copulation) and when responding slowly might be especially costly (e.g., during physical challenges)" (p. 1404). This led them to hypothesize that testosterone biases decision making away from reflective and deliberate responses and toward rapid and intuitive ones, thereby elucidating one potential mechanism by which testosterone might cause behaviors such as aggression, sensation seeking, and impulse control disorders.

To study their hypothesis, NNZC conducted a single experiment (n=243) in which they randomly administered either exogenous testosterone or placebo to participants and then measured their performance on the Cognitive Reflection Test (CRT), a simple three-item assessment of intuitive versus deliberate decision making (Frederick, 2005). Each CRT item has an intuitive but incorrect response with which most people respond; discerning the correct response requires one to inhibit this intuitive response and to perform deliberate but easy calculations. For example, one item reads

> *In a lake, there is a patch of lily pads. Every day, the patch doubles in size. If it takes 48 days for the patch to cover the entire lake, how long would it take for the patch to cover half of the lake?*

When asked this question, many people automatically respond with the perhaps intuitive but ultimately incorrect response of 24 days; discerning the correct response (47 days) requires inhibiting the automatic response and deliberating on the question. Consistent with their hypothesis, the NNZC experiment found that exogenous testosterone caused a decrease in performance on the CRT by increasing intuitive-but-incorrect responses.

We report three new experiments (total n=628) that also examine the effect of exogenous testosterone on CRT performance. When pooling the data across experiments, we find (i) substantial variation in CRT performance across experiments, treatment groups, and participants and (ii) variable treatment effects of testosterone on CRT performance across experiments with any average effect being weak relative to this underlying variability – regardless of whether we considered the three new experiments or all four. We explore potential explanations for the pattern of results observed across the four experiments.

Materials for the three new experiments; data from the three new experiments and the original NNZC experiment; and code that implements all analyses presented in this manuscript and in our Supplementary Online Materials, which provides further detail on Methods, Results, and other matters related to this manuscript, are available at https://osf.io/6ppdv/. Materials for and data from the original experiment were obtained from the corresponding publication, supplemental materials (https://osf.io/79r2v), and personal communication with Nave.

Methods

The three new experiments were designed independently of and executed prior to the publication of NNZC and therefore differ with one another and with NNZC with regards to the experimental design as discussed below (Table S1). Like NNZC, these experiments included tasks completed prior to the CRT as part of larger protocols, including competitive and pro-social decision-making tasks (Experiment 1); an aggression task and public goods game (Experiment 2); and emotion recognition tasks, empathy tests, and pro-social decision-making tasks (Experiment 3).

Testosterone versus Placebo Administration

Exogenous testosterone or placebo was administered to three samples of men aged 18-41 (Experiment 1: *n*=116, Oregon, USA; Experiment 2, *n*=396, Ontario, Canada; Experiment 3, *n*=116, Bratislava, Slovakia) prior to the CRT topically (150-mg dose, Experiments 1 and 3) or intranasally (11-mg dose, Experiment 2).

Cognitive Reflection Task

Each of the three new experiments presented the CRT items in random order. Experiment 3 presented them in Slovak, the native language of the participants. Experiments 1 and 2 did not include financial incentives for CRT performance, but, in an effort to increase attention and engagement with the task Experiment 3 did as did NNZC; specifically, Experiment 3 paid €0.30 per correct response, a value chosen to reflect the local, part-time job salary for students (€4 per hour at the time of experiment). We note that financial incentives may improve effort but not performance in laboratory experiments, or they may improve performance only for individuals with higher cognitive skills (Camerer & Hogarth, 1999). Consistent with this reasoning, a large-scale meta-analysis suggests that financial incentives do not impact CRT performance (Brañas-Garza et al., 2015).

Methodological Difference Variables

Experimental Manipulations

All manipulations in the three new experiments were randomized and administered prior to the CRT. Two of the experiments included manipulations in addition to testosterone or placebo. Experiment 1

manipulated blinding by informing half of all participants (*n*=58) whether they had been assigned to testosterone or placebo; experimenters remained fully blind. Experiment 3 assigned participants to one of two experimental stressors (cold pressor, *n*=39; a socially-evaluated cold pressor, *n*=37) or control (warm pressor, *n*=40).

Experimenter Gender

Experiments 1 and 2 used male and female experimenters while Experiment 3 used female only; NNZC used male only. Prior work suggests that experimenter gender may alter testosterone levels and behavior in young men in an ecological setting (Ronay & von Hippel, 2010). Other work has shown such experimenter gender effects may generalize to a laboratory setting, but the effects may be weaker and may depend on the time of day (Roney et al., 2007). To our knowledge, no experiment has found that experimenter gender impacts the effect of testosterone treatment on behavior.

Time of Day

The new experiments administered the CRT at a range of times from approximately 11:00 AM to 7:00 PM; NNZC administered it at approximately 4:00 PM. In all experiments, the CRT was administered in the time period that pharmacokinetic analyses suggest should coincide with peak testosterone levels for each method (Eisenegger et al., 2013; Geniole et al., 2019). Although testosterone levels fluctuate with a diurnal rhythm, whether the time of day impacts the effect of testosterone treatment on CRT performance is unknown.

In sum, the three new experiments administered testosterone or placebo prior to the CRT like NNZC, but they differed with one another and with NNZC with regard to some details. These differences provide a valuable opportunity to examine the generalizability of the NNZC finding regarding the effect of testosterone treatment on CRT performance across diverse experimental populations and designs as well as heterogeneity in the treatment effect that may result from these or other unknown factors – an important consideration when conducting replications of psychological research studies (McShane et al., 2019).

Individual Difference Variables

Prior research reports that several individual difference variables including basal cortisol, the ratio between the lengths of the second and fourth digits (2D:4D ratio), and trait impulsivity may affect the relationship between testosterone and social cognition and behavior. Although these variables have not been examined in studies of the effect of testosterone on CRT performance, exploring their effects may provide insight into potential moderators that could be investigated in future studies.

Basal Cortisol

A recent meta-analysis suggests that testosterone is more strongly associated with status-relevant behavior when cortisol levels are low, though heterogeneity is evident in the direction and magnitude of this interaction effect across studies (Dekkers et al., 2019). In the three new experiments, basal cortisol was measured prior to testosterone or placebo administration.

2D:4D Ratio

The 2D:4D ratio is believed to be associated with prenatal testosterone exposure, which in turn may moderate the effects of testosterone administration on socio-cognitive behavior among men. Accordingly, prior work has reported reduced empathic accuracy in individuals with lower 2D:4D ratios (van Honk et al., 2011; Carré et al., 2015). In the three new experiments, participants' left and right hands were scanned on a flatbed scanner; trained research assistants digitally measured the lengths of the second and fourth digits between the ventral proximal creases of the digits to the fingertips.

Trait Impulsivity

Recent work reports that the effect of testosterone on reactive aggression is associated with trait impulsivity (Carré et al., 2017; Geniole et al., 2019). In the three new experiments, trait impulsivity was measured via three questionnaires: Experiment 1 used the impulsivity subscale of the Zuckerman-Kuhlman Impulsive Sensation-Seeking Scale (Zuckerman et al., 1993); Experiment 2 used a summed composite of the Barrett Impulsivity (Patton et al., 1995) and Brief Self-Control Scale (Tangey et al., 2004); and Experiment 3 used the fun-seeking subscale of the Behavioral Inhibition/Behavior Activation Scales (Carver & White, 1994).

Models

Primary

To estimate the effect of testosterone treatment on CRT performance, we meta-analyzed the data from the three new experiments as well as all four experiments by fitting a multilevel logistic regression to the response of each participant to each CRT item (Correct=1, Incorrect=0) jointly (McShane and Böckenholt, 2017; 2018). The model treated effects for the interaction of each item and primary treatment condition (i.e., testosterone or placebo) as "fixed" and effects for (i) each experiment across all items, (ii) each experiment for each item, (iii) each treatment group (i.e., primary treatment condition crossed with blinding or stressor condition as applicable) across all items, (iv) each treatment group for each item, and (v) each participant across all items as "random." We also expanded the model to directly compare the degree to which the treatment effect pooled across the three new experiments differed from the treatment effect in NNZC.

Secondary

For comparability with NNZC, we also meta-analyzed aggregated data. Specifically, we fit a multilevel linear regression specified *mutatis mutandis* analogously to our primary model to the score of each participant (i.e., number of CRT items correct out of three).

We also expanded the primary model to include covariates included by NNZC, namely age, treatment expectancy, right hand 2D:4D ratio, basal cortisol levels, positive/negative affect (Experiments 1, 3, and NNZC only), and mathematics aptitude (Experiment 1 and NNZC only). Like NNZC, we also report the effect of testosterone treatment separately for each CRT item as well as the effect on intuitive-but-incorrect responses (1=intuitive-but-incorrect, 0=all other responses) instead of correct responses.

We also examined potential moderators of the effect of testosterone on CRT performance. We did so for methodological differences across the experiments in two ways: (i) by re-fitting our primary model with the single-blind and stressor groups removed from Experiments 1 and 3 respectively and (ii) by expanding our primary model to include the interaction of each item, primary treatment condition, and various methodological difference variables [experimenter gender, time of day, experimental blinding conditions (Experiment 1), and experimental stressor conditions (Experiment 3)]. We did so for individual difference variables (basal cortisol, right- and left-hand 2D:4D ratio, and trait impulsivity) by expanding the model to include interactions in the same manner.

Models fit to subsets of experiments (e.g., because one or more did not measure a given variable) were specified analogously to our primary model with effects treated as random removed when they were not identified.

Estimation

We estimate all models in a fully Bayesian manner (Gelman, et al., 2013) and present point and 95% interval estimates for each coefficient or effect of interest. All estimates are presented on the scale of a logistic regression coefficient unless otherwise noted, with point estimates given by the median of the estimated posterior distribution and interval estimates given by the 2.5 and 97.5 percentiles. Positive estimates imply better CRT performance.

Results

Distributions of CRT Performance

Experiments differed in terms of CRT performance as reflected in the mean (**Table S2**) and the distribution of the scores of the participants (**Figure S1** and **Table S3**) with lower performance in the three new experiments as compared to NNZC. The distributions in the three new experiments were relatively more similar to the distribution in a large meta-analysis (Brañas-Garza et al., 2015) whereas the distribution in NNZC was relatively more similar to the distributions in the highest performing samples in prior research (e.g., MIT and Princeton students; Frederick, 2005; Iyer et al., 2012).

Primary

We begin by discussing the estimates of the variance components from our primary model as they inform our discussion of the estimates of the treatment effect. These estimates indicated substantial variation in CRT performance from (i) experiment to experiment, thus reflecting the differences in CRT performance across experiments discussed above; (ii) treatment group to treatment group, thus reflecting differences in the treatment effect from experiment to experiment; and (iii) participant to participant, thus reflecting individual differences in CRT performance – regardless of whether we considered the three new experiments or all four (Table S4).

To illustrate the extent of this variation, we use our point estimates of the variance components to create three comparisons that correspond to each of the above three points respectively and that are scaled relative to the point estimate of the meta-analytic average treatment effect. First, the difference in CRT performance from experiment to experiment was estimated to be 15.50 times larger than the meta-analytic average treatment effect when we considered the three new experiments or 4.01 times larger when we considered all four. Second, the difference in the treatment effect from experiment to experiment was estimated to be 6.71 times larger than the meta-analytic average treatment effect when we considered the three new experiments or 2.05 times larger when we considered all four. Third, the difference in CRT performance from participant to participant was estimated to be 46.25 times larger than the meta-analytic average treatment effect when we considered the three new experiments or 10.20 times larger when we considered all four. We note the larger relative estimates when we considered the three new experiments as compared to all four do not so much reflect differences in the estimates of the variance components; instead, they primarily reflect the scaling by the estimate of the meta-analytic average treatment effect, which, as we discuss immediately below, was considerably smaller when we considered the three new experiments as compared to all four.

Given this degree of variation, the meta-analytic average treatment effect was unsurprisingly estimated with considerable uncertainty regardless of whether we considered the three new

experiments (*Point Estimate*: -0.07; *95%CI*: [-0.76, 0.69]; Figure 1 and Table S4) or all four (-0.32; [-0.96, 0.46]; Figure 1 and Table S4). Put differently, given our modeling assumptions, an average treatment effect of a 7% decrease in the odds of correctly responding to a CRT item is the value most compatible with the data from the three new experiments; however, anything from a 53% decrease to a 99% increase is also reasonably compatible. Similarly, a 27% decrease is the value most compatible with the data from all four experiments; however, anything from a 62% decrease to a 58% increase is also reasonably compatible. A comparison of the treatment effect in the three new experiments to the treatment effect in NNZC within our modeling framework also resulted, again unsurprisingly, in an estimate with considerable uncertainty (-1.01; [-2.44, 0.53]; Table S6); while the point estimate suggests a stronger (i.e., more negative) treatment effect in NNZC as compared to the three new experiments, a similar or even weaker treatment effect is also reasonably compatible with the data from all four experiments given our modeling assumptions.

In sum, our results suggest variable treatment effects of testosterone on CRT performance across experiments with any average effect being weak relative to this underlying variability.

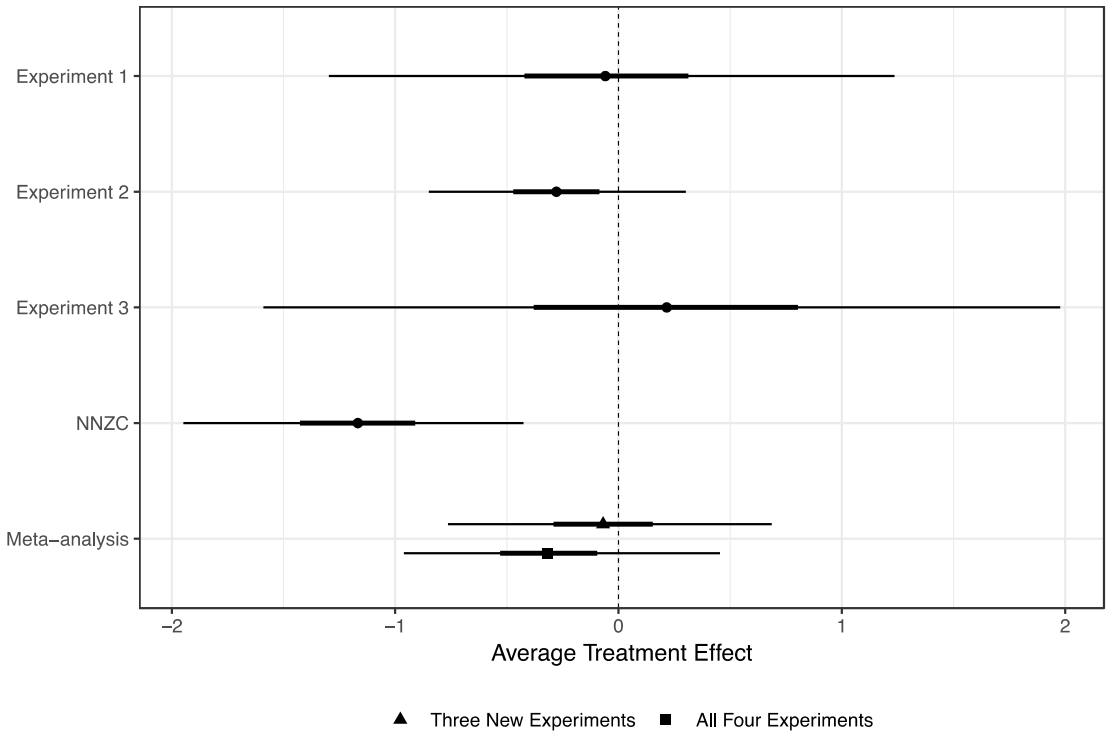


Figure 1. Primary Results. Point estimates are given by the points; 50% and 95% interval estimates are given by the thick and thin lines, respectively. Estimates are based on models fit to data from each experiment separately and based on our primary meta-analytic model fit to the data from the experiments jointly (Tables S4-S5).

Secondary

CRT Score

The multilevel linear regression fit to the score of each participant (i.e., number of CRT items correct out of three) yielded results in line with those presented above (Table S7). Variance component estimates again indicated substantial variation across experiments, treatment groups, and participants. The meta-analytic average treatment effect was again estimated with considerable uncertainty regardless of whether we considered only the three new experiments (-0.03; [-0.31, 0.28]) or all four (-0.13; [-0.39, 0.21]). Put differently, given our modeling assumptions, an average treatment effect of a 0.03 point decrease in the score is the value most compatible with the data from the three new experiments; however, anything from a 0.31 point decrease to a 0.28 point increase is also reasonably compatible. Similarly, a 0.13 point decrease is the value most compatible with the data from all four experiments; however, anything from a 0.39 point decrease to a 0.21 point increase is also reasonably compatible.

Covariates, Individual Item Responses, and Intuitive-but-Incorrect Responses

Results remained substantively similar when including covariates included by NNZC (Table S8). Results also remained substantively similar when the meta-analytic average treatment effect was broken down at the CRT item-level (Table S4). Finally, results remained substantively similar when examining the effect of testosterone on intuitive-but-incorrect (as opposed to correct) responses both on average and at the item-level (Figure S2 and Table S9).

Methodological Difference Variables

Estimates of variance components and the meta-analytic average treatment effect remained substantively similar to those from the primary model when we excluded the single-blind and stressor groups from Experiments 1 and 3 respectively (Table S10); the result concerning the stability of the variance component estimates is particularly notable because it suggests our conclusions regarding differences in the treatment effect from experiment to experiment are not driven by the single-blind or stressor conditions of the respective experiments. In addition, methodological difference variables showed no substantial moderating effects (Table S11).

Individual Difference Variables

Individual difference variables showed no substantial moderating effects (Table S12) but the results may suggest a moderating effect of trait impulsivity. Specifically, the effect of testosterone on CRT performance may be associated with trait impulsivity, with a potential negative treatment effect at lower levels of trait impulsivity and a potential positive treatment effect at higher levels of trait impulsivity (0.52; [0.06, 0.99]; Figure S3 and Table S12).

Discussion

NNZC presented a single experiment suggesting that exogenous testosterone causes a decrease in CRT performance. We report three new experiments that also examine the effect of exogenous testosterone on CRT performance. When pooling the data across experiments, we find (i) substantial variation in CRT performance across experiments, treatment groups, and participants and (ii) variable treatment effects of testosterone on CRT performance across experiments with any average effect being weak relative to this underlying variability – regardless of whether we considered the three new experiments or all four. The extent of this relative variability suggests the notion of *the* effect of testosterone on CRT performance is not particularly meaningful. Instead, to the degree that testosterone does affect CRT performance, potential moderators that drive this variability would seem to be of greater interest.

Our results suggest two possible moderators. First, CRT performance in the three new experiments was relatively more similar to that in a large meta-analysis whereas CRT performance in NNZC was relatively more similar to that in the highest performing samples in prior research. It is therefore possible that testosterone causes impaired CRT performance only in high performing populations. Second, our results suggest that trait impulsivity may moderate the effect of testosterone on CRT performance with a potential negative treatment effect at lower levels of trait impulsivity and a potential positive treatment effect at higher levels of trait impulsivity. This finding may be related to recent work suggesting that trait impulsivity moderates the effect of testosterone on reactive aggression but with a positive treatment effect at lower levels of trait impulsivity and a negative treatment effect at higher levels of trait impulsivity (Carré et al., 2017; Geniole et al., 2019).

It is perhaps of interest to consider these two possible moderators jointly and alongside prior work linking high CRT performance with low trait impulsivity (Frederick, 2005). Specifically, although trait impulsivity was not measured in NNZC, the participants in that higher performing sample may have been less impulsive and therefore more vulnerable to any negative effect of testosterone on CRT performance as compared to participants in the three new experiments. Nonetheless, this would suggest that testosterone causes impaired CRT performance only in populations low in trait impulsivity.

However, we urge due caution in interpreting our moderation results particularly given the number of experiments, the sample sizes of the experiments, and the number of moderator variables examined. We also note we examined the moderating effects only of variables studied either in NNZC or in testosterone research more broadly; other variables may moderate the effect of testosterone on CRT performance. Nonetheless, insofar as future research continues to examine the effects of testosterone

treatment on cognitive reflection – perhaps in search of such moderators – our results suggest something akin to a "one phenomenon, many labs" approach that features systematic variation of methodological difference variables and examines potential moderating effects of relevant variables in larger and more diverse samples seems necessary (McShane et al., 2019).

Author Contributions

Experiment 1: E.L. Knight, U. Mayr, W.T. Harbaugh, P.H. Mehta designed the experimental protocol, with input specific to the CRT from C. Ma-Kellams; E.L. Knight, C.B. Christian, P.J. Morales executed data collection. Experiment 2: J.M. Carré, T.L. Ortiz, N.V. Watson designed the experimental protocol; T.L. Ortiz performed hormone assays; T.L. Ortiz & K. Gilbert executed data collection. Experiment 3: H.H. Kutlikova, I. Riečanský, C. Eisenegger, C. Lamm designed the experimental protocol; H.H. Kutlikova executed data collection. E.L. Knight and B.B. McShane analyzed data for the manuscript. E.L. Knight wrote the initial manuscript; E.L. Knight and B.B. McShane wrote the revised manuscript(s). J.M. Carré, P.H. Mehta, J.M. Carré and H.H. Kutlikova wrote segments specific to their respective experiments in the Supplementary Online Materials methods section. All surviving authors approved the final version of the manuscript for submission. Please see Supplementary Online Materials for acknowledgements.

Funding

Experiment 1 was supported by National Science Foundation grants to PHM (#1451848) and to WTH and UM (#1063561). Experiment 2 was supported by funds from the Natural Sciences and Engineering Research Council of Canada to JMC (RGPIN-2014-06676), a Northern Ontario Heritage Fund Corporation grant to JMC, and a Discovery Grant (RGPIN-2016-05706) from the Natural Sciences and Engineering Research Council of Canada to NVW. Experiment 3 was supported by the Vienna Science and Technology Fund (WWTF VRG 13-007). ELK is partially supported by a National Institute on Aging Grant AG049676 to The Pennsylvania State University.

References

Brañas-Garza, P., Kujal, P., & Lenkei, B. (2015). Cognitive Reflection Test: Whom, how, when (ESI Working Paper 15-25). Retrieved from https://mpra.ub.uni-muenchen.de/68049/

Camerer, C. F., & Hogarth, R. M. (1999). The effects of financial incentives in experiments: A review and capital-labor-production framework. *Journal of risk and uncertainty*, *19*(1-3), 7-42.

Carré, J. M., Geniole, S. N., Ortiz, T. L., Bird, B. M., Videto, A., & Bonin, P. L. (2017). Exogenous testosterone rapidly increases aggressive behavior in dominant and impulsive men. *Biological psychiatry*, *82*(4), 249-256.

Carré, J. M., Ortiz, T. L., Labine, B., Moreau, B. J., Viding, E., Neumann, C. S., & Goldfarb, B. (2015). Digit ratio (2D: 4D) and psychopathic traits moderate the effect of exogenous testosterone on socio-cognitive processes in men. *Psychoneuroendocrinology*, *62*, 319-326.

Carver, C. S., & White, T. L. (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: The BIS/BAS Scales. *Journal of personality and social psychology*, *67*(2), 319.

Dekkers, T. J., van Rentergem, J. A. A., Meijer, B., Popma, A., Wagemaker, E., & Huizenga, H. M. (2019). A meta-analytical evaluation of the dual-hormone hypothesis: Does cortisol moderate the relationship between testosterone and status, dominance, risk taking, aggression, and psychopathy? *Neuroscience and Biobehavioral Reviews*, *96*, 250-271.

Eisenegger, C., von Eckardstein, A., Fehr, E., & von Eckardstein, S. (2013). Pharmacokinetics of testosterone and estradiol gel preparations in healthy young men. *Psychoneuroendocrinology*, *38*(2), 171-178.

Frederick, S. (2005). Cognitive reflection and decision making. *J Econ Perspect*, *19*(4), 25-42.

Gelman, Andrew, Carlin, John B., Stern, Hal S., Dunson, David B., Vehtari, Aki, and Rubin, Donald B. (2013). *Bayesian Data Analysis*. Chapman and Hall/CRC, Boca Raton.

Geniole, S.N., Procyshyn, T.L., Marley, N., Ortiz, T.L., Bird, B.M., Marcellus, A.L., Welker, K.M., Bonin, P.L., Goldfarb, B.,Watson, N.V. & Carré, J.M. (2019). Using a psychopharmacogenomic approach to identify the pathways through which and people for whom testosterone promotes aggression. *Psychological Science*, *30*(4), 481-494.

van Honk, J., Schutter, D. J., Bos, P. A., Kruijt, A. W., Lentjes, E. G., & Baron-Cohen, S. (2011). Testosterone administration impairs cognitive empathy in women depending on second-to-fourth digit ratio. *Proceedings of the National Academy of Sciences*, *108*(8), 3448-3452.

Iyer, R., Koleva, S., Graham, J., Ditto, P., & Haidt, J. (2012). Understanding libertarian morality: The psychological dispositions of self-identified libertarians. *PloS One*, *7*(8), e42366.

McShane, B. B., & Böckenholt, U. (2017). Single-paper meta-analysis: Benefits for study summary, theory testing, and replicability. *J Consum Res*, *43*(6), 1048-1063.

McShane, B.B. and Böckenholt, U. (2018) Multilevel Multivariate Meta-analysis with Application to Choice Overload. *Psychometrika*, *83*(1), 255-271.

McShane, B. B., Tackett, J. L., Gelman, A., & Bockenholt, U. (2019). Large scale replication projects in contemporary psychological research. *The American Statistician*, *73:sup1*, 99-105.

Nave, G., Nadler, A., Zava, D., & Camerer, C. (2017). Single dose testosterone administration impairs cognitive reflection in men. *Psychological Science*, *28*(10), 1398-1407.

Patton, J. H., & Stanford, M. S. (1995). Factor structure of the Barratt impulsiveness scale. *Journal of Clinical Psychology*, *51*(6), 768-774.

Ronay, R., & Hippel, W. V. (2010). The presence of an attractive woman elevates testosterone and physical risk taking in young men. *Soc Psychol and Personal Sci*, *1*(1), 57-64.

Roney, J. R., Lukaszewski, A. W., Simmons, Z. L. (2007). Rapid endocrine responses of young men to social interactions with young women. *Hormones and Behavior*, *52*, 326–333.

Tangney, J. P., Baumeister, R. F., & Boone, A. L. (2004). High self-control predicts good adjustment, less pathology, better grades, and interpersonal success. *Journal of Personality*, *72*(2), 271-324.

Zuckerman, M., Kuhlman, D. M., Joireman, J., Teta, P., & Kraft, M. (1993). A comparison of three structural models for personality: The Big Three, the Big Five, and the Alternative Five. *Journal of personality and social psychology*, *65*(4), 757.

Supplementary Materials for:

Weak and variable effects of exogenous testosterone on cognitive reflection task performance in three experiments: Commentary on Nave et al. (2017)

Erik L. Knight, Blakeley B. McShane, Hana H. Kutlikova, Pablo J. Morales, Colton B. Christian, William T. Harbaugh, Ulrich Mayr, Triana L. Ortiz, Kimberly Gilbert, Christine Ma-Kellams, Igor Riečanský, Neil V. Watson, Christoph Eisenegger, Claus Lamm, Pranjal H. Mehta, & Justin M. Carré

Acknowledgements

Due to space constraints in the main text we were unable to thank the long list of colleagues and collaborators who assisted on our three experiments. Experiment 1: We thank Smrithi Prasad, Bethany Lassetter, Cassandra Brandes, Jason Isbell, and Jeffrey Whitaker for their help with data collection and Craig Davidson for his medical advice. We are grateful for input from Jennifer Lerner on testosterone and the CRT. Experiment 2: We thank Caelan Mathers, Emily Jeanneault, Nicole Marley, Kendra Maracle, Victoria Bass-Parcher, Nadia Desrosiers, Charlotte Miller, Brittney Robinson, Dalton Rogers, Megan Phillips, Brandon Reimer, Camille Gray, Christine Jessamine, and Brandon Reimer for their help with data collection and Dr. Pierre Bonin and Dr. Bernard Goldfarb for providing medical supervision. Experiment 3: We thank Jaroslava Babková Durdiaková and Karina Rerichová for their help with data collection and Bernhard Wagner and Miriam Ehrnhoefer-Ressler for their help with hormone assays. We thank Dusti Jones for helpful comments on the manuscript.

Methods

The three new experiments were designed independently of and executed prior to the publication of Nave et al. (2017) and therefore differ with one another and with Nave et al. with regards to the experimental design as discussed below. See Table S1 for a summary.

Participants

Experiment 1. Participants were recruited on and around the University of Oregon campus via emails to campus listservs and flyers placed around campus. Interested participants were screened via telephone for medical conditions that would prevent participation in the experiment (see Knight et al., (2017) for details). These conditions included mental illness, including recurrent major depression, antisocial personality disorder, schizophrenia, bipolar disorder, Tourette's syndrome, conduct disorder, serious emotional disturbance, and intermittent explosive disorder; physical health conditions, including any hormone or immune disorder, autonomic disorders, liver, heart, lung, obstructive respiratory, kidney, cerebrovascular disease, metabolic syndrome, and diabetes; alcohol and drug dependencies, including any use of anabolic steroids; and any neurological disorders. Participants arrived at the laboratory between 9:00 and 11:00 AM for a daylong protocol and consisted of undergraduate students (91%), graduate students (3%), and non-students (6%).

Experiment 2. Participants were recruited from two cities in Northern Ontario via flyers placed around college and university campuses and online advertisements (Facebook and Kijiji). Interested participants were screened via telephone for medical conditions that would prevent participation in the

experiment. Participants were excluded from the experiment if they were not between the ages of 18 and 40; on a sports team where testosterone is a banned substance; drug or alcohol dependent; on any prescription medication known to interfere with steroid hormone concentrations including corticosteroids, anabolic steroids; had a medical condition including prostate cancer, diabetes, or a heart condition; or had then been diagnosed with any developmental or psychological disorders including schizophrenia, bipolar disorder, borderline personality disorder, anxiety disorder, depression, PTSD, obsessive compulsive disorder, attention deficit hyperactive disorder, panic disorder. Participants arrived at the laboratory between 10:00 AM and 5:30 PM for a 2-hour long protocol and consisted of university students (39%), community-college students (37%), and non-students (24%).

Experiment 3. Participants were recruited in Bratislava, Slovakia via flyers placed around university campuses, and online advertisements (Facebook). Interested participants were screened via online questionnaire and telephone for medical conditions that would prevent participation in the experiment. These conditions included mental illness, including major depression, antisocial personality disorder, schizophrenia, bipolar disorder; physical health conditions, including any hormone disorder, autonomic disorders, liver, heart, lung, cerebrovascular disease, obesity, and diabetes; alcohol or drug dependencies, including any use of anabolic steroids or corticosteroids; and any neurological disorders. Participants arrived at the laboratory between 12:00 and 2:45 PM for a four hour-long protocol and consisted of undergraduate students (53%), graduate students (34%), and non-students (14%).

Testosterone versus Placebo Administration

The testosterone administration methods differed across the three experiments. Consequently, the rate at which the testosterone absorbed into the blood stream and traversed the blood-brain barrier to affect the central nervous system (i.e., the pharmacokinetics or pK) likely differed as well.

Experiment 1. Testosterone was administered via a 150-mg dose of the topical testosterone gel, Androgel (AbbVie, Chicago, IL). A placebo gel was created in a local compounding pharmacy to exactly match the vehicle of the testosterone gel; the only difference between the two gels was that the placebo lacked testosterone. Testosterone and placebo gels were randomized into individual doses within amber colored blunted-tip syringes. Participants rubbed the gel onto their upper arms and shoulders in small increments until the full sample was rubbed into their skin. Prior pharmacokinetic research showed peak testosterone concentrations as well as physiological differences occurred between three and six hours after testosterone gel application (Eisenegger et al., 2013; Tuiten et al., 2000). Participants waited three hours in the laboratory prior to beginning lab tasks.

Experiment 2. Testosterone was administered via an 11-mg dose of intranasal testosterone gel, Natesto (Acerus Pharmaceuticals Corporation, Mississauga, Ontario). A placebo gel was created in a local compounding pharmacy to exactly match the vehicle of the testosterone gel; the only difference between the two gels was that the placebo lacked testosterone. Testosterone and placebo gels were randomized into individual doses within amber colored blunted-tip syringes. Under the supervision of a research assistant (blind to drug condition), participants self-administered 11-mg of gel into their nostrils (5.5-mg per nostril). Pharmacokinetic research with hypogonadal men indicates that 11-mg of Natesto increases serum testosterone concentrations within 30 mins of application (Geniole et al., 2019). Further, research on healthy eugonadal men indicates that administration of 11-mg intranasal

testosterone gel (Natesto) increased serum testosterone within fifteen minutes ($M_{increase}$ = 47.76%, Cohen's d = 1.41) and it remained elevated up to three hours post application (Geniole et al., 2019).

Experiment 3. Testosterone was administered via a topical cream that contained a 150-mg dose of testosterone (Euro OTC Pharma GmbH, Bönen, Germany). Both testosterone and placebo gel were created in a local compounding pharmacy; the only difference between the two creams was that the placebo cream lacked testosterone. Testosterone and placebo creams were randomized into individual doses within disposable plastic containers. Participants rubbed the cream onto their upper arms and shoulders in small increments until the full sample was rubbed into their skin. Participants waited two hours in the laboratory prior to beginning lab tasks.

Endocrine concentration measurement

Experiment 1. Participants were asked to drool approximately 2 mL of saliva directly into a polyethylene tube at three time points: at baseline, prior to gel application; three hours after gel application; and immediately after the cognitive reflection task (CRT; Frederick, 2005; see Knight et al., 2017 for details and analyses on later samples). Saliva samples were immediately frozen on site. In order to assay testosterone and cortisol concentrations, samples were thawed and refrozen into approximately 500 µL aliquots. Hormones were assayed via commercially available enzyme immunoassay (EIA) kits according to the kits' instructions (DRG International).

Testosterone concentrations were outside the maximum value in 26.9% of samples from those assigned testosterone (0% of those assigned placebo; 13.8% of all participants). For these samples, the concentration was replaced with the kit's maximum value of 5250 pg/mL. This conservative data replacement strategy produces a low-end estimate of the average testosterone concentration among participants treated with testosterone and thus of any differences between testosterone and placebo groups.

Experiment 2. Participants were asked to drool approximately 2 mL of saliva directly into a polystyrene tube at baseline (pre-drug) and at the end of the experiment (post-drug). Hormones were assayed via commercially available EIA kits (DRG International). Although previous research indicates that 11-mg Natesto increases serum testosterone concentrations to within the high-normal range (Geniole et al., 2019), our unpublished work indicates that a substantial number of saliva samples from men receiving Natesto had salivary testosterone values that were outside the maximum value measured by the EIA kit (1,000 pg/mL). Thus, for Experiment 2, post-drug saliva samples from men assigned to testosterone were diluted prior to performing the assay, enabling us to estimate testosterone concentrations within the effective range of the EIA kit.

Experiment 3. Participants were asked to drool approximately 2 mL of saliva directly into a polyethylene tube at baseline and 2.5 hours after cream application. Saliva samples were immediately frozen on site and kept at -30°C until analysis. Testosterone, cortisol, and androstenedione were measured by liquid chromatography tandem mass spectrometry (LC-MS/MS; Experiment 3) using an Agilent 6460 with electrospray ionization coupled to a 1290 UHPLC system. 100 µl internal standards (5 ng/mL) were added to 500µl plasma or saliva and the steroids were extracted using 4 mL MTBE. After ten minutes overhead shacking, the samples were centrifuged for five minutes at 3000 rpm, and the top MTBE layer was transferred to a test tube. MTBE was evaporated using a centrivap concentrator (Labconco). The residual sample was then re-dissolved in 30% methanol and analyzed by LC-MS/MS. Agilent Poroshell 120 EC-C18 was used for chromatographic separation.

Cognitive Reflection Task

Each of the three new experiments presented the CRT items in random order. Experiment 3 presented them in Slovak, the native language of the participants (professional translation into Slovak and a back translation into English are included as part of these Supplementary Online Materials). Experiments 1 and 2 did not include financial incentives for CRT performance; Experiment 3 paid €0.30 per correct response, a value chosen to reflect the local, part-time job salary for students (€4 per hour at the time of experiment).

Methodological Difference Variables

Experimental Manipulations. All manipulations in the three new experiments were randomized and administered prior to the CRT. Two of the experiments included manipulations in addition to testosterone or placebo. Experiment 1 randomly assigned participants to one of two blinding conditions (i.e., single versus double) in addition to testosterone versus placebo. To produce the blinding conditions, each participant was given a sealed envelope that either revealed whether the participant had been given testosterone or placebo (single-blind) or simply stated that the participant had an equal chance of receiving testosterone or placebo (double-blind). Experimenters remained fully blind. Experiment 3 randomly assigned participants to one of three stressor conditions prior to the CRT in addition to testosterone versus placebo: A cold pressor test (Hines & Brown, 1932), a socially-evaluated cold pressor test (SECPT; Schwabe et al., 2008), or a warm pressor test (as a control condition).

Additional Differences. Experiments 1 and 2 used male and female experimenters while Experiment 3 used female only. Also, the experiments administered the CRT at a range of times from approximately 11:00 AM to 7:00 PM. In all experiments, the CRT was administered in the time period that pharmacokinetic analyses suggest should coincide with peak testosterone levels for each method (Eisenegger et al., 2013; Geniole et al., 2019), specifically approximately four hours after gel application in Experiment 1 (M = 3.83 hours, SD = 0.15); approximately one hour after gel application in Experiment 2 (M = 1.15 hours, SD = 0.20); and approximately three hours after gel application in Experiment 3 (M = 2.84 hours, SD = 0.27). For all statistical analyses, time was measured as hours after noon local time.

Individual Difference Variables

Basal Cortisol. As discussed above, basal cortisol was measured prior to testosterone or placebo administration in the three new experiments.

2D:4D Ratio. In the three new experiments, participants' left and right hands were scanned on a flatbed scanner. In Experiments 1 and 2, two trained research assistants measured lengths of the second and fourth digits of each hand between the ventral proximal creases of the digits to the fingertips, using AutoMetric (Experiment 1) and ImageJ Software (Experiment 2). In Experiment 3, one research assistant measured each hand twice in AutoMetric with a time difference of three weeks between measurements. Research assistants then computed the ratio between these two lengths (i.e., the 2D:4D ratio). Cronbach's α was 0.81 in Experiment 1, 0.86 in Experiment 2, and 0.88 in Experiment 3.

***Trait Impulsivity*.** Trait impulsivity was measured via different questionnaires in each of the three new experiments. Consequently, we selected subscales from each measurement that conceptually relate to

one another most closely across the three experiments. For all statistical analyses, the values discussed below were first converted to *z*-scores.

Experiment 1. Trait impulsivity was measured using the impulsivity subscale from the Zuckerman-Kuhlman Impulsive Sensation Seeking scale (Zuckerman et al., 1993). Participants responded to eight True/False items that make up the impulsive factor of this subscale (e.g., "I am an impulsive person"). The remaining eleven items on the subscale that describe sensation seeking traits were not used. Items were scored one for impulsive responses and zero for less impulsive responses and summed for each participant. Cronbach's α was 0.73.

Experiment 2. Trait impulsivity was measured using the Barratt Impulsivity Scale (Patton et al., 1995) and the Brief Self-Control Scale (BCBS; Tangey, Baumeister, & Boone, 2004). The Barratt Impulsivity Scale consists of thirty items that measure trait impulsivity. Participants were asked to rate the extent to which each statement was true for them on an integer scale ranging from 1 (rarely/never) to 4 (almost always/always). The BCBS consists of thirteen items related to a tendency to be disciplined and lack impulsivity. Participants were asked to rate the extent to which each statement applied to them on an integer scale ranging from 1 (not at all like me) to 5 (very much like me). Cronbach's α was 0.82 for the Barratt Impulsivity Scale and 0.85 for the BSCS. Because the two measures correlated highly (r = -0.67), they were combined into a single measure by summing them after each was converted to a *z*-score and the latter was reverse-coded.

*Experiment 3***.** Trait impulsivity was measured using the Behavioral Inhibition/Behavior Activation Scales (BIS/BAS) which consists of twenty-four items across one BIS scale and three BAS subscales (Carver & White, 1994). We used the four-item BAS Fun-seeking subscale because it correlated most strongly with the Barratt Impulsivity Scale compared to other measures in prior work [e.g., in Stanford et al. (2009), r = -0.31, which is negative due to how the scales are scored]. Participants responded on an integer scale ranging from 1 (very true of me) to 4 (very false for me) to items related to a tendency to seek rewarding events impulsively (e.g., "I'm always willing to try something new if I think it will be fun" and "I often act on the spur of the moment"). Items were reverse-coded and summed for each participant. Cronbach's α was 0.65.

Covariates

Age. Participants self-reported their age in each experiment.

Treatment Expectancy.

*Experiment 1***.** At the end of the laboratory day, participants reported whether they believed they had received testosterone or placebo. 61% of all participants (84% of those assigned placebo, 37% of those assigned testosterone) believed they received placebo; 55% of participants in the single-blind condition (100% of those assigned placebo, 7% of those assigned testosterone) believed they received placebo while 66% of participants in the double-blind condition (67% of those assigned placebo, 66% of those assigned testosterone) believed they received placebo. Participants also indicated the confidence with which they felt they had received the treatment they reported on 0 (not at all confident) to 100 (certain) integer scale but this was not used in our analysis.

Experiment 2. At the end of the laboratory session, participants reported whether they believed they had received testosterone or placebo (i.e., binary choice). 70% of all participants (67% of those assigned placebo, 73% of those assigned testosterone) believed they received placebo.

Experiment 3. At the end of the laboratory session, participants reported whether they believed they had received testosterone or placebo (i.e., binary choice) and were asked to explain their choice. 81% of all participants (75% of those assigned placebo, 87% of those assigned testosterone) believed they received placebo.

***Right Hand 2D:4D Ratio*.** As discussed above, right hand 2D:4D ratio was measured in the three new experiments.

Basal Cortisol. As discussed above, basal cortisol was measured prior to testosterone or placebo administration in the three new experiments.

Positive and Negative Affect.
Experiment 1. Positive and negative affect was measured at baseline via the positive and negative subscales from the PANAS-X (Watson & Clark, 1994). Participants responded to ten positive and ten negative items on a 1 (Not at all) to 4 (Quite a bit) integer scale; scores were computed as the average across items.

Experiment 2. Positive and negative affect was not measured.

Experiment 3. Positive and negative affect was measured at baseline via the Brief PANAS (Watson, Clark, & Tellegen, 1988). Participants responded to ten positive and ten negative items on a 1 (very slightly or not at all) to 5 (extremely) integer scale; scores were computed as the average across items.

Mathematics Aptitude. In Experiment 1, participants were shown a series of simple equations (e.g., 9 + 2 - 4 = 7) and asked to report whether the equation was true or false. They had ten seconds to respond to as many of these equations as they were able. This task was repeated across sixteen trials, and the number of equations responded to correctly on average across the trials was used as the measure of the participants' mathematics aptitude. For all statistical analyses, these values were first converted to *z*-scores. In Experiments 2 and 3, mathematics aptitude was not measured.

Models

Primary. To estimate the effect of testosterone treatment on CRT performance, we meta-analyzed the data from the three new experiments as well as all four experiments by fitting a multilevel logistic regression to the response of each participant to each CRT item (Correct=1, Incorrect=0; Correct responses are: bat and ball item = 5 cents; widgets item = 5 minutes; lily pads item = 47 days) jointly (McShane and Böckenholt, 2017; 2018). The model treated effects for the interaction of each item and primary treatment condition (i.e., testosterone or placebo) as "fixed" and effects for (i) each experiment across all items, (ii) each experiment for each item, (iii) each treatment group (i.e., primary treatment condition crossed with blinding or stressor condition as applicable) across all items, (iv) each treatment group for each item, and (v) each participant across all items as "random." Specifically, our model specification is given by

$$y_{i,j} \sim \text{Bernoulli}(p_{i,j})$$
$$\text{logit}(p_{i,j}) = \alpha_{T_i,j} + b_{1,e[i]} + b_{2,e[i],j} + b_{3,g[i]} + b_{4,g[i],j} + b_{5,i}$$

where $y_{i,j}$ denotes whether participant *i* responded to CRT item *j* correctly, $p_{i,j}$ denotes the probability that participant *i* responded to CRT item *j* correctly, T_i denotes the primary treatment condition to which participant *i* was assigned, *e[i]* denotes the experiment to which participant *i* belongs, and *g[i]*

denotes the treatment group to which participant *i* belongs. Terms given by an α are treated as "fixed" and terms given by a *b* are treated as "random" (and independent).

We also expanded the model to directly compare the degree to which the treatment effect pooled across the three new experiments differed from the treatment effect in Nave et al. by introducing separate α terms for the three new experiments on one hand and Nave et al. on the other.

Secondary. For comparability with Nave et al., we also meta-analyzed aggregated data. Specifically, we fit a multilevel linear regression specified *mutatis mutandis* analogously to our primary model to the score of each participant (i.e., number of CRT items correct out of three). Specifically, our model specification is given by

$$y_i \sim \text{Normal}(\alpha_0 + \alpha_1 T_i + b_{1,e[i]} + b_{2,g[i]}, \sigma^2)$$

where y_i denotes the score of participant *i*, T_i is a binary variable indicating that participant *i* was assigned testosterone, and other terms are given and treated as above.

We also expanded the primary model to include covariates included by Nave et al., namely age, treatment expectancy, right hand 2D:4D ratio, basal cortisol levels, positive/negative affect (Experiments 1, 3, and Nave et al. only), and mathematics aptitude (Experiment 1 and Nave et al. only); we did so by introducing α terms for each covariate and treating each linearly. As in Nave et al., we also report the effect of testosterone treatment separately for each CRT item as well as the effect on intuitive-but-incorrect responses (1=intuitive-but-incorrect, 0=all other responses; Intuitive-but-incorrect responses are: bat and ball item = 10 cents; widgets item = 100 minutes; lily pads item = 24 days) instead of correct responses.

We also examined potential moderators of the effect of testosterone on decision-making. We did so for methodological differences across the experiments in two ways: (i) by re-fitting our primary model with the single-blind and stressor groups removed from Experiments 1 and 3 respectively and (ii) by introducing separate α terms to model the interaction of each item, primary treatment condition, and various methodological difference variables [experimenter gender, time of day (treating it linearly), experimental blinding conditions (Experiment 1), and experimental stressor conditions (Experiment 3)]. We did so for individual difference variables (basal cortisol, right- and left-hand 2D:4D ratio, and trait impulsivity) by expanding the model to include interactions in the same manner and treating each linearly.

Models fit to subsets of experiments (e.g., because one or more did not measure a given variable) were specified analogously to our primary model with terms given by a *b* removed when they were not identified.

Estimation. We estimated all models in R (v3.4.1; R Core Team, 2016) using *rstanarm* (Stan Development Team, 2016) with the default (weakly informative) prior distributions. For each model, we ran four Hamiltonian Monte Carlo Markov Chains for 10,000 iterations each with the first 5,000 iterations discarded as burn in and the target average proposal acceptance probability for adaptation set to 0.99.

We summarize estimated posterior distributions by presenting 2.5%, 25%, 50%, 75%, and 97.5% percentile estimates for each coefficient or effect of interest. All estimates are presented on the scale of a logistic regression coefficient unless otherwise noted (and thus variance component estimates are presented as a standard deviation). Positive estimates imply better CRT performance.

Our analysis scripts are included as part of the Supplementary Online Materials.

Results

Preliminary

Distributions of CRT Performance & Other Descriptive Statistics. Four participants did not complete the CRT in each of the three experiments; they were removed from all analyses, leaving final sample sizes of n = 116 (Experiment 1), n = 396 (Experiment 2), and n = 116 (Experiment 3). Table S2 presents the mean scores of the participants and other descriptive statistics from all four experiments. Table S3 presents the distribution of the scores of the participants from all four experiments as well as three other studies (Brañas-Garza et al., 2015, Bosch-Domènech et al., 2014; Frederick, 2005). Figure S1 presents the distribution of the scores of the participants from all four experiments along with a comparison to the distribution in a large meta-analysis (Brañas-Garza et al., 2015).

Baseline testosterone concentrations. Visual inspection of baseline testosterone concentrations revealed notably elevated testosterone concentrations – especially in Experiments 2 and 3 – compared to previous population studies of testosterone concentrations. For example, Keevil et al. (2017) report an average of 90.8 pg/mL for men aged 18-24 which is substantially lower compared to our results (Experiment 1: *Point Estimate:* 125.0 pg/mL, *95%CI:* [92.1, 157.9]; Experiment 2: 321.9 pg/mL, [286.0, 357.7]; and Experiment 3: 504.6 pg/mL, [401.0, 608.1]). Topical testosterone gel can transfer from washed hands after topical gel use leading to contaminated assay results in a clinical laboratory (Wolthuis & de Vreeze, 2005).

Nave et al. also report high baseline levels of testosterone (545.4 pg/mL, [426.4, 664.3]) as well as evidence that the contamination likely occurred via contact with contaminated laboratory surfaces and equipment that then transferred exogenous testosterone to the saliva collection containers. They also show, via their extensive panel of hormone assays, that these elevated concentrations were not evident for testosterone metabolites thereby demonstrating the contamination was specific to testosterone entering the saliva tubes and therefore did not alter physiological functioning. Their supplemental materials provide extensive evidence of contamination and discussion of how to prevent it in hormone administration research.

Given these results of Nave et al., we suspect residual testosterone contamination may also explain the elevated concentrations in the three new experiments. Although we lack the panel of hormones measured in Nave et al. to provide clear support for this interpretation in Experiments 1 and 2, Experiment 3 did measure concentrations of androstenedione – a prohormone in the biosynthesis of testosterone (Haring et al., 2012) – in addition to testosterone and cortisol. Androstenedione levels were at a relatively normal physiological concentration in Experiment 3 (0.34 ng/mL, [0.30, 0.39]). These results are consistent with those of Nave et al. and suggest that the elevated baseline testosterone levels observed in the three new experiments were driven by contamination of saliva tubes without any physiological contamination.

Intranasal delivery of testosterone as used in Experiment 2 may also contaminate salivary measures of testosterone concentration. That is, the levels reflected in the saliva might be artificially inflated due to the presence of exogenous testosterone in the saliva rather than due to testosterone that had been absorbed into the bloodstream and which then entered the saliva.

Post-treatment testosterone concentrations. To confirm that testosterone treatment increased testosterone concentrations compared to placebo, we first winsorized pre- and post-gel testosterone concentrations to ± 3SD of the experiment- and sample-specific mean of the log-transformed testosterone concentrations (Experiment 1: pre-gel samples from two participants; Experiment 2: post-

gel samples from two participants; Experiment 3: pre-gel from two participants, post-gel samples from one participant). We then fit a multilevel model to these transformed testosterone concentrations as a function of the interaction of time (pre- to post-gel administration) and treatment (testosterone or placebo). Across all three experiments, the estimate of this interaction indicates that testosterone treatment was associated with a substantial increase in salivary testosterone concentration compared to placebo treatment (Experiment 1: 2.59, [2.24, 2.94]; Experiment 2: 2.35, [2.14, 2.57]; Experiment 3: 2.55, [1.88, 3.22]; see also Table S2).

Even though the high post-treatment salivary testosterone levels we observed are outside the normal physiological range (Keevil et al., 2017), prior pharmacokinetic work indicates that the dosages of testosterone administered in the three new experiments typically increase serum testosterone concentrations to a high-normal physiological range (Eisenegger et al., 2013; Geniole et al., 2019). Although serum and salivary measures of endogenous bioavailable testosterone generally correlate (Wang et al., 1981; Granger et al., 2004), salivary testosterone concentrations are prone to exaggerated increases after topical testosterone gel administration (Schönfelder et al., 2011; Thieme et al., 2013). Lipophilic molecules like testosterone absorb into lipid layers when applied to the skin (Prausnitz & Langer, 2008) and may subsequently be directed to the salivary glands via lymphatic vessels (Ahern et al., 2017). Another possible explanation for elevated salivary testosterone concentrations is dysregulation of the molecules that bind with testosterone to allow it to be transported in the blood (e.g., sex hormone-binding globulin, or SHBG, Thieme et al., 2013). The effect may be specific to topical testosterone treatment: Intramuscular testosterone injections and oral testosterone administration increased serum testosterone and salivary testosterone at an approximately equivalent rate in several studies (Wang et al., 1981; Schürmeyer & Nieschlag, 1984; Schürmeyer, et al., 1983).

Primary

Table S4 presents estimates from our primary model fit to the data from the three new (all four) experiments (Table S5 presents estimates from models fit to each experiment separately used in Figure 1 of the main text). Table S6 presents estimates from the expanded model that directly compares the degree to which the treatment effect pooled across the three new experiments differed from the treatment effect in Nave et al.

Secondary

CRT Score. Table S7 presents estimates from the model fit to the score of each participant (i.e., number of CRT items correct out of three).

Covariates, Individual Item Responses, and Intuitive-but-Incorrect Responses. Table S8 presents estimates from models including covariates included by Nave et al. Figure S2 presents the fraction of participants giving correct, intuitive-but-incorrect, and other incorrect responses to each item by experiment and primary treatment condition. Tables S4 present estimates of the treatment effect at the CRT item-level. Table S9 presents estimates of the treatment effect on intuitive-but-incorrect responses on average and at the CRT item-level.

Methodological Difference Variables. Table S10 presents estimates from models with the single-blind and stressor groups removed from Experiments 1 and 3 respectively. Table S11 presents estimates from models including the interaction of each item, primary treatment condition, and various methodological difference variables [experimenter gender, time of day, experimental blinding conditions (Experiment 1), and experimental stressor conditions (Experiment 3)].

Individual Difference Variables. Figures S3 and Tables S12 present estimates from models including the interaction of each item, primary treatment condition, and various individual difference variables (basal cortisol, right- and left-hand 2D:4D ratio, and trait impulsivity).

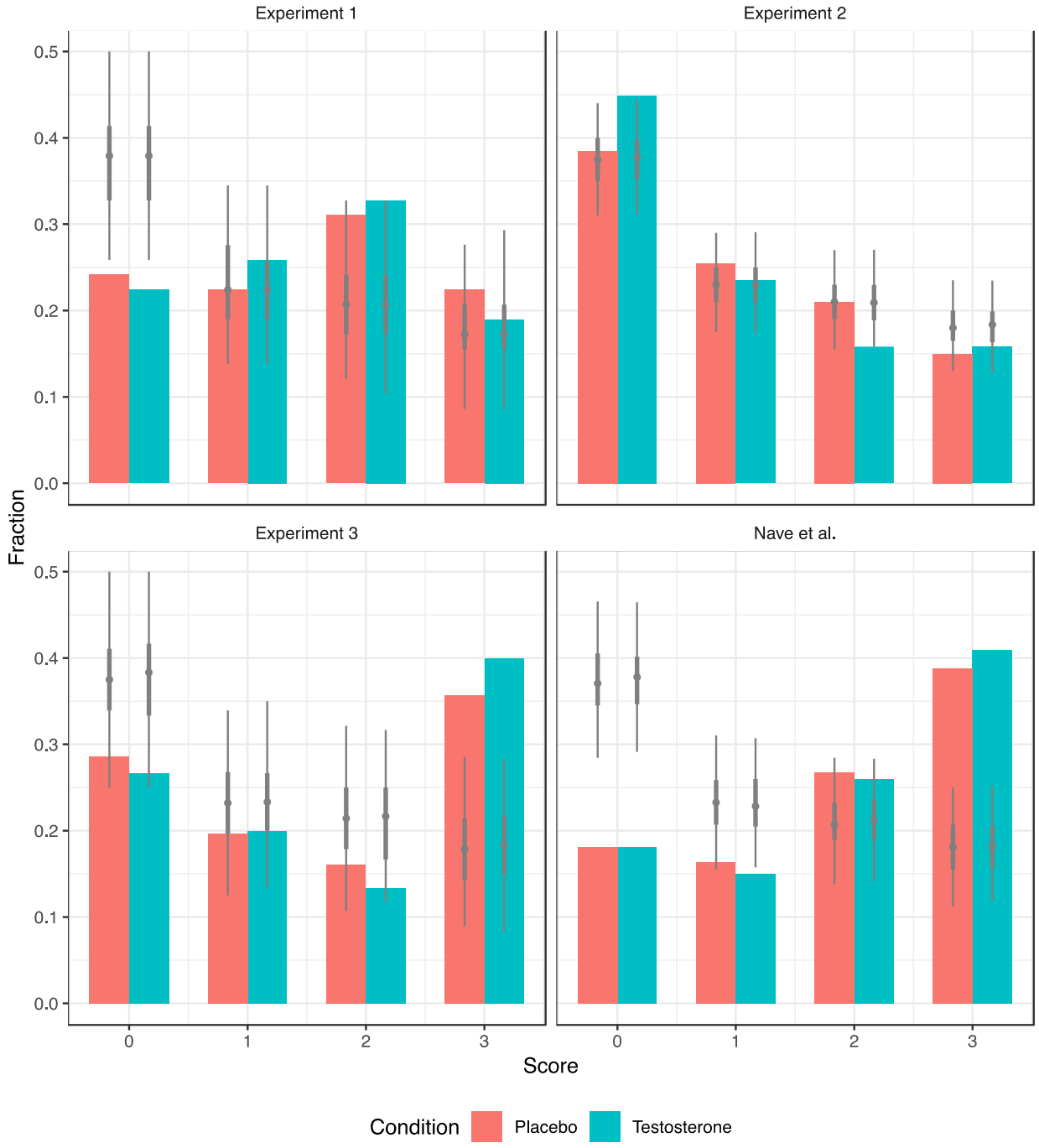


Figure S1. Distributions of CRT Performance. The fraction of participants with each score in each experiment and primary treatment condition is given by the bars. Median and 50% and 95% interval estimates based on the performance in the Brañas-Garza (2015) meta-analysis (Table A1) and the sample sizes in the four experiments are given by the grey points and thick and thin lines, respectively.

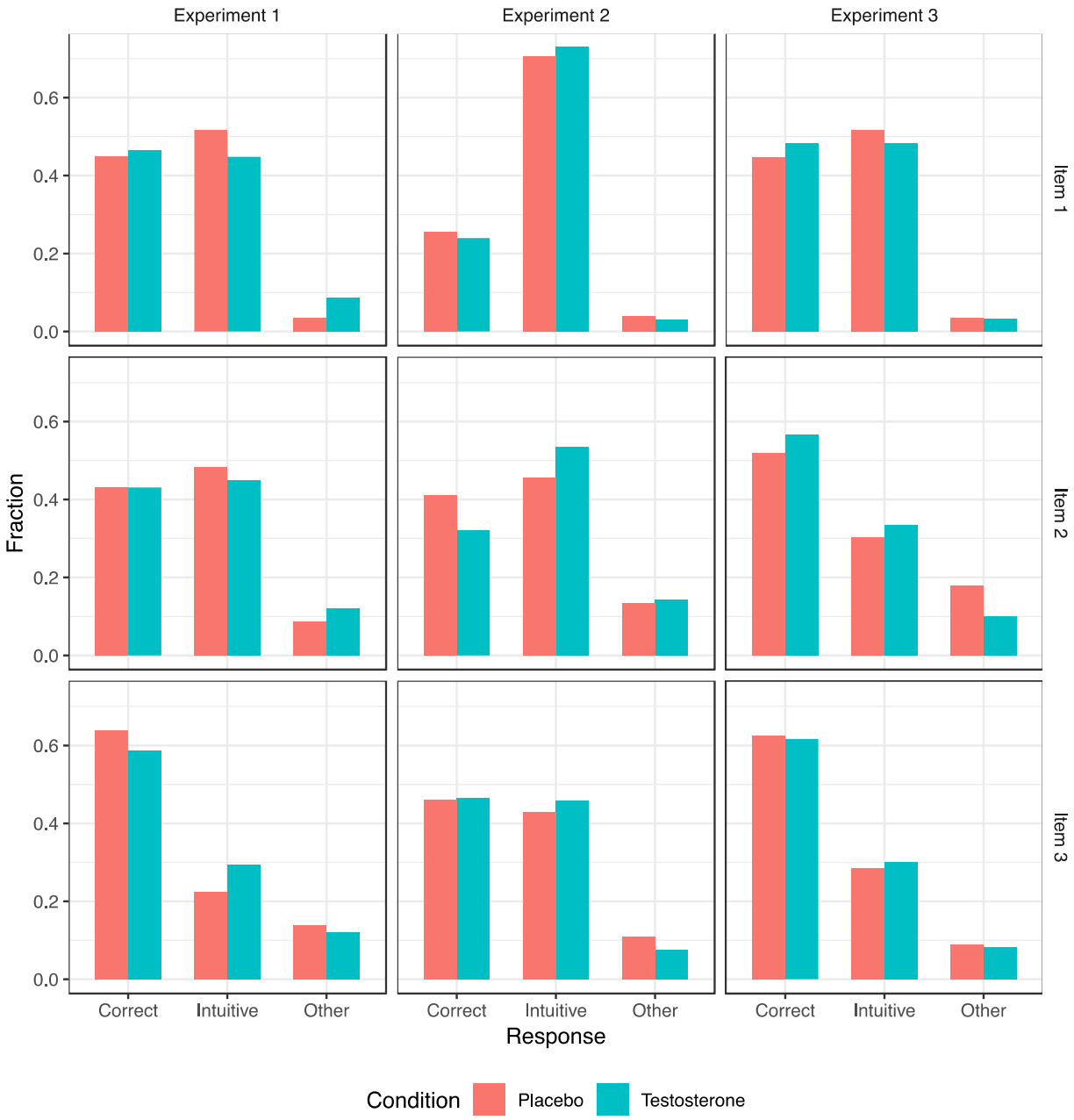


Figure S2. Responses by Item and Experiment. The fraction of participants giving correct, intuitive-but-incorrect, and other incorrect responses to each item in experiment and primary treatment condition is given by the bars.

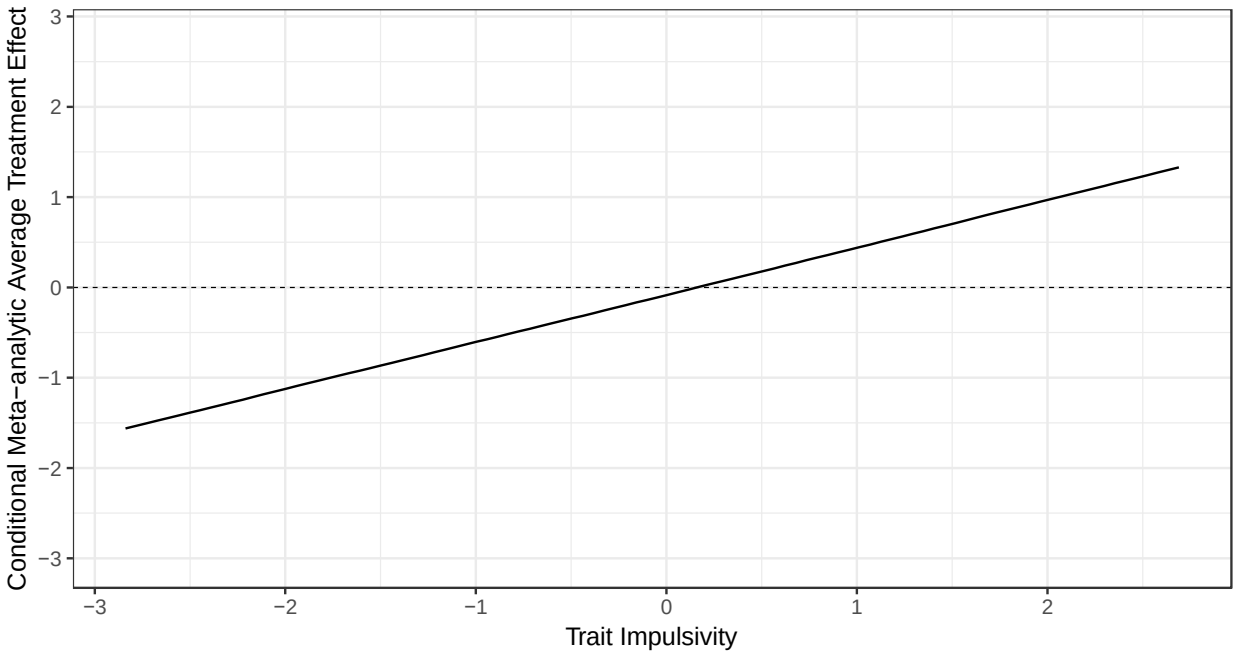


Figure S3. Conditional Meta-analytic Average Treament Effect of Trait Impulsivity. The point estimates are given by the line; 50% and 95% interval estimates are given by the dark and light shaded regions, respectively. The figure suggests a potential negative treatment effect of testosterone on CRT performance at lower levels of trait impulsivity and a potential positive treatment effect at higher levels.

Table S1. Comparison of Nave et al. and the three new experiments.

	Nave et al.	Experiment 1	Experiment 2	Experiment 3
Testosterone Dose	2 x 50 mg topical gel	150 mg topical gel	11 mg nasal spray	150 mg topical cream
Testosterone brand	Vogelxo	Androgel	Natesto	Compounded in local pharmacy
Blinding	Double-blind	50% double-blind, 50% single-blind	Double-blind	Double-blind
Protocol	Participants leave between gel application and tasks	Daylong protocol; participants remain in lab throughout	2-hour protocol; participants remain in lab throughout	4-hour protocol; participants remain in lab throughout
CRT administration time	Approximately 4pm	1pm - 4pm	11am - 7pm	3pm – 7pm
Delay in CRT after gel application	4.5 hours	4.5 hours	1.15 hours	3 hours
CRT Incentives	$1 per correct response; bonus $2 for all correct responses ($5 total possible)	None	None	€0.30 per correct response (€0.90 total possible)
Trait Impulsivity Measure	None	Zuckerman-Kuhlman Impulsivity subscale	Composite of Barratt Impulsivity Survey and Brief Self-Control Scale	Behavior Activation Scale Fun-seeking subscale
Experimenter Gender	Male	Male and female	Male and female	Female

Table S2: Descriptive statistics [Mean (SD), unless otherwise noted] for Nave et al. and three new experiments.

	Nave et al.			Experiment 1			Experiment 2			Experiment 3		
	Testost.	*Placebo*	*All*	*Testost.*	*Placebo*	*All*	*Testost.*	*Placebo*	*All*	*Testost.*	*Placebo*	*All*
Final Sample Size	125	118	243	58	58	116	196	200	396	60	56	116
Age (years)	24.4 (8.6)	22.8 (5.3)	23.6 (7.2)	22.2 (3.2)	22.9 (3.8)	22.5 (3.5)	23.1 (4.9)	22.6 (4.5)	22.8 (4.7)	24.2 (4.8)	23.7 (4.1)	23.9 (4.5)
Pre-gel testosterone (pg/mL)	480.1 (827.0)	614.5 (1048.6)	545.4 (941.6)	137.2 (172.0)	112.8 (186.4)	125.0 (179.0)	320.8 (380.8)	323.8 (353.0)	322.3 (366.6)	529.2 (696.6)	477.7 (371.7)	504.6 (563.3)
Post-gel testosterone (pg/mL)	11433.7 (15298.3)	250.8 (273.6)	6004.7 (12302.4)	2768.5[a] (2130.7)	108.4 (94.5)	1438.4[a] (2009.8)	8802.4 (19505.8)	398.5 (359.1)	4557.8 (14338.1)	67489.8 (196277.2)	641.0 (1849.1)	35518.6 (145136.9)
Basal Cortisol (ng/mL)	3.44 (2.20)	3.61 (3.93)	3.52 (3.15)	3.64 (2.11)	3.17 (1.89)	3.40 (2.00)	3.28 (2.30)	3.22 (2.67)	3.25 (2.49)	6.73 (5.01)	8.45 (6.71)	7.55 (5.92)
Positive Affect	2.63 (0.92)	2.60 (0.95)	2.61 (0.93)	2.53 (0.53)	2.41 (0.70)	2.47 (0.63)	--	--	--	3.58 (0.47)	3.75 (0.50)	3.66 (0.49)
Negative Affect	1.46 (0.57)	1.43 (0.55)	1.45 (0.56)	1.18 (0.18)	1.23 (0.35)	1.20 (0.28)	--	--	--	2.12 (0.70)	1.98 (0.68)	2.05 (0.69)
Right hand 2D:4D	0.94 (0.03)	0.95 (0.03)	0.95 (0.03)	0.95 (0.03)	0.95 (0.03)	0.95 (0.03)	0.95 (0.04)	0.95 (0.03)	0.95 (0.03)	0.97 (0.03)	0.96 (0.04)	0.96 (0.04)

	Nave et al.			Experiment 1			Experiment 2			Experiment 3		
	Testost.	*Placebo*	*All*	*Testost.*	*Placebo*	*All*	*Testost.*	*Placebo*	*All*	*Testost.*	*Placebo*	*All*
Treatment expectancy (% guessing testosterone)	20.8% [b]	27.6% [b]	24.1% [b]	32.1% [c]	33.3% [c]	32.7% [c]	27.7%	33.0%	30.4%	13.3%	25.0%	19.0%
Mathematics Aptitude [d]	10.80 (4.18)	10.76 (4.10)	10.78 (4.13)	3.03 (0.72)	2.95 (0.63)	2.99 (0.68)	--	--	--	--	--	--
Trait Impulsivity [e]	--	--	--	2.59 (1.90)	2.55 (2.23)	2.57 (2.07)	-0.07 (1.84)	0.06 (1.86)	0.00 (1.85)	13.3 (1.6)	13.3 (1.4)	13.3 (1.5)
CRT Score	1.66 (1.18)	2.10 (1.02)	1.88 (1.13)	1.48 (1.05)	1.52 (1.10)	1.50 (1.07)	1.03 (1.12)	1.13 (1.09)	1.08 (1.10)	1.67 (1.26)	1.59 (1.25)	1.63 (1.25)

Notes:

a) Values for post-gel testosterone were capped at 5250 ng/dL due to limits on the EIA kits used in this experiment.

b) In Nave et al., participants reported whether they believed they had received testosterone or placebo on a 5-point Likert scale (1 = received placebo, 5 = received testosterone). Participants responding 4 or 5 were coded as guessing testosterone. The percentage guessing testosterone is lower in this experiment compared to the other three likely because participants were given an "unsure" option (i.e., 3, which was given by 33.2% of all participants; 32.0% of those assigned testosterone; and 34.4% of those assigned placebo). To facilitate comparison with the dichotomous measure used in the three new experiments, we subtracted one from this response and divided by four for all statistical analyses.

c) Treatment expectancy is presented from only the double-blind condition in Experiment 1. In the single-blind condition, participants were told which treatment they were administered. See text of this SOM for more discussion.

d) In Nave et al., mathematics aptitude was determined by how many math problems a participant could respond to correctly in a five-minute period. In Experiment 1, mathematics aptitude was indexed by the average number of math equations solved correctly across sixteen, ten-second trials. For all statistical analyses, these values were first converted to *z*-scores.

e) In Experiment 1, trait impulsivity was measured using the Zuckerman-Kuhlman Impulsivity subscale which ranges from 0 to 8. In Experiment 2, trait impulsivity was measured using the sum of the score from the Barratt Impulsivity Scale and the Brief Self-Control Scale after each was converted to a *z*-score and the latter was reverse-coded. In Experiment 3, impulsivity was measured using the (reverse-coded) BAS fun-seeking subscale which ranges from 4 to 16. In each experiment, higher values indicate higher trait impulsivity. For all statistical analyses, these values were first converted to *z*-scores.

Table S3. Distributions of CRT Performance. The first column gives the total sample size (and testosterone and placebo sample sizes respectively as applicable). All other columns give the percentage of participants with the score indicated by the column heading.

Experiment	*n*	*Testosterone*				*Placebo*				*All*			
		0	*1*	*2*	*3*	*0*	*1*	*2*	*3*	*0*	*1*	*2*	*3*
Nave et al.	243 (125, 118)	24.8	17.6	24.0	33.6	11.0	14.4	28.0	46.6	18.1	16.0	25.9	39.9
Experiment 1	116 (58, 58)	22.4	25.9	32.8	19.0	24.1	22.4	31.0	22.4	23.3	24.1	31.9	20.7
Experiment 2	394 (196, 200)	44.9	23.5	15.8	15.8	38.5	25.5	21.0	15.0	41.7	21.5	18.4	15.4
Experiment 3	116 (60, 56)	26.7	20.0	13.3	40.0	28.6	19.6	16.1	35.7	27.6	19.8	14.7	37.9
Brañas-Garza et al., 2015 (Table A1)[a]	44,558									37.5	21.2	21.1	18.2
Bosch-Domènech et al., 2014 (Table 2, men only)	260									43.5	28.9	16.2	11.5
Frederick, 2005 (Table 1; MIT)	61									7	16	30	48
Frederick, 2005 (Table 1; Princeton)	121									18	27	28	26

Notes:
a. Includes data from Bosch-Domènech et al. (2014) and Frederick (2005).

Table S4. Estimates from the primary model.

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Three New Experiments					
Meta-analytic Treatment Effects					
Average	**-0.764**	**-0.291**	**-0.069**	**0.154**	**0.686**
Item #1 (bat & ball)	-0.781	-0.224	0.052	0.336	0.940
Item #2 (widgets)	-1.029	-0.476	-0.205	0.074	0.715
Item #3 (lily pads)	-0.926	-0.341	-0.055	0.218	0.823
Coefficients					
Placebo, Item #1 (bat & ball)	-1.935	-1.189	-0.837	-0.481	0.331
Placebo, Item #2 (widgets)	-1.301	-0.561	-0.215	0.143	0.950
Placebo, Item #3 (lily pads)	-0.548	0.200	0.547	0.897	1.699
Testosterone, Item #1 (bat & ball)	-1.861	-1.112	-0.782	-0.429	0.382
Testosterone, Item #2 (widgets)	-1.510	-0.752	-0.408	-0.052	0.739
Testosterone, Item #3 (lily pads)	-0.598	0.148	0.488	0.841	1.620
Variance Components					
Experiment	0.059	0.406	0.646	0.98	2.052
Experiment × Item	0.013	0.126	0.243	0.395	0.895
Group	0.010	0.118	0.257	0.451	0.938
Group × Item	0.009	0.093	0.186	0.295	0.530
Participant	1.956	2.151	2.262	2.381	2.619
Three New Experiments & Nave et al.					
Meta-analytic Treatment Effects					
Average	**-0.961**	**-0.530**	**-0.318**	**-0.095**	**0.455**
Item #1 (bat & ball)	-0.969	-0.452	-0.199	0.069	0.666
Item #2 (widgets)	-1.151	-0.649	-0.394	-0.129	0.500
Item #3 (lily pads)	-1.149	-0.613	-0.358	-0.090	0.513
Coefficients					
Placebo, Item #1 (bat & ball)	-1.396	-0.687	-0.358	-0.024	0.696
Placebo, Item #2 (widgets)	-1.112	-0.371	-0.045	0.277	0.996
Placebo, Item #3 (lily pads)	-0.043	0.674	1.006	1.340	2.057
Testosterone, Item #1 (bat & ball)	-1.581	-0.871	-0.547	-0.205	0.519
Testosterone, Item #2 (widgets)	-1.485	-0.759	-0.425	-0.091	0.625
Testosterone, Item #3 (lily pads)	-0.393	0.329	0.658	0.994	1.701
Variance Components					
Experiment	0.074	0.488	0.729	1.032	1.990
Experiment × Item	0.041	0.232	0.342	0.473	0.880
Group	0.020	0.190	0.354	0.556	1.012
Group × Item	0.009	0.098	0.191	0.297	0.516
Participant	2.017	2.193	2.290	2.389	2.592

Table S5. Estimates from models fit to each experiment separately used in Figure 1 of the main text.

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Experiment 1					
Average Treatment Effect	**-1.297**	**-0.421**	**-0.059**	**0.313**	**1.236**
Coefficients					
Placebo, Item #1 (bat & ball)	-1.435	-0.652	-0.309	0.027	0.768
Placebo, Item #2 (widgets)	-1.543	-0.751	-0.416	-0.076	0.669
Placebo, Item #3 (lily pads)	-0.340	0.444	0.788	1.128	1.883
Testosterone, Item #1 (bat & ball)	-1.273	-0.529	-0.191	0.142	0.878
Testosterone, Item #2 (widgets)	-1.505	-0.725	-0.387	-0.054	0.702
Testosterone, Item #3 (lily pads)	-0.612	0.145	0.480	0.815	1.570
Variance Components					
Group	0.012	0.129	0.294	0.550	1.424
Group × Item	0.008	0.090	0.198	0.354	0.829
Participant	1.014	1.342	1.524	1.717	2.148
Experiment 2					
Average Treatment Effect	**-0.850**	**-0.471**	**-0.278**	**-0.085**	**0.301**
Coefficients					
Placebo, Item #1 (bat & ball)	-2.430	-2.046	-1.849	-1.657	-1.304
Placebo, Item #2 (widgets)	-1.140	-0.810	-0.636	-0.467	-0.148
Placebo, Item #3 (lily pads)	-0.777	-0.453	-0.280	-0.110	0.222
Testosterone, Item #1 (bat & ball)	-2.649	-2.241	-2.039	-1.840	-1.476
Testosterone, Item #2 (widgets)	-1.885	-1.515	-1.324	-1.143	-0.788
Testosterone, Item #3 (lily pads)	-0.741	-0.405	-0.231	-0.057	0.268
Variance Components					
Participant	1.908	2.158	2.298	2.447	2.758
Experiment 3					
Average Treatment Effect	**-1.590**	**-0.380**	**0.216**	**0.803**	**1.978**
Coefficients					
Placebo, Item #1 (bat & ball)	-2.073	-1.038	-0.528	-0.021	1.009
Placebo, Item #2 (widgets)	-1.392	-0.369	0.131	0.646	1.668
Placebo, Item #3 (lily pads)	-0.343	0.692	1.199	1.725	2.821
Testosterone, Item #1 (bat & ball)	-1.706	-0.670	-0.167	0.322	1.384
Testosterone, Item #2 (widgets)	-0.990	0.066	0.580	1.071	2.071
Testosterone, Item #3 (lily pads)	-0.504	0.547	1.046	1.562	2.638
Variance Components					
Group	0.018	0.206	0.464	0.828	1.831
Group × Item	0.024	0.249	0.480	0.739	1.348
Participant	2.440	3.044	3.407	3.818	4.742
Nave et al.					
Average Treatment Effect	**-1.948**	**-1.426**	**-1.167**	**-0.910**	**-0.426**
Coefficients					
Placebo, Item #1 (bat & ball)	0.614	1.042	1.282	1.526	2.006

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Placebo, Item #2 (widgets)	0.050	0.472	0.695	0.930	1.392
Placebo, Item #3 (lily pads)	1.926	2.429	2.708	2.997	3.602
Testosterone, Item #1 (bat & ball)	-0.395	0.021	0.242	0.465	0.892
Testosterone, Item #2 (widgets)	-1.006	-0.578	-0.354	-0.134	0.290
Testosterone, Item #3 (lily pads)	0.637	1.069	1.303	1.539	2.023
Variance Components					
Participant	1.869	2.196	2.378	2.580	3.007

Table S6. Estimates from the expanded model.

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Meta-analytic Effects					
Difference in Treatment Effects	**-2.437**	**-1.447**	**-1.009**	**-0.566**	**0.532**
Nave et al. Treatment Effect	-2.322	-1.466	-1.094	-0.707	0.294
Three new experiments Treatment Effect	-0.778	-0.300	-0.081	0.146	0.676
Coefficients					
Nave et al., Placebo, Item #1 (bat & ball)	-0.848	0.359	0.911	1.437	2.472
Nave et al., Placebo, Item #2 (widgets)	-1.388	-0.208	0.349	0.878	1.913
Nave et al., Placebo, Item #3 (lily pads)	0.436	1.696	2.269	2.818	3.887
Nave et al., Testosterone, Item #1 (bat & ball)	-1.780	-0.581	-0.034	0.485	1.528
Nave et al., Testosterone, Item #2 (widgets)	-2.356	-1.155	-0.611	-0.085	0.947
Nave et al., Testosterone, Item #3 (lily pads)	-0.838	0.392	0.951	1.482	2.505
Three new exps., Placebo, Item #1 (bat & ball)	-1.899	-1.186	-0.855	-0.516	0.232
Three new exps., Placebo, Item #2 (widgets)	-1.277	-0.563	-0.224	0.108	0.837
Three new exps., Placebo, Item #3 (lily pads)	-0.507	0.198	0.536	0.878	1.618
Three new exps., Testosterone, Item #1 (bat & ball)	-1.846	-1.140	-0.805	-0.463	0.292
Three new exps., Testosterone, Item #2 (widgets)	-1.474	-0.763	-0.434	-0.094	0.663
Three new exps., Testosterone, Item #3 (lily pads)	-0.590	0.136	0.471	0.814	1.553
Variance Components					
Experiment	0.056	0.405	0.634	0.933	1.881
Experiment × Item	0.013	0.125	0.242	0.390	0.829
Group	0.011	0.117	0.250	0.443	0.912
Group × Item	0.010	0.092	0.189	0.298	0.531
Participant	2.038	2.214	2.310	2.410	2.610

Table S7. Estimates from models fit to the score of each participant (i.e., number of CRT items correct out of three). Estimates are presented on the scale of the score.

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Three New Experiments					
Coefficients					
Intercept	0.650	1.254	1.418	1.584	2.170
Meta-analytic Average Treatment Effect	**-0.306**	**-0.118**	**-0.032**	**0.056**	**0.277**
Variance Components					
Experiment	0.065	0.238	0.376	0.608	1.634
Group	0.005	0.051	0.110	0.190	0.399
Participant	1.063	1.102	1.123	1.145	1.189
Three New Experiments & Nave et al.					
Coefficients					
Intercept	0.980	1.426	1.579	1.727	2.160
Meta-analytic Average Treatment Effect	**-0.390**	**-0.209**	**-0.126**	**-0.033**	**0.214**
Variance Components					
Experiment	0.066	0.257	0.377	0.559	1.268
Group	0.011	0.094	0.160	0.240	0.435
Participant	1.068	1.101	1.119	1.138	1.175

Table S8. Estimates from models including covariates. All covariates were not available in all experiments.

Table S8A. Covariates: Age, Treatment Expectancy, Right Hand 2D:4D, Basal Cortisol.

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Three New Experiments					
Meta-analytic Average Treatment Effect	**-0.656**	**-0.184**	**0.043**	**0.277**	**0.798**
Coefficients					
Placebo, Item #1 (bat & ball)	-2.824	-1.513	-0.809	-0.118	1.238
Placebo, Item #2 (widgets)	-2.191	-0.873	-0.180	0.519	1.854
Placebo, Item #3 (lily pads)	-1.403	-0.072	0.622	1.319	2.652
Testosterone, Item #1 (bat & ball)	-2.628	-1.308	-0.618	0.076	1.437
Testosterone, Item #2 (widgets)	-2.230	-0.909	-0.199	0.490	1.839
Testosterone, Item #3 (lily pads)	-1.419	-0.090	0.610	1.306	2.657
Age	-0.091	-0.055	-0.036	-0.017	0.020
Treatment Expectancy	-0.892	-0.534	-0.353	-0.168	0.177
Right Hand 2D:4D	-1.718	0.033	0.935	1.830	3.617
Basal Cortisol	-0.420	-0.192	-0.076	0.038	0.258
Variance Components					
Experiment	0.055	0.399	0.662	1.027	2.262
Experiment × Item	0.016	0.141	0.269	0.429	0.945
Group	0.010	0.104	0.230	0.408	0.880
Group × Item	0.016	0.151	0.266	0.382	0.627
Participant	1.980	2.194	2.312	2.435	2.691
Three New Experiments and Nave et al.					
Meta-analytic Average Treatment Effect	**-0.841**	**-0.406**	**-0.200**	**0.022**	**0.552**
Coefficients					
Placebo, Item #1 (bat & ball)	-2.319	-1.009	-0.327	0.358	1.675
Placebo, Item #2 (widgets)	-2.059	-0.741	-0.046	0.641	1.955
Placebo, Item #3 (lily pads)	-0.989	0.342	1.037	1.712	3.026
Testosterone, Item #1 (bat & ball)	-2.401	-1.097	-0.417	0.270	1.577
Testosterone, Item #2 (widgets)	-2.252	-0.938	-0.256	0.438	1.742
Testosterone, Item #3 (lily pads)	-1.235	0.086	0.760	1.456	2.756
Age	-0.092	-0.067	-0.053	-0.040	-0.015
Treatment Expectancy	-0.755	-0.421	-0.244	-0.072	0.263
Right Hand 2D:4D	-1.102	0.485	1.323	2.152	3.771
Basal Cortisol	-0.335	-0.142	-0.043	0.056	0.251
Variance Components					
Experiment	0.084	0.516	0.773	1.117	2.230
Experiment × Item	0.038	0.240	0.363	0.508	0.937
Group	0.013	0.143	0.292	0.485	0.954
Group × Item	0.016	0.156	0.266	0.377	0.605
Participant	2.029	2.211	2.312	2.416	2.633

Table S8B. Covariates: Age, Treatment Expectancy, Right Hand 2D:4D, Basal Cortisol, Positive and Negative Affect.

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Experiments 1 & 3					
Meta-analytic Average Treatment Effect	**-0.973**	**-0.304**	**0.010**	**0.331**	**0.973**
Coefficients					
Placebo, Item #1 (bat & ball)	-2.393	-0.988	-0.255	0.477	1.872
Placebo, Item #2 (widgets)	-2.272	-0.913	-0.175	0.555	1.959
Placebo, Item #3 (lily pads)	-0.991	0.390	1.125	1.848	3.241
Testosterone, Item #1 (bat & ball)	-2.320	-0.900	-0.165	0.561	1.969
Testosterone, Item #2 (widgets)	-1.997	-0.594	0.154	0.883	2.271
Testosterone, Item #3 (lily pads)	-1.399	0.011	0.747	1.486	2.898
Age	-0.166	-0.096	-0.061	-0.028	0.039
Treatment Expectancy	-0.709	-0.097	0.222	0.539	1.198
Right Hand 2D:4D	-2.628	-0.022	1.336	2.686	5.431
Basal Cortisol	-0.510	-0.147	0.039	0.223	0.574
Positive Affect	-0.983	-0.541	-0.326	-0.116	0.285
Negative Affect	-0.205	0.271	0.518	0.768	1.264
Variance Components					
Experiment	0.019	0.195	0.462	0.928	2.678
Experiment × Item	0.012	0.119	0.257	0.472	1.217
Group	0.013	0.137	0.295	0.514	1.096
Group × Item	0.009	0.101	0.212	0.355	0.682
Participant	1.811	2.138	2.325	2.524	2.953
Experiments 1, 3, and Nave et al.					
Meta-analytic Average Treatment Effect	-1.112	-0.566	-0.304	-0.025	0.613
Coefficients					
Placebo, Item #1 (bat & ball)	-1.776	-0.437	0.275	0.957	2.251
Placebo, Item #2 (widgets)	-1.996	-0.632	0.071	0.762	2.070
Placebo, Item #3 (lily pads)	-0.454	0.894	1.604	2.303	3.603
Testosterone, Item #1 (bat & ball)	-2.067	-0.691	0.019	0.727	2.026
Testosterone, Item #2 (widgets)	-2.057	-0.676	0.025	0.728	2.071
Testosterone, Item #3 (lily pads)	-1.060	0.310	1.010	1.715	3.051
Age	-0.114	-0.081	-0.064	-0.048	-0.017
Treatment Expectancy	-0.455	0.076	0.347	0.622	1.174
Right Hand 2D:4D	-1.293	0.642	1.612	2.569	4.484
Basal Cortisol	-0.385	-0.113	0.026	0.163	0.434
Positive Affect	-0.633	-0.398	-0.280	-0.164	0.060
Negative Affect	-0.180	0.135	0.308	0.479	0.818
Variance Components					
Experiment	0.019	0.233	0.472	0.817	2.102
Experiment × Item	0.015	0.148	0.271	0.429	0.904
Group	0.018	0.189	0.368	0.570	1.062
Group × Item	0.007	0.078	0.172	0.291	0.560
Participant	1.933	2.175	2.309	2.451	2.744

Table S8C. Covariates: Age, Treatment Expectancy, Right Hand 2D:4D, Basal Cortisol, Positive and Negative Affect, Mathematics Aptitude.

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Experiment 1					
Average Treatment Effect	**-2.260**	**-0.907**	**-0.341**	**0.226**	**1.566**
Coefficients					
Placebo, Item #1 (bat & ball)	-2.149	-0.653	0.160	0.972	2.466
Placebo, Item #2 (widgets)	-2.481	-1.011	-0.196	0.613	2.166
Placebo, Item #3 (lily pads)	-0.992	0.476	1.279	2.082	3.617
Testosterone, Item #1 (bat & ball)	-2.471	-0.971	-0.172	0.626	2.140
Testosterone, Item #2 (widgets)	-2.512	-0.972	-0.181	0.627	2.141
Testosterone, Item #3 (lily pads)	-1.741	-0.205	0.576	1.390	2.880
Age	-0.125	-0.043	-0.001	0.040	0.123
Treatment Expectancy	-0.288	0.430	0.819	1.215	2.004
Right Hand 2D:4D	-5.386	-2.378	-0.875	0.635	3.721
Basal Cortisol	-0.512	-0.050	0.182	0.425	0.904
Positive Affect	-0.494	-0.061	0.156	0.384	0.838
Negative Affect	-1.859	-0.833	-0.338	0.162	1.110
Mathematics Aptitude	0.207	0.477	0.625	0.773	1.087
Variance Components					
Group	0.052	0.440	0.749	1.151	2.398
Group × Item	0.010	0.116	0.257	0.468	1.090
Participant	0.920	1.283	1.488	1.703	2.179
Experiment 1 and Nave et al.					
Meta-analytic Average Treatment Effect	**-2.039**	**-0.982**	**-0.572**	**-0.137**	**1.023**
Coefficients					
Placebo, Item #1 (bat & ball)	-1.677	-0.229	0.516	1.240	2.640
Placebo, Item #2 (widgets)	-2.184	-0.750	-0.023	0.722	2.176
Placebo, Item #3 (lily pads)	-0.452	0.989	1.730	2.461	3.937
Testosterone, Item #1 (bat & ball)	-2.229	-0.776	-0.043	0.694	2.108
Testosterone, Item #2 (widgets)	-2.454	-1.047	-0.300	0.433	1.865
Testosterone, Item #3 (lily pads)	-1.280	0.153	0.896	1.638	3.073
Age	-0.110	-0.078	-0.062	-0.046	-0.016
Treatment Expectancy	-0.140	0.475	0.809	1.141	1.827
Right Hand 2D:4D	-2.311	0.087	1.157	2.190	4.213
Basal Cortisol	-0.350	-0.044	0.113	0.268	0.578
Positive Affect	-0.593	-0.356	-0.242	-0.126	0.100
Negative Affect	-0.482	-0.093	0.108	0.312	0.710
Mathematics Aptitude	0.518	0.720	0.829	0.939	1.166
Variance Components					
Experiment	0.029	0.288	0.614	1.140	3.063
Experiment × Item	0.009	0.090	0.204	0.396	1.132
Group	0.063	0.442	0.706	1.036	2.022
Group × Item	0.007	0.070	0.154	0.274	0.623
Participant	1.533	1.783	1.920	2.067	2.364

Table S9. Estimates from models fit to intuitive-but-incorrect responses.

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Three New Experiments					
Meta-analytic Treatment Effects					
Average	**-0.598**	**-0.099**	**0.122**	**0.327**	**0.773**
Item #1 (bat & ball)	-0.965	-0.363	-0.093	0.163	0.695
Item #2 (widgets)	-0.640	-0.034	0.231	0.495	1.014
Item #3 (Lily pads)	-0.651	-0.058	0.215	0.485	1.059
Coefficients					
Placebo, Item #1 (bat & ball)	-0.512	0.222	0.568	0.912	1.709
Placebo, Item #2 (widgets)	-1.653	-0.911	-0.571	-0.219	0.578
Placebo, Item #3 (lily pads)	-2.290	-1.552	-1.199	-0.842	-0.030
Testosterone, Item #1 (bat & ball)	-0.638	0.114	0.464	0.814	1.610
Testosterone, Item #2 (widgets)	-1.427	-0.687	-0.344	0.001	0.808
Testosterone, Item #3 (lily pads)	-2.070	-1.331	-0.982	-0.635	0.174
Variance Components					
Experiment	0.032	0.326	0.576	0.896	1.928
Experiment × Item	0.048	0.262	0.402	0.587	1.129
Group	0.010	0.107	0.237	0.419	0.873
Group × Item	0.008	0.085	0.181	0.305	0.578
Participant	1.714	1.895	1.996	2.099	2.308
Three New Experiments and Nave et al.					
Meta-analytic Treatment Effects					
Average	**-0.371**	**0.111**	**0.300**	**0.479**	**0.858**
Item #1 (bat & ball)	-0.642	-0.101	0.130	0.351	0.790
Item #2 (widgets)	-0.412	0.119	0.354	0.571	1.020
Item #3 (Lily pads)	-0.352	0.166	0.401	0.634	1.127
Coefficients					
Placebo, Item #1 (bat & ball)	-0.840	-0.181	0.144	0.469	1.198
Placebo, Item #2 (widgets)	-1.659	-0.999	-0.684	-0.354	0.376
Placebo, Item #3 (lily pads)	-2.603	-1.946	-1.621	-1.295	-0.542
Testosterone, Item #1 (bat & ball)	-0.721	-0.064	0.259	0.587	1.338
Testosterone, Item #2 (widgets)	-1.306	-0.660	-0.347	-0.017	0.730
Testosterone, Item #3 (lily pads)	-2.188	-1.546	-1.226	-0.888	-0.143
Variance Components					
Experiment	0.051	0.399	0.634	0.930	1.873
Experiment × Item	0.136	0.346	0.462	0.612	1.040
Group	0.014	0.141	0.284	0.462	0.875
Group × Item	0.007	0.067	0.142	0.247	0.497
Participant	1.682	1.836	1.920	2.008	2.179

Table S10. Estimates from models with single-blind and stressor groups removed from Experiments 1 and 3 respectively.

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Three New Experiments					
Meta-analytic Treatment Effects					
Average	**-0.997**	**-0.291**	**0.010**	**0.331**	**1.206**
Item #1 (bat & ball)	-1.111	-0.303	0.078	0.468	1.441
Item #2 (widgets)	-1.390	-0.587	-0.213	0.191	1.209
Item #3 (Lily pads)	-1.097	-0.200	0.172	0.561	1.496
Coefficients					
Placebo, Item #1 (bat & ball)	-2.212	-1.432	-1.038	-0.626	0.363
Placebo, Item #2 (widgets)	-1.667	-0.853	-0.462	-0.061	0.873
Placebo, Item #3 (lily pads)	-1.119	-0.289	0.090	0.488	1.394
Testosterone, Item #1 (bat & ball)	-2.092	-1.343	-0.940	-0.518	0.428
Testosterone, Item #2 (widgets)	-1.836	-1.051	-0.649	-0.235	0.708
Testosterone, Item #3 (lily pads)	-0.952	-0.127	0.270	0.681	1.626
Variance Components					
Experiment	0.019	0.205	0.433	0.756	1.814
Experiment × Item	0.027	0.224	0.391	0.598	1.166
Group	0.014	0.138	0.306	0.553	1.309
Group × Item	0.010	0.100	0.221	0.384	0.793
Participant	2.007	2.242	2.372	2.513	2.788
Three New Experiments and Nave et al.					
Meta-analytic Treatment Effects					
Average	**-1.264**	**-0.603**	**-0.329**	**-0.022**	**0.828**
Item #1 (bat & ball)	-1.306	-0.583	-0.249	0.109	1.018
Item #2 (widgets)	-1.520	-0.782	-0.455	-0.097	0.813
Item #3 (Lily pads)	-1.353	-0.610	-0.268	0.088	0.990
Coefficients					
Placebo, Item #1 (bat & ball)	-1.589	-0.771	-0.383	0.011	0.855
Placebo, Item #2 (widgets)	-1.383	-0.560	-0.157	0.231	1.026
Placebo, Item #3 (lily pads)	-0.448	0.395	0.791	1.181	2.017
Testosterone, Item #1 (bat & ball)	-1.806	-1.002	-0.609	-0.208	0.654
Testosterone, Item #2 (widgets)	-1.783	-0.982	-0.596	-0.195	0.641
Testosterone, Item #3 (lily pads)	-0.670	0.143	0.536	0.943	1.764
Variance Components					
Experiment	0.043	0.400	0.680	1.003	1.990
Experiment × Item	0.057	0.324	0.464	0.638	1.127
Group	0.026	0.240	0.458	0.735	1.410
Group × Item	0.008	0.090	0.194	0.328	0.657
Participant	2.070	2.262	2.371	2.482	2.712

Table S11. Estimates from models including methodological difference variables.

Table S11A. Experimenter Gender.

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Three New Experiments					
Treatment × Gender	**-1.496**	**-0.771**	**-0.408**	**-0.053**	**0.643**
Meta-analytic Avg Treatment Effect, Female	-0.693	-0.183	0.064	0.319	0.884
Meta-analytic Avg Treatment Effect, Male	-1.362	-0.681	-0.342	0.001	0.682
Coefficients					
Placebo, Item #1 (bat & ball), Female	-1.956	-1.274	-0.923	-0.570	0.174
Placebo, Item #2 (widgets), Female	-1.507	-0.809	-0.462	-0.110	0.600
Placebo, Item #3 (lily pads), Female	-0.537	0.157	0.499	0.856	1.549
Testosterone, Item #1 (bat & ball), Female	-1.857	-1.197	-0.857	-0.505	0.269
Testosterone, Item #2 (widgets), Female	-1.428	-0.746	-0.407	-0.055	0.683
Testosterone, Item #3 (lily pads), Female	-0.452	0.240	0.582	0.929	1.667
Placebo, Item #1 (bat & ball), Male	-1.727	-0.965	-0.581	-0.178	0.647
Placebo, Item #2 (widgets), Male	-0.823	-0.065	0.313	0.708	1.509
Placebo, Item #3 (lily pads), Male	-0.504	0.266	0.659	1.050	1.857
Testosterone, Item #1 (bat & ball), Male	-1.667	-0.891	-0.472	-0.046	0.812
Testosterone, Item #2 (widgets), Male	-1.596	-0.794	-0.378	0.044	0.894
Testosterone, Item #3 (lily pads), Male	-1.014	-0.190	0.230	0.645	1.472
Variance Components					
Experiment	0.058	0.405	0.643	0.972	2.032
Experiment × Item	0.016	0.152	0.287	0.462	0.983
Group	0.011	0.118	0.259	0.454	0.936
Group × Item	0.009	0.095	0.191	0.305	0.553
Participant	1.983	2.187	2.303	2.419	2.654
Three New Experiments and Nave et al.					
Treatment × Gender	**-1.610**	**-1.003**	**-0.682**	**-0.364**	**0.273**
Meta-analytic Avg Treatment Effect, Female	-0.757	-0.245	0.001	0.244	0.778
Meta-analytic Avg Treatment Effect, Male	-1.456	-0.955	-0.695	-0.417	0.225
Coefficients					
Placebo, Item #1 (bat & ball), Female	-1.722	-1.012	-0.666	-0.319	0.401
Placebo, Item #2 (widgets), Female	-1.499	-0.781	-0.436	-0.092	0.601
Placebo, Item #3 (lily pads), Female	-0.264	0.457	0.800	1.139	1.843
Testosterone, Item #1 (bat & ball), Female	-1.726	-1.026	-0.680	-0.325	0.369
Testosterone, Item #2 (widgets), Female	-1.473	-0.762	-0.414	-0.064	0.635
Testosterone, Item #3 (lily pads), Female	-0.252	0.439	0.791	1.133	1.836
Placebo, Item #1 (bat & ball), Male	-1.092	-0.377	-0.029	0.315	1.001
Placebo, Item #2 (widgets), Male	-0.709	-0.001	0.346	0.700	1.394
Placebo, Item #3 (lily pads), Male	0.140	0.860	1.209	1.561	2.234
Testosterone, Item #1 (bat & ball), Male	-1.528	-0.790	-0.423	-0.049	0.641
Testosterone, Item #2 (widgets), Male	-1.571	-0.849	-0.481	-0.115	0.612
Testosterone, Item #3 (lily pads), Male	-0.723	0.041	0.410	0.773	1.459
Variance Components					
Experiment	0.066	0.459	0.695	0.988	1.915
Experiment × Item	0.032	0.245	0.385	0.549	1.011
Group	0.011	0.118	0.261	0.454	0.917
Group × Item	0.010	0.100	0.200	0.311	0.537
Participant	2.042	2.220	2.318	2.418	2.626

Table S11B. Time of Day.

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Three New Experiments					
Treatment × Time of Day	**-0.080**	**0.067**	**0.144**	**0.218**	**0.364**
Placebo, Time of Day effect	-0.262	-0.145	-0.085	-0.025	0.088
Testosterone, Time of Day effect	-0.100	0.005	0.058	0.111	0.214
Coefficients					
Placebo, Item #1 (bat & ball)	-1.928	-1.111	-0.707	-0.302	0.588
Placebo, Item #2 (widgets)	-1.198	-0.389	0.017	0.420	1.261
Placebo, Item #3 (lily pads)	-0.332	0.443	0.841	1.242	2.086
Testosterone, Item #1 (bat & ball)	-2.055	-1.240	-0.848	-0.434	0.459
Testosterone, Item #2 (widgets)	-2.065	-1.258	-0.869	-0.458	0.396
Testosterone, Item #3 (lily pads)	-0.673	0.120	0.513	0.908	1.753
Placebo, Item #1 (bat & ball), Time of day	-0.283	-0.131	-0.051	0.028	0.176
Placebo, Item #2 (widgets), Time of day	-0.309	-0.169	-0.096	-0.022	0.118
Placebo, Item #3 (lily pads), Time of day	-0.321	-0.180	-0.108	-0.035	0.099
Testosterone, Item #1 (bat & ball), Time of day	-0.182	-0.046	0.024	0.094	0.225
Testosterone, Item #2 (widgets), Time of day	-0.032	0.095	0.162	0.229	0.362
Testosterone, Item #3 (lily pads), Time of day	-0.206	-0.077	-0.012	0.053	0.178
Variance Components					
Experiment	0.068	0.424	0.666	1.001	2.091
Experiment × Item	0.015	0.138	0.251	0.404	0.903
Group	0.011	0.111	0.241	0.438	0.929
Group × Item	0.009	0.087	0.179	0.292	0.530
Participant	1.991	2.195	2.306	2.425	2.661
Three New Experiments and Nave et al.					
Treatment × Time of Day	**-0.117**	**0.028**	**0.106**	**0.184**	**0.335**
Placebo, Time of Day effect	-0.240	-0.120	-0.060	0.000	0.115
Testosterone, Time of Day effect	-0.111	-0.007	0.047	0.101	0.202
Coefficients					
Placebo, Item #1 (bat & ball)	-1.502	-0.714	-0.311	0.101	0.945
Placebo, Item #2 (widgets)	-1.022	-0.221	0.177	0.578	1.416
Placebo, Item #3 (lily pads)	0.063	0.827	1.230	1.635	2.462
Testosterone, Item #1 (bat & ball)	-1.801	-0.985	-0.580	-0.183	0.636
Testosterone, Item #2 (widgets)	-2.082	-1.264	-0.859	-0.459	0.351
Testosterone, Item #3 (lily pads)	-0.456	0.351	0.741	1.131	1.928
Placebo, Item #1 (bat & ball), Time of day	-0.253	-0.100	-0.021	0.058	0.207
Placebo, Item #2 (widgets), Time of day	-0.307	-0.159	-0.084	-0.010	0.131
Placebo, Item #3 (lily pads), Time of day	-0.291	-0.146	-0.072	0.001	0.137
Testosterone, Item #1 (bat & ball), Time of day	-0.187	-0.051	0.019	0.088	0.220
Testosterone, Item #2 (widgets), Time of day	-0.054	0.076	0.145	0.213	0.344
Testosterone, Item #3 (lily pads), Time of day	-0.215	-0.087	-0.022	0.045	0.171
Variance Components					
Experiment	0.050	0.438	0.698	1.016	1.994
Experiment × Item	0.041	0.250	0.361	0.497	0.911
Group	0.030	0.251	0.427	0.625	1.102
Group × Item	0.008	0.084	0.179	0.295	0.530
Participant	2.042	2.221	2.320	2.423	2.632

Table S11C. Experimental Blinding Conditions.

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Three New Experiments					
Treatment × Blinding	**-2.462**	**-1.145**	**-0.502**	**0.132**	**1.440**
Meta-analytic Avg Treatment Effect, Double-blind	-0.792	-0.248	0.009	0.283	0.937
Meta-analytic Avg Treatment Effect, Single-blind	-2.223	-1.064	-0.491	0.086	1.311
Coefficients					
Placebo, Item #1 (bat & ball), Double-blind	-2.025	-1.287	-0.938	-0.585	0.153
Placebo, Item #2 (widgets), Double-blind	-1.445	-0.697	-0.348	0.004	0.712
Placebo, Item #3 (lily pads), Double-blind	-0.695	0.052	0.399	0.755	1.497
Testosterone, Item #1 (bat & ball), Double-blind	-1.969	-1.253	-0.900	-0.545	0.252
Testosterone, Item #2 (widgets), Double-blind	-1.512	-0.788	-0.441	-0.079	0.661
Testosterone, Item #3 (lily pads), Double-blind	-0.560	0.169	0.518	0.874	1.632
Placebo, Item #1 (bat & ball), Single-blind	-2.119	-0.985	-0.392	0.183	1.334
Placebo, Item #2 (widgets), Single-blind	-1.484	-0.288	0.290	0.871	2.031
Placebo, Item #3 (lily pads), Single-blind	-0.535	0.656	1.250	1.833	3.010
Testosterone, Item #1 (bat & ball), Single-blind	-1.860	-0.698	-0.123	0.469	1.642
Testosterone, Item #2 (widgets), Single-blind	-2.064	-0.917	-0.327	0.266	1.436
Testosterone, Item #3 (lily pads), Single-blind	-1.621	-0.464	0.130	0.708	1.857
Variance Components					
Experiment	0.047	0.366	0.610	0.928	1.988
Experiment × Item	0.011	0.114	0.237	0.407	0.921
Group	0.014	0.141	0.304	0.523	1.043
Group × Item	0.010	0.105	0.212	0.340	0.623
Participant	1.979	2.182	2.294	2.412	2.655
Three New Experiments and Nave et al.					
Treatment × Blinding	**-2.336**	**-0.878**	**-0.211**	**0.453**	**1.806**
Meta-analytic Avg Treatment Effect, Double-blind	-1.027	-0.513	-0.269	-0.004	0.667
Meta-analytic Avg Treatment Effect, Single-blind	-2.343	-1.095	-0.476	0.152	1.448
Coefficients					
Placebo, Item #1 (bat & ball), Double-blind	-1.461	-0.754	-0.407	-0.072	0.589
Placebo, Item #2 (widgets), Double-blind	-1.244	-0.505	-0.164	0.174	0.844
Placebo, Item #3 (lily pads), Double-blind	-0.161	0.581	0.915	1.258	1.923
Testosterone, Item #1 (bat & ball), Double-blind	-1.662	-0.966	-0.623	-0.281	0.411
Testosterone, Item #2 (widgets), Double-blind	-1.522	-0.809	-0.465	-0.127	0.546
Testosterone, Item #3 (lily pads), Double-blind	-0.387	0.337	0.686	1.030	1.731
Placebo, Item #1 (bat & ball), Single-blind	-2.115	-0.896	-0.293	0.318	1.513
Placebo, Item #2 (widgets), Single-blind	-1.430	-0.231	0.383	0.991	2.163
Placebo, Item #3 (lily pads), Single-blind	-0.487	0.730	1.354	1.982	3.183
Testosterone, Item #1 (bat & ball), Single-blind	-1.820	-0.608	0.006	0.634	1.810
Testosterone, Item #2 (widgets), Single-blind	-2.033	-0.827	-0.207	0.416	1.622
Testosterone, Item #3 (lily pads), Single-blind	-1.590	-0.376	0.251	0.862	2.061
Variance Components					
Experiment	0.051	0.431	0.696	1.006	1.958
Experiment × Item	0.035	0.240	0.357	0.495	0.917
Group	0.028	0.250	0.444	0.657	1.123
Group × Item	0.012	0.110	0.216	0.340	0.592
Participant	2.043	2.219	2.316	2.416	2.620

Table S11D. Experimental Stressor Conditions.

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Three New Experiments					
Treatment × (Cold Pressor versus Control)	**-0.775**	**0.658**	**1.345**	**2.040**	**3.393**
Treatment × (SCEPT versus Control)	**-3.291**	**-1.918**	**-1.211**	**-0.524**	**0.853**
Meta-analytic Avg Treatment Effect, Control	-0.851	-0.347	-0.107	0.138	0.745
Meta-analytic Avg Treatment Effect, Cold Pressor	-0.675	0.599	1.244	1.879	3.171
Meta-analytic Avg Treatment Effect, SECPT	-3.225	-1.969	-1.328	-0.665	0.635
Coefficients					
Placebo, Item #1 (bat & ball), Control	-1.972	-1.283	-0.937	-0.578	0.193
Placebo, Item #2 (widgets), Control	-1.373	-0.669	-0.333	0.015	0.765
Placebo, Item #3 (lily pads), Control	-0.932	-0.147	0.203	0.552	1.266
Testosterone, Item #1 (bat & ball), Control	-1.873	-1.196	-0.851	-0.489	0.284
Testosterone, Item #2 (widgets), Control	-1.691	-0.993	-0.660	-0.307	0.441
Testosterone, Item #3 (lily pads), Control	-0.983	-0.200	0.148	0.505	1.229
Placebo, Item #1 (bat & ball), Cold Pressor	-3.099	-1.826	-1.168	-0.511	0.746
Placebo, Item #2 (widgets), Cold Pressor	-2.756	-1.444	-0.795	-0.135	1.104
Placebo, Item #3 (lily pads), Cold Pressor	-1.295	-0.056	0.589	1.248	2.519
Testosterone, Item #1 (bat & ball), Cold Pressor	-1.592	-0.345	0.307	0.962	2.219
Testosterone, Item #2 (widgets), Cold Pressor	-2.022	-0.754	-0.113	0.530	1.790
Testosterone, Item #3 (lily pads), Cold Pressor	0.143	1.461	2.149	2.836	4.214
Placebo, Item #1 (bat & ball), SECPT	-1.786	-0.518	0.152	0.818	2.090
Placebo, Item #2 (widgets), SECPT	-1.391	-0.117	0.549	1.233	2.556
Placebo, Item #3 (lily pads), SECPT	0.219	1.557	2.279	3.017	4.479
Testosterone, Item #1 (bat & ball), SECPT	-3.481	-2.235	-1.583	-0.942	0.282
Testosterone, Item #2 (widgets), SECPT	-1.450	-0.235	0.399	1.037	2.224
Testosterone, Item #3 (lily pads), SECPT	-1.582	-0.362	0.264	0.880	2.119
Variance Components					
Experiment	0.030	0.270	0.499	0.802	1.815
Experiment × Item	0.027	0.214	0.359	0.546	1.074
Group	0.010	0.099	0.215	0.389	0.872
Group × Item	0.009	0.084	0.176	0.296	0.577
Participant	2.000	2.204	2.319	2.439	2.675
Three New Experiments and Nave et al.					
Treatment × (Cold Pressor versus Control)	**-0.597**	**0.926**	**1.642**	**2.328**	**3.677**
Treatment × (SCEPT versus Control)	**-3.008**	**-1.604**	**-0.898**	**-0.196**	**1.235**
Meta-analytic Avg Treatment Effect, Control	-1.076	-0.611	-0.393	-0.162	0.442
Meta-analytic Avg Treatment Effect, Cold Pressor	-0.779	0.590	1.262	1.909	3.164
Meta-analytic Avg Treatment Effect, SECPT	-3.268	-1.948	-1.285	-0.614	0.765
Coefficients					
Placebo, Item #1 (bat & ball), Control	-1.444	-0.731	-0.392	-0.061	0.630
Placebo, Item #2 (widgets), Control	-1.168	-0.465	-0.123	0.215	0.891
Placebo, Item #3 (lily pads), Control	-0.309	0.429	0.774	1.107	1.773
Testosterone, Item #1 (bat & ball), Control	-1.632	-0.951	-0.617	-0.275	0.406
Testosterone, Item #2 (widgets), Control	-1.669	-0.974	-0.644	-0.297	0.370
Testosterone, Item #3 (lily pads), Control	-0.687	0.038	0.382	0.712	1.378
Placebo, Item #1 (bat & ball), Cold Pressor	-3.062	-1.753	-1.098	-0.433	0.840
Placebo, Item #2 (widgets), Cold Pressor	-2.789	-1.491	-0.825	-0.141	1.123
Placebo, Item #3 (lily pads), Cold Pressor	-1.215	0.062	0.740	1.399	2.669

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Testosterone, Item #1 (bat & ball), Cold Pressor	-1.589	-0.273	0.382	1.055	2.282
Testosterone, Item #2 (widgets), Cold Pressor	-2.127	-0.796	-0.133	0.531	1.775
Testosterone, Item #3 (lily pads), Cold Pressor	0.263	1.596	2.275	2.993	4.365
Placebo, Item #1 (bat & ball), SECPT	-1.813	-0.478	0.212	0.896	2.221
Placebo, Item #2 (widgets), SECPT	-1.486	-0.171	0.512	1.211	2.507
Placebo, Item #3 (lily pads), SECPT	0.269	1.642	2.375	3.139	4.613
Testosterone, Item #1 (bat & ball), SECPT	-3.507	-2.157	-1.501	-0.852	0.394
Testosterone, Item #2 (widgets), SECPT	-1.510	-0.252	0.396	1.052	2.315
Testosterone, Item #3 (lily pads), SECPT	-1.484	-0.231	0.408	1.051	2.277
Variance Components					
Experiment	0.066	0.461	0.705	0.997	1.930
Experiment × Item	0.053	0.288	0.411	0.570	1.026
Group	0.017	0.159	0.312	0.512	0.983
Group × Item	0.008	0.084	0.171	0.287	0.531
Participant	2.062	2.236	2.334	2.435	2.639

Table S12. Estimates from models including individual difference variables.

Table S12A. Basal Cortisol

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Three New Experiments					
Treatment × Basal Cortisol	**-0.428**	**-0.025**	**0.179**	**0.381**	**0.781**
Placebo, Basal Cortisol effect	-0.531	-0.248	-0.103	0.044	0.329
Testosterone, Basal Cortisol effect	-0.364	-0.078	0.077	0.226	0.522
Coefficients					
Placebo, Item #1 (bat & ball)	-2.101	-1.267	-0.852	-0.428	0.485
Placebo, Item #2 (widgets)	-1.165	-0.332	0.074	0.492	1.374
Placebo, Item #3 (lily pads)	-0.703	0.142	0.556	0.976	1.858
Testosterone, Item #1 (bat & ball)	-2.109	-1.257	-0.840	-0.403	0.495
Testosterone, Item #2 (widgets)	-2.005	-1.165	-0.738	-0.324	0.600
Testosterone, Item #3 (lily pads)	-0.653	0.174	0.589	1.009	1.912
Placebo, Item #1 (bat & ball), Cortisol	-0.582	-0.212	-0.022	0.168	0.543
Placebo, Item #2 (widgets), Cortisol	-0.810	-0.449	-0.268	-0.079	0.264
Placebo, Item #3 (lily pads), Cortisol	-0.548	-0.203	-0.019	0.162	0.520
Testosterone, Item #1 (bat & ball), Cortisol	-0.534	-0.156	0.043	0.240	0.619
Testosterone, Item #2 (widgets), Cortisol	-0.294	0.074	0.271	0.462	0.841
Testosterone, Item #3 (lily pads), Cortisol	-0.641	-0.277	-0.089	0.105	0.475
Variance Components					
Experiment	0.062	0.412	0.661	1.000	2.074
Experiment × Item	0.016	0.142	0.263	0.421	0.920
Group	0.010	0.107	0.239	0.425	0.902
Group × Item	0.009	0.084	0.175	0.287	0.523
Participant	1.986	2.191	2.304	2.422	2.660
Three New Experiments and Nave et al.					
Treatment × Basal Cortisol	**-0.403**	**-0.045**	**0.137**	**0.325**	**0.682**
Placebo, Basal Cortisol effect	-0.396	-0.146	-0.012	0.117	0.373
Testosterone, Basal Cortisol effect	-0.264	-0.006	0.124	0.257	0.521
Coefficients					
Placebo, Item #1 (bat & ball)	-1.514	-0.720	-0.344	0.040	0.807
Placebo, Item #2 (widgets)	-1.135	-0.373	-0.002	0.369	1.164
Placebo, Item #3 (lily pads)	-0.190	0.601	0.984	1.367	2.146
Testosterone, Item #1 (bat & ball)	-1.887	-1.105	-0.722	-0.338	0.433
Testosterone, Item #2 (widgets)	-1.954	-1.166	-0.776	-0.390	0.398
Testosterone, Item #3 (lily pads)	-0.348	0.414	0.799	1.176	1.956
Placebo, Item #1 (bat & ball), Cortisol	-0.519	-0.198	-0.030	0.140	0.470
Placebo, Item #2 (widgets), Cortisol	-0.515	-0.206	-0.041	0.121	0.435
Placebo, Item #3 (lily pads), Cortisol	-0.465	-0.140	0.028	0.199	0.519
Testosterone, Item #1 (bat & ball), Cortisol	-0.329	-0.010	0.164	0.333	0.670
Testosterone, Item #2 (widgets), Cortisol	-0.185	0.144	0.312	0.484	0.816
Testosterone, Item #3 (lily pads), Cortisol	-0.597	-0.269	-0.101	0.067	0.391
Variance Components					
Experiment	0.074	0.472	0.718	1.030	2.017
Experiment × Item	0.040	0.240	0.347	0.479	0.877
Group	0.020	0.193	0.363	0.563	1.014
Group × Item	0.009	0.091	0.185	0.298	0.523
Participant	2.042	2.221	2.319	2.423	2.627

Table S12B. Right Hand 2D:4D

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Three New Experiments					
Treatment × R2D:4D	**-4.067**	**-1.460**	**-0.150**	**1.167**	**3.698**
Placebo, R2D:4D effect	-2.737	-0.861	0.095	1.058	2.919
Testosterone, R2D:4D effect	-2.865	-1.038	-0.074	0.923	2.825
Coefficients					
Placebo, Item #1 (bat & ball)	-5.029	-2.287	-0.844	0.620	3.399
Placebo, Item #2 (widgets)	-5.123	-2.405	-0.994	0.452	3.194
Placebo, Item #3 (lily pads)	-3.131	-0.376	1.081	2.493	5.230
Testosterone, Item #1 (bat & ball)	-5.178	-2.326	-0.880	0.559	3.435
Testosterone, Item #2 (widgets)	-4.851	-2.076	-0.644	0.871	3.634
Testosterone, Item #3 (lily pads)	-3.101	-0.340	1.137	2.589	5.400
Placebo, Item #1 (bat & ball), R2D:4D	-4.530	-1.564	0.022	1.586	4.524
Placebo, Item #2 (widgets), R2D:4D	-3.654	-0.710	0.846	2.331	5.316
Placebo, Item #3 (lily pads), R2D:4D	-4.979	-2.073	-0.540	0.991	3.965
Testosterone, Item #1 (bat & ball), R2D:4D	-4.440	-1.354	0.207	1.738	4.821
Testosterone, Item #2 (widgets), R2D:4D	-4.226	-1.264	0.308	1.872	4.879
Testosterone, Item #3 (lily pads), R2D:4D	-5.265	-2.224	-0.682	0.881	3.840
Variance Components					
Experiment	0.053	0.387	0.640	1.002	2.204
Experiment × Item	0.015	0.152	0.278	0.443	0.967
Group	0.010	0.109	0.240	0.426	0.910
Group × Item	0.013	0.129	0.241	0.359	0.607
Participant	1.963	2.178	2.295	2.417	2.671
Three New Experiments and Nave et al.					
Treatment × R2D:4D	**-4.096**	**-1.613**	**-0.310**	**1.006**	**3.520**
Placebo, R2D:4D effect	-2.554	-0.716	0.236	1.167	3.055
Testosterone, R2D:4D effect	-2.832	-1.037	-0.077	0.878	2.724
Coefficients					
Placebo, Item #1 (bat & ball)	-4.723	-2.044	-0.626	0.770	3.481
Placebo, Item #2 (widgets)	-5.089	-2.439	-1.025	0.371	3.011
Placebo, Item #3 (lily pads)	-2.423	0.258	1.665	3.066	5.727
Testosterone, Item #1 (bat & ball)	-4.864	-2.181	-0.747	0.654	3.330
Testosterone, Item #2 (widgets)	-3.966	-1.304	0.123	1.518	4.190
Testosterone, Item #3 (lily pads)	-3.455	-0.727	0.706	2.115	4.814
Placebo, Item #1 (bat & ball), R2D:4D	-4.065	-1.179	0.285	1.812	4.683
Placebo, Item #2 (widgets), R2D:4D	-3.265	-0.449	1.037	2.562	5.363
Placebo, Item #3 (lily pads), R2D:4D	-5.060	-2.160	-0.688	0.850	3.719
Testosterone, Item #1 (bat & ball), R2D:4D	-4.108	-1.223	0.304	1.827	4.703
Testosterone, Item #2 (widgets), R2D:4D	-4.810	-2.017	-0.511	1.038	3.862
Testosterone, Item #3 (lily pads), R2D:4D	-4.431	-1.543	-0.033	1.494	4.448
Variance Components					
Experiment	0.065	0.468	0.724	1.047	2.002
Experiment × Item	0.036	0.241	0.365	0.507	0.941
Group	0.018	0.183	0.345	0.542	1.016
Group × Item	0.016	0.136	0.242	0.356	0.581
Participant	2.033	2.209	2.308	2.413	2.624

Table S12C. Left Hand 2D:4D

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Three New Experiments					
Treatment × L2D:4D	**-3.910**	**-1.399**	**-0.067**	**1.257**	**3.752**
Placebo, L2D:4D effect	-2.555	-0.678	0.293	1.275	3.173
Testosterone, L2D:4D effect	-2.636	-0.767	0.217	1.227	3.117
Coefficients					
Placebo, Item #1 (bat & ball)	-4.304	-1.527	-0.101	1.364	4.230
Placebo, Item #2 (widgets)	-5.421	-2.650	-1.228	0.211	2.920
Placebo, Item #3 (lily pads)	-3.918	-1.226	0.200	1.596	4.377
Testosterone, Item #1 (bat & ball)	-5.991	-3.139	-1.647	-0.177	2.685
Testosterone, Item #2 (widgets)	-4.835	-2.055	-0.580	0.887	3.649
Testosterone, Item #3 (lily pads)	-3.062	-0.263	1.202	2.656	5.466
Placebo, Item #1 (bat & ball), L2D:4D	-5.393	-2.321	-0.725	0.814	3.774
Placebo, Item #2 (widgets), L2D:4D	-3.262	-0.345	1.190	2.736	5.697
Placebo, Item #3 (lily pads), L2D:4D	-4.100	-1.086	0.452	1.971	4.894
Testosterone, Item #1 (bat & ball), L2D:4D	-3.592	-0.531	1.044	2.649	5.743
Testosterone, Item #2 (widgets), L2D:4D	-4.196	-1.232	0.339	1.891	4.890
Testosterone, Item #3 (lily pads), L2D:4D	-5.294	-2.278	-0.703	0.874	3.892
Variance Components					
Experiment	0.051	0.395	0.648	0.994	2.261
Experiment × Item	0.011	0.123	0.239	0.395	0.916
Group	0.010	0.108	0.242	0.434	0.899
Group × Item	0.012	0.112	0.213	0.325	0.567
Participant	1.962	2.168	2.284	2.408	2.658
Three New Experiments and Nave et al.					
Treatment × L2D:4D	**-4.266**	**-1.811**	**-0.517**	**0.793**	**3.266**
Placebo, L2D:4D effect	-2.167	-0.373	0.576	1.523	3.347
Testosterone, L2D:4D effect	-2.688	-0.882	0.081	1.041	2.837
Coefficients					
Placebo, Item #1 (bat & ball)	-4.010	-1.425	-0.027	1.373	4.014
Placebo, Item #2 (widgets)	-5.234	-2.628	-1.255	0.098	2.759
Placebo, Item #3 (lily pads)	-3.631	-0.936	0.441	1.828	4.487
Testosterone, Item #1 (bat & ball)	-5.498	-2.775	-1.395	0.070	2.767
Testosterone, Item #2 (widgets)	-3.927	-1.288	0.121	1.563	4.224
Testosterone, Item #3 (lily pads)	-3.163	-0.478	0.958	2.364	5.075
Placebo, Item #1 (bat & ball), L2D:4D	-4.642	-1.811	-0.322	1.211	4.005
Placebo, Item #2 (widgets), L2D:4D	-2.905	-0.062	1.389	2.864	5.643
Placebo, Item #3 (lily pads), L2D:4D	-3.659	-0.827	0.693	2.155	5.011
Testosterone, Item #1 (bat & ball), L2D:4D	-3.432	-0.567	1.006	2.497	5.417
Testosterone, Item #2 (widgets), L2D:4D	-4.844	-1.998	-0.474	1.045	3.901
Testosterone, Item #3 (lily pads), L2D:4D	-4.649	-1.774	-0.266	1.267	4.108
Variance Components					
Experiment	0.066	0.454	0.714	1.037	2.077
Experiment × Item	0.036	0.236	0.355	0.495	0.922
Group	0.017	0.184	0.352	0.553	1.009
Group × Item	0.013	0.123	0.228	0.340	0.565
Participant	2.033	2.211	2.311	2.416	2.624

Table S12D. Trait Impulsivity

	2.5%	*25%*	*50%*	*75%*	*97.5%*
Three New Experiments					
Treatment × Trait Impulsivity	**0.061**	**0.363**	**0.522**	**0.681**	**0.988**
Placebo, Trait Impulsivity effect	-0.612	-0.390	-0.278	-0.167	0.043
Testosterone, Trait Impulsivity effect	-0.085	0.131	0.241	0.356	0.579
Coefficients					
Placebo, Item #1 (bat & ball)	-1.939	-1.202	-0.863	-0.511	0.311
Placebo, Item #2 (widgets)	-1.328	-0.573	-0.227	0.129	0.944
Placebo, Item #3 (lily pads)	-0.524	0.202	0.544	0.902	1.720
Testosterone, Item #1 (bat & ball)	-1.910	-1.165	-0.820	-0.466	0.352
Testosterone, Item #2 (widgets)	-1.499	-0.780	-0.439	-0.085	0.726
Testosterone, Item #3 (lily pads)	-0.619	0.146	0.495	0.840	1.654
Placebo, Item #1 (bat & ball), Trait Impulsivity	-0.774	-0.484	-0.338	-0.196	0.077
Placebo, Item #2 (widgets), Trait Impulsivity	-0.925	-0.649	-0.505	-0.362	-0.097
Placebo, Item #3 (lily pads), Trait Impulsivity	-0.406	-0.126	0.010	0.147	0.412
Testosterone, Item #1 (bat & ball), Trait Impulsivity	-0.043	0.239	0.390	0.542	0.830
Testosterone, Item #2 (widgets), Trait Impulsivity	-0.259	0.017	0.161	0.306	0.589
Testosterone, Item #3 (lily pads), Trait Impulsivity	-0.234	0.037	0.176	0.317	0.589
Variance Components					
Experiment	0.063	0.423	0.666	1.005	2.110
Experiment × Item	0.013	0.128	0.247	0.404	0.897
Group	0.010	0.101	0.225	0.403	0.869
Group × Item	0.011	0.113	0.218	0.334	0.585
Participant	1.995	2.199	2.314	2.437	2.677

Notes: In Experiment 1, trait impulsivity was measured using the Zuckerman-Kuhlman Impulsivity subscale. In Experiment 2, trait impulsivity was measured using the Barratt Impulsivity Scale and the Brief Self-Control Scale. In Experiment 3, impulsivity was measured using the BAS fun-seeking subscale.

SM References

Ahern, T., Adaway, J., Monaghan, P., Trainer, P., & Keevil, B. (2017). Can salivary testosterone be used in the monitoring of men using transdermal testosterone replacement therapy? *Endocrine Abstracts*, 49, EP1169.

Bosch-Domènech, A., Brañas-Garza, P., & Espín, A. M. (2014). Can exposure to prenatal sex hormones (2D: 4D) predict cognitive reflection? *Psychoneuroendocrinology*, *43*, 1-10.

Brañas-Garza, P., Kujal, P., Lenkei, B. (2015). Cognitive Reflection Test: Whom, how, when (ESI Working Paper 15-25). Retrieved from http://digitalcommons.chapman.edu/esi_working_papers/174 Google Scholar

Carver, C. S., & White, T. L. (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: The BIS/BAS Scales. *Journal of personality and social psychology*, *67*(2), 319.

Eisenegger, C., von Eckardstein, A., Fehr, E., & von Eckardstein, S. (2013). Pharmacokinetics of testosterone and estradiol gel preparations in healthy young men. *Psychoneuroendocrinology*, *38*(2), 171-178.

Frederick, S. (2005). Cognitive reflection and decision making. *The Journal of Economic Perspectives*, *19*(4), 25-42.

Geniole, S.N., Procyshyn, T.L., Marley, N., Ortiz, T.L., Bird, B.M., Marcellus, A.L., Welker, K.M., Bonin, P.L., Goldfarb, B.,Watson, N.V. & Carré, J.M. (2019). Using a psychopharmacogenomic approach to identify the pathways through which and people for whom testosterone promotes aggression. *Psychological Science*, *30*(4), 481-494.

Granger, D. A., Shirtcliff, E. A., Booth, A., Kivlighan, K. T., & Schwartz, E. B. (2004). The "trouble" with salivary testosterone. *Psychoneuroendocrinology*, *29*(10), 1229-1240.

Haring, R., Hannemann, A., John, U., Radke, D., Nauck, M., Wallaschofski, H., ... & Brabant, G. (2012). Age-specific reference ranges for serum testosterone and androstenedione concentrations in women measured by liquid chromatography-tandem mass spectrometry. *Clinical Chemistry and Laboratory Medicine*, *50*(9), A242.

Hines, E.A. & Brown, G.E. (1932). A standard stimulus for measuring vasomotor reactions: Its application in the study of hypertension. *Mayo Clinic Proceedings*, *7*, 332.

Keevil, B. G., Clifton, S., Tanton, C., Macdowall, W., Copas, A. J., Lee, D., ... & Mercer, C. H. (2017). Distribution of salivary testosterone in men and women in a British general population-based sample: the third national survey of sexual attitudes and lifestyles (Natsal-3). *Journal of the Endocrine Society*, *1*(1), 14-25.

Knight, E. L., Christian, C. B., Morales, P. J., Harbaugh, W. T., Mayr, U., & Mehta, P. H. (2017). Exogenous testosterone enhances cortisol and affective responses to social-evaluative stress in dominant men. *Psychoneuroendocrinology*, 85, 151-157.

McShane, B. B., & Böckenholt, U. (2017). Single-paper meta-analysis: Benefits for study summary, theory testing, and replicability. *Journal of Consumer Research*, 43(6), 1048-1063.

McShane, B.B. and Böckenholt, U. (2018) "Multilevel Multivariate Meta-analysis with Application to Choice Overload." *Psychometrika*, 83(1), 255-271.

Nave, G., Nadler, A., Zava, D., & Camerer, C. (2017). Single-dose testosterone administration impairs cognitive reflection in men. *Psychological Science*, 28(10), 1398-1407.

Patton, J. H., & Stanford, M. S. (1995). Factor structure of the Barratt impulsiveness scale. *Journal of Clinical Psychology*, *51*(6), 768-774.

Prausnitz, M. R., & Langer, R. (2008). Transdermal drug delivery. *Nature Biotechnology*, *26*(11), 1261-1268.

R Core Team (2016). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/.

Schönfelder, M., Hofmann, H., Anielski, P., Thieme, D., Oberhoffer, R., & Michna, H. (2011). Gene expression profiling in human whole blood samples after controlled testosterone application and exercise. *Drug Testing and Analysis*, *3*(10), 652-660.

Schürmeyer, T., & Nieschlag, E. (1984). Comparative pharmacokinetics of testosterone enanthate and testosterone cyclohexanecarboxylate as assessed by serum and salivary testosterone levels in normal men. *International Journal of Andrology*, *7*(3), 181-187.

Schürmeyer, T. H., Wickings, E. J., Freischem, C. T., & Nieschlag, E. (1983). Saliva and serum testosterone following oral testosterone undecanoate administration in normal and hypogonadal men. *Acta Endocrinologica*, *102*(3), 456-462.
Schwabe, L., Haddad, L., & Schachinger, H. (2008). HPA axis activation by a socially evaluated cold-pressor test. *Psychoneuroendocrinology*, *33*(6), 890-895.
Stan Development Team (2016). rstanarm: Bayesian applied regression modeling via Stan. R package version 2.13.1. http://mc-stan.org/.
Stanford, M. S., Mathias, C. W., Dougherty, D. M., Lake, S. L., Anderson, N. E., & Patton, J. H. (2009). Fifty years of the Barratt Impulsiveness Scale: An update and review. *Personality and Individual Differences*, *47*(5), 385-395.
Tangney, J. P., Baumeister, R. F., & Boone, A. L. (2004). High self-control predicts good adjustment, less pathology, better grades, and interpersonal success. *Journal of Personality*, *72*(2), 271-324.
Thieme, D., Rautenberg, C., Grosse, J., & Schoenfelder, M. (2013). Significant increase of salivary testosterone levels after single therapeutic transdermal administration of testosterone: suitability as a potential screening parameter in doping control. *Drug Testing and Analysis*, *5*(11-12), 819-825.
Tuiten, A., Van Honk, J., Koppeschaar, H., Bernaards, C., Thijssen, J., & Verbaten, R. (2000). Time course of effects of testosterone administration on sexual arousal in women. *Archives of General Psychiatry*, *57*(2), 149-153.
Wang, C., Plymate, S., Nieschlag, E., & Paulsen, C. A. (1981). Salivary testosterone in men: further evidence of a direct correlation with free serum testosterone. *The Journal of Clinical Endocrinology & Metabolism*, *53*(5), 1021-1024.
Watson, D., Clark, L.A., (1994). The PANAS-X: Manual for the Positive and Negative Affect Schedule – Expanded Form http://www2.psychology.uiowa.edu/faculty/watson/PANAS-X.pdf.
Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. *Journal of Personality and Social Psychology*, *54*(6), 1063.
Wolthuis, A., & de Vreeze, J. (2005). Unexpected testosterone result for external quality assessment scheme sample. *Clinical Chemistry*, *51*(2), 475-476.
Zuckerman, M., Kuhlman, D. M., Joireman, J., Teta, P., & Kraft, M. (1993). A comparison of three structural models for personality: The Big Three, the Big Five, and the Alternative Five. *Journal of personality and social psychology*, *65*(4), 757.

Chapter 6

STUDY 5:
THINKING FAST OR SLOW UNDER TESTOSTERONE - EXPLORING VARIABILITY THROUGH COMPUTATIONAL PHARMACOGENETICS

Non-peer reviewed manuscript as submitted to a peer-review journal

Nace Mikus[a,b] *, Hana, H. Kutlikova[a]*, Christoph Eisenegger[a†], Claus Lamm[a,c]

[a] Neuropsychopharmacology and Biopsychology Unit, Department of Cognition, Emotion, and Methods in Psychology, Faculty of Psychology, University of Vienna, Vienna, Austria

[b] Interacting Minds Centre, Aarhus University, Aarhus, Denmark

[c] Vienna Cognitive Science Hub, University of Vienna, Liebiggasse 5, 1010 Vienna, Austria

Correspondence to:
Nace Mikus: nace.mikus@univie.ac.at
Hana H. Kutlikova: hana.kutlikova@univie.ac.at

Notes:
* Shared first co-authorship
† Deceased February 27, 2017

Abstract

The sex steroid testosterone has been linked to increased aggression and disorders of compulsivity, but also to enhanced motivation and better performance in cognitive tasks. To explore the pathways through which testosterone may impact these behaviors, we used a pharmacogenetic approach together with computational modeling and investigated the effect of testosterone administration on the trade-off between deliberate ('model-based') or intuitive ('model-free') decision-making. 216 healthy men underwent a placebo-controlled testosterone administration and completed a sequential decision-making paradigm. We found no effect of testosterone on the trade-off between the two types of decision-making but did observe an increase in the choice stochasticity parameter, indicating testosterone increases randomness in decision-making. Genetic phenotyping revealed that this randomness following testosterone administration was driven by the carriers of the 9-repeat allele of the dopamine transporter gene, associated with higher striatal dopamine. Our findings support the notion that although testosterone does not influence the arbitration between intuitive versus deliberate choices per se, it does affect decision-making, potentially through interacting with the dopaminergic system.

Introduction

Decision-making has been described as either deliberate and thought-through or intuitive and "quick and dirty" (Dickinson, 1985; Kahneman, 2011). Deliberate decision-making is goal-directed and involves a prospective consideration of alternatives but is time-intensive and cognitively effortful (Kool et al., 2016, 2017; Otto et al., 2013). In contrast, intuitive decision-making relies on past experiences to make quick decisions and is useful in situations where time is limited, or the stakes are low.

Testosterone is a sex hormone naturally produced by the body, primarily in the testes of males and the ovaries of females. Testosterone can be released into the bloodstream and act on the brain and body in response to external stimuli, such as the presence of an attractive mating partner or winning a competition, hence modulating physiological processes (Schultheiss & Mehta, 2019). While testosterone's effects on physiology are well-established, its role in decision-making and, specifically, in the arbitration between intuitive and deliberate behavior is less clear. Testosterone has been shown to increase impulsive and aggressive behavior in animals (Svensson et al., 2003) and humans (Carré et al., 2017; Geniole et al., 2019; Wu et al., 2020). Endogenous testosterone levels in humans also correlate positively with disorders of compulsivity, such as disorders of impulse control (Rodríguez-Nieto et al., 2021), eating disorders (Cotrufo et al., 2000), and substance use disorder (Reynolds et al., 2007) – i.e., conditions characterized by an overreliance on intuitive habitual actions (Gillan et al., 2016; Voon et al., 2015, 2017). These findings suggest that testosterone biases decision-making towards intuitive and away from effortful and deliberate processes, yet conclusive evidence is lacking.

A commonly used paradigm for measuring the trade-off between the two decision-making styles is the Cognitive Reflection Test (CRT, Frederick, 2005). The CRT consists of three questions. To answer them correctly, one must resist reporting the first intuitive response that comes to mind and, instead, engage in deliberate processing. In one study, testosterone administration increased incorrect intuitive responses in the CRT compared to placebo but had no effect on an arithmetic task of comparable difficulty (Nave et al., 2017). Based on these findings, the authors suggested that testosterone did not impair the capacity for deliberate behavior but decreased the probability of exerting cognitive effort. However, a subsequent study that combined data from the same test across three different experiments showed that the effects of testosterone on cognitive reflection are, on average, weak and associated with high variability (Knight et al., 2020). Importantly, the CRT has several limitations as a paradigm for assessing decision-making styles. With only three items, CRT may not be sensitive enough to capture individual differences in decision-making. Responses in the CRT might be thus influenced by increased impulsivity or increased noisiness in responding, leading to sloppier but not more intuitive decision-making.

In the present study, we used an alternative approach to provide a fine-grained, comprehensive investigation of testosterone's causal effects on the trade-off between deliberate and intuitive decision-making while controlling for testosterone's effects on other decision-making processes. To measure the degree to which participants (fail to) act deliberately when their testosterone levels are pharmacologically increased, we used the Two-step task (Daw et al., 2005), an incentivized decision-making task designed to measure an individual's contribution of intuitive and deliberate thinking to their decisions (Kool et al., 2016). The task is embedded in a reinforcement learning framework where a weighting of a model-free and a model-based valuation system influences decision-making. The model-free system learns from experience, is fast, computationally cheap, and is considered analogous to intuitive decision-making (Thorndike, 1911). The model-based system, on the other hand, is computationally expensive and uses its knowledge of the regularities in the world to make deliberate, prospective choices that, however, require cognitive effort. The degree of model-based (MB) or model-free (MF) decision-making is defined by the weight that one or the other system has on participants' choices. Choice behavior not accounted for by this trade-off is captured by a noise parameter.

To estimate the effects of testosterone on the relative engagement of the two systems while accounting for other decision-making processes, we analyzed participants' behavior in one hierarchical model, estimating the effects of testosterone on all parameters of the computational model simultaneously. If testosterone indeed impairs deliberate decision-making processes, we expected the weight to shift away from model-based and towards the model-free valuation system ("fast intuitive thinking hypothesis"). On the other hand, if testosterone has no effect on the trade-off between MF and MB systems but impairs performance in decision-making overall, we expected to detect increased noise in responding ("sloppy thinking hypothesis").

Finally, the responses to testosterone administration might interact with neural pathways related to the capacity for deliberate or intuitive behavior, which could account for some of the heterogeneity reported in other studies investigating testosterone's effects on the trade-off between the two systems. There is ample evidence that the dopaminergic system is involved in arbitrating between effortful deliberate and intuitive decisions (Kroemer et al., 2019; Mikus et al., 2022; Wunderlich et al., 2012) and that genetic variation related to the dopaminergic system accounts for some variation in behavior in the two-step task across participants (Doll et al., 2016). Similarly, there is evidence that testosterone affects aggressive behavior through the androgenic pathway (Geniole et al., 2019). We thus included in our hierarchical computational model three genotypes (COMT for prefrontal dopamine, DAT1 for striatal dopamine, and CAG-repeat for androgen receptor efficiency) to 1) account for the effects of baseline variation in these genes on behavior in the two-step task and 2) explore potential pathways through which testosterone might affect the trade-off between the two types of decision-making.

Method

Participants

The study sample consisted of 216 healthy adult men aged between 18 and 40 years (M =24.56, 95%CI = [24.03, 25.09] and was part of a larger experimental cohort (other studies reported elsewhere, e.g., Kutlikova et al., 2023). With this sample, we had more than 80% power to detect an effect size of 0.4, an effect size of testosterone's effects on the arbitration between deliberate and intuitive decision-making reported by Nave et al.(2017)

Participants were recruited using flyers placed around university campuses and online advertisements. The volunteers, who replied to these advertisements, were screened via an online questionnaire and a telephone interview. The exclusion criteria consisted of a history of neurological or psychiatric disorders, endocrine or other internal diseases, obesity, substance dependence, and the use of steroids. Only male participants were included as testosterone metabolism is subject to sex differences, and the pharmacokinetics of topical administration of testosterone is only known precisely in men (Eisenegger et al., 2013).

All participants gave written informed consent and received a financial reward for their participation consisting of a flat fee and a bonus based on their task performance. Due to technical problems, the data of three participants were not recorded, and these participants were excluded from the analysis. All procedures were approved by the local research ethics board and conducted in accordance with the latest revision of the Declaration of Helsinki (World Medical Association., 2001).

Procedure

Testing took place in groups of three to five participants, who were seated individually in small cubicles within the same testing room. To account for testosterone circadian variation (Plymate et al., 1989), testing sessions started between 01:00 and 02:30 p.m. First, a buccal smear sample for CAG repeat, DAT1, and COMT gene polymorphism analyses was taken (See SI for details). 20 min after arrival, participants were asked to drool 2 mL of saliva into a polyethylene collection tube. All salivary samples were frozen on-site and stored at -30°C until analysis. Afterward, participants were administered topical testosterone or placebo gel in a double-blind between-subjects design with random group allocation. These groups did not differ in baseline testosterone levels, AR CAG polymorphism, and trait impulsivity (see SI). Participants of a testing session were always assigned to the same drug treatment condition to minimize the risk of potential testosterone contamination of the laboratory equipment (Nave et al., 2017, see SI). Those allocated to the testosterone group received a single dose of testosterone gel containing 150 mg of testosterone [Androgel®]. Participants in the placebo group received an equivalent amount of placebo gel. The only difference between the testosterone and placebo gel was that the placebo gel

was void of testosterone. Participants rubbed the gel onto their upper arms and shoulders in small increments using disposable latex gloves. Gel administration was followed by a waiting period, during which participants remained in the laboratory premises, completed the Barratt Impulsiveness Scale (Patton et al., 1995) and demographic questionnaires, and were offered leisure-time materials (such as geographic magazines and documentaries). One hour and 50 minutes after the gel application, participants provided a second saliva sample and completed a battery of tasks and questionnaires unrelated to the current research question as part of a larger study protocol. 180 min after administration, participants provided a third saliva sample and started the Two-step task. A final saliva sample was taken at the end of the session (240 min after the administration).

Analysis of hormone data

After data collection was complete, saliva samples were shipped on dry ice to Dresden LabService GmbH and analyzed by liquid chromatography-tandem mass spectrometry. To verify the effectiveness of the gel administration, we compared the testosterone levels between placebo and testosterone group measured at baseline, 120 min after administration, just before the task (180 min after administration), and at the end of the session (240 min after the administration) using a GLMM with factors time, drug treatment, their interaction, and a random intercept. Due to the high skewness, hormone data were log-transformed.

Behavioral task

The two-step task is an incentivized sequential decision-making task that was designed to measure the trade-off between intuitive and deliberate behavior (Daw et al., 2005, 2011). Participants are required to earn points in a dynamically changing environment. Each trial consists of two steps or stages. In the first stage, participants see one of two possible starting scenarios, each featuring a pair of spaceships that fly deterministically to one of the two second stages that feature planets, where they encounter an alien that gives them points ranging from -4 to +5 (Fig. 1B). How many points each alien gives changes throughout the experiment according to a Gaussian random walk. The deterministic transition between the spaceships and the planets stays the same throughout the experiment and participants are explicitly instructed about it. This represents the participants' "knowledge about the regularities in the world".

Participants' best strategy to maximize the payoff in the game is simply choosing the spaceship that flies to the same planet as in the previous trial if the previous reward was high and changing to the other planet if the points were low. However, to do this in trials where the first-stage state is different from that of the previous trial, participants need to keep the mapping between spaceships and planets online when making choices (Fig. 1C). Within this task, a more intuitive player relies completely on their direct experience and will choose the spaceship related to reward in the previous trial regardless of their experience with the other pair of spaceships. A more deliberate player will be more goal-directed and use the causal structure of the task to their advantage and

always choose the spaceship that leads them to the planet (i.e., goal) that they want to reach. Importantly, in this version of the task, behaving in a more goal-directed manner leads to more points (Kool et al., 2016).

Participants have 2000 ms to choose in the first step and then again 2000 ms to press the space bar once they have encountered the alien. Each acquired point was translated to 4 cents and added to the overall compensation of the participant at the end of the experiment. The task was wrapped in a cover story to increase comprehension (Decker et al., 2016). Each participant first went through a rigorous automated explanation of the task, followed by 25 practice trials before completing 200 trials of the task.

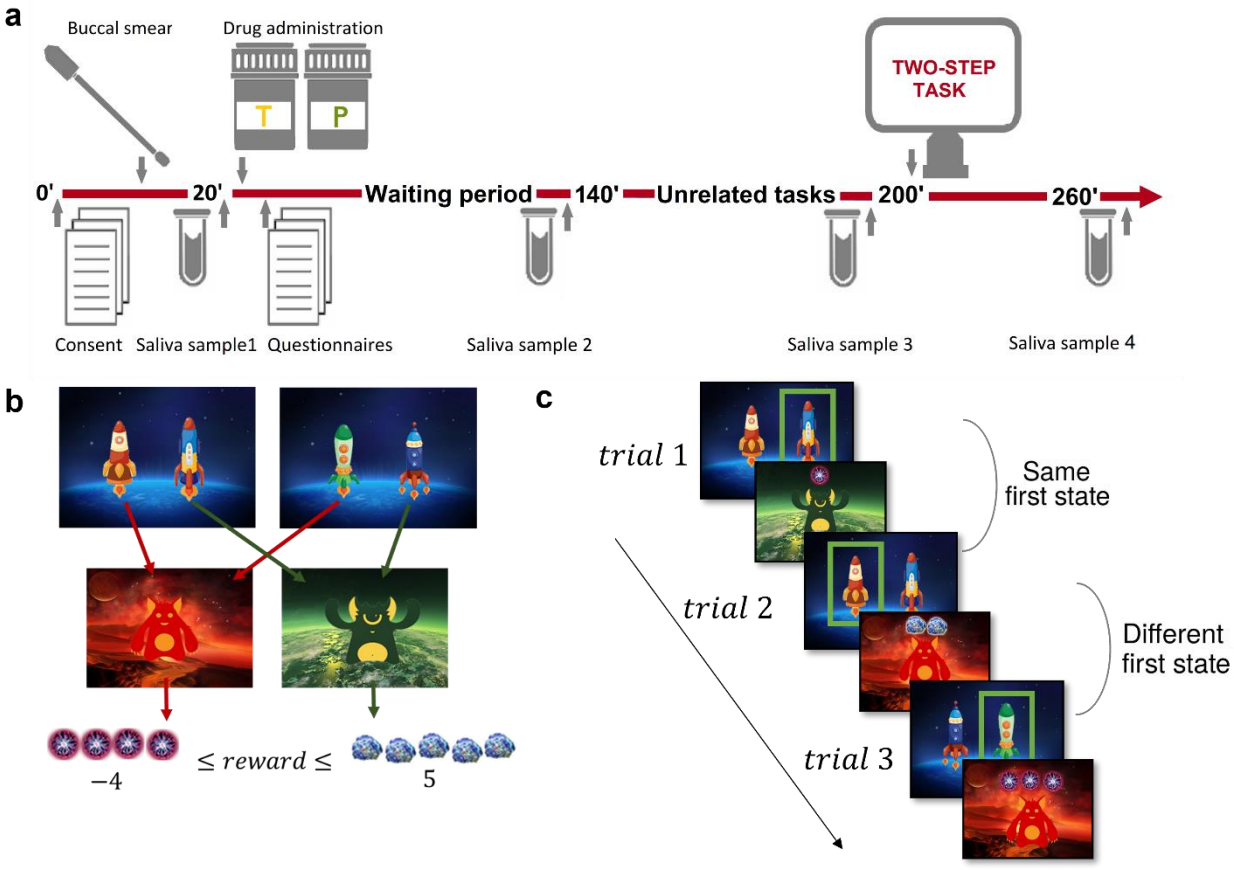


Fig. 1. Study and task design. (a) timeline of the experimental session. (b) the two-step task is an incentivized decision-making task that can be played either in a habitual, reflexive, or deliberate, goal-directed manner. Participants first see one of the two pairs of spaceships that fly deterministically to one of the two planets, where they receive points from an alien ranging from -4 to 5. (c) the number of points in a certain trial should either encourage switching (trial 1) or staying with the same choice (i.e., choosing the spaceship that flies to the same planet, trial 2). When the first state of the trial is different from that of the previous trial (trial 3), staying with the same planet requires that participants keep the mapping from spaceships to planets online.

Main analysis

We analyzed testosterone's effects on behavior in the Two-step task from two complementary angles. We first analyzed the participants' trial-by-trial choice data with a computational model. The aim of this analysis is to model how latent trial-level values of model-based and model-free

systems affect participants' choices and whether the parameters that determine these variables are affected by the testosterone administration.

To see what implications this analysis has more directly on behavioral patterns, we also conducted three behavioral analyses. We investigated how previous points affect choice repetition and how this effect differs in trials where the first-stage state is the same as in the previous trial, compared to those where it is different. On top of this, we analyzed points earned across the two trial types, as well as reaction times.

We used a hierarchical Bayesian approach in our analysis, report estimates in the parameter estimation space, and provide estimated precisions of estimates with the credibility interval and with the proportion of the credibility interval that is above (or below) zero.

Computational Model

To derive a measure for the degree to which participants were model-based (deliberate) or model-free (intuitive), we applied a computational model to the trial-by-trial choice data. The computational model assumes that there are two competing valuation systems that contribute to spaceship selection: a model-free system that is reflective and computationally cheap and a model-based system that is goal-directed and computationally more expensive. In particular, the model-free agent learns only from experience and repeats choices of the spaceships that were more favorable and avoids those that were punishing. The model-based agent, on the other hand, is always aware of the mapping between spaceships and planets and therefore focuses on the goal (planet) it wants to achieve. For each participant, we estimate three parameters: the weight of how much model-based, relative to model-free, system affects trial-by-trial choice; the discounting factor that accounts for the devaluation of unobserved stimulus outcome association across time; and a noise parameter, that determines the degree of behavior that is not accounted by the model.

For the model-free agent, the subjective value of each of the spaceships is simply the last encountered outcome following the choice of that spaceship, and for the model-based agent, the subjective value of each spaceship is the subjective value of the last encountered outcome following the planet that this spaceship flies to. That means that the update equation of the model-free agent after receiving outcome $r(s_2, t)$ following an action a, in trial t, with first state s_1, is defined as

$$Q_{MF}(a, s_1, t) = r(s_2, t).$$

whereas the value the unchosen actions a' across both first-level states s_1' are discounted with a parameter γ:

$$Q_{MF}(a', s_1, t) = (1 - \gamma)\, Q_{MF}(a', s_1, t - 1),$$

$$Q_{MF}(a, s_1{}', t) = (1 - \gamma)\, Q_{MF}(a, s_1', t - 1),$$

$$Q_{MF}(a', s_1', t) = (1 - \gamma)\, Q_{MF}(a', s_1', t - 1),$$

The model-based agent, on the other hand, after receiving outcome $r(t)$ following an action a, in trial t, with first state s_1, updates not only the experienced first stage state, but also the unencountered first stage state, that would have led to the same outcome:

$$Q_{MB}(a, s_1, t) = Q_2(s_2, t) = r(s_2, t)\,,$$

$$Q_{MB}(a, s_1{}', t) = Q_2(s_2, t) = r(s_2, t)\,,$$

where, $Q_2(s_2, t)$ is the subjective value of the second stage state that action a deterministically leads to. We then predicted participants' choices based on a soft-max transformation of the weighted sum of model-based (Q_{MB}) and model-free (Q_{MF}) subjective values of the spaceships in each trial t,

$$Q_{mix}(a, s, t) = \omega Q_{MB}(\mathrm{a}, \mathrm{s}, t) + (1 - \omega) Q_{MF}(\mathrm{a}, \mathrm{s}, t)$$

$$P(a, s, t) = \frac{1}{1 + e^{\eta Q_{mix}}}$$

where a is the action of choosing a spaceship in state s, ω is the trade-off between the weight on model-based and model-free values (with higher values implying more model-based relative to model-free behavior), and η is the decision temperature parameter (with lower values implying more stochastic or exploratory behaviors). In a previous study (Mikus et al., 2022), we show that this model outperforms two versions of a Dual-system Reinforcement learning model inspired by Kool et al., (2016, 2017). In the two versions of the model, the model-free agent learns the subjective values of spaceships and planets through a temporal difference learning algorithm (Daw et al., 2011; Sutton & Barto, 2018), with either two different learning rates across the stages, or with a single learning rate.

Model estimation

We estimated the model parameters in one hierarchical (multilevel) Bayesian model. This pools information across different levels (treatment groups and participants), as well as across random effects, and thus leads to more stable individual parameter estimates (Ahn et al., 2017) and reduces overfitting (McElreath, 2016). Furthermore, it allows us to estimate both individual- and group-level parameters, as well as group-level regression coefficients in one inferential step (Lengersdorff et al., 2020). Models were implemented in Stan (Carpenter et al., 2017) using R as the interface. Stan uses a Markov Chain Monte Carlo sampling method to describe posterior distributions of model parameters. We ran each candidate model with four independent chains and 3000 iterations (1000 warm-up). The convergence of sampling chains was estimated through the Gelman-Rubin $\hat{R}$ statistic (Gelman & Rubin, 1992), whereby we considered $\hat{R}$ values smaller than 1.01 as acceptable.

The participant-level parameters (ω, β, γ) were drawn from a multivariate Gaussian distribution with a vector of means μ and a covariance matrix that was factored into a diagonal matrix with standard deviations and the correlation matrix R (Bürkner, 2017; McElreath, 2016). The effects of testosterone on the three parameters were included as an additive regression term:

$$\begin{pmatrix} \omega' \\ \eta' \\ \gamma' \end{pmatrix} \sim MVNormal \begin{pmatrix} \mu_\omega + \beta_\omega * \mathrm{T} \\ \mu_\eta + \beta_\eta * \mathrm{T}, \\ \mu_\gamma + \beta_\gamma * \mathrm{T} \end{pmatrix} \quad S \Bigg)$$

where β_* are coefficients drawn from $N(0,1)$ and T is the testosterone administration variable. The parameters that were fully constrained (i.e. γ and ω) were estimated in the inverse probit space and the parameters that only had a lower bound (i.e. η) were estimated in log space. The prime denotes that the parameter is in estimation space.

Table 1: Prior distributions for the computational analysis

Group-level mean	$\boldsymbol{\mu_* \sim N(0,1)}$
Standard Deviations	$\boldsymbol{\sigma_* \sim HN(0,1)}$
Regression Coefficients	$\beta \sim N(0,1)$
Participant-level parameters (ω, η, γ)	$\omega' \sim N(\mu_\omega, \sigma_\omega)$
Prior for the correlation matrix	$R \sim LKJcorr(2)$

The priors for all group-level means (Table 1) were weakly informative, $\mu_\omega \sim N(0,1)$, the prior for group-level standard deviations were $\sigma_\omega \sim HalfNormal(0,1)$, and the prior for the correlation matrix was $R \sim LKJcorr(2)$. We defined the effect sizes (d) by dividing the regression coefficients β with the estimated standard deviation for that parameter.

Analysis of the genetic data

DNA was extracted from buccal swabs and isolated using a resin-based method with Chelex®100 (Sigma Aldrich, USA); for extraction details, see SI.

To estimate how the effects of testosterone on model parameters were moderated by the genotype variables, we included all three genotype variables and their interaction with testosterone effects on all three model parameters as group-level effects in the hierarchical model using the same priors as above.

Behavioral analysis

To analyze choice behavior, we focused on predicting the probability of staying with the previous choice (choose the spaceship that flies to the same planet as in the previous trial). We fitted a multilevel logistic regression model that predicts staying with the previous choice from three variables and their interactions: 1) points obtained in the previous trial, 2) a categorical predictor

for the first stage in the previous trial as well as 3) a variable for the testosterone administration. The effects of the previous state and previous points as well as the intercept, were allowed to vary for each participant and were drawn from a multivariate normal distribution, meaning we also explicitly estimated correlations between them, allowing for pooling across random effects (McElreath, 2016). We report 95% credibility intervals of odd ratios (the ratio between probability to stay and probability to switch) as well as estimates in the log-odds scale.

To analyze points earned and reaction times, we used a hierarchical linear regression with the previous state and hormone administration as well as their interaction as predictors, where we allowed the effect for the previous state to vary per participant. When analyzing reaction time data, we considered trials with responses faster than 200 ms (0.016% of all trials) as not conscious decisions and excluded them from the analysis. Because of the lower bound and a skew in the distribution of reaction times, we log-transformed the data. We report total effect sizes (d) that are calculated by normalizing the regression coefficients with the square root of the sum of all squared estimated standard deviations (Nalborczyk et al., 2019).

All models were run with the *brms* package in R (Bürkner, 2017), using MCMC sampling procedures, with 4 chains, each 3000 iterations (1000 warm-up), and priors depicted in Table 2.

Table 2: Prior distributions for the behavioral analysis.

Standard Deviations	$\sigma \sim HalfCauchy(0,2)$
Regression Coefficients	$\beta \sim N(0,3)$
Intercept	$\beta_0 \sim Student(3,0,10)$
Prior for the correlation matrix	$R \sim LKJcorr(2)$

Open practices statement

The motivation for the study comes as a continuation of an ongoing debate on testosterone's role in reflective vs reflexive behavior (Nave et al., 2017), to which we have also contributed (Knight et al., 2020). We have made all the data and the code available online. The study was, however, planned before our lab had switched to persistent pre-registration and thus has not been pre-registered.

Results

Testosterone manipulation check

120 minutes after gel administration, we observed considerably higher testosterone levels in the testosterone compared to the placebo group (drug treatment x time: $F(3,609.09) = 84.58$, $p < .001$; 120 min: $b = 3.62$, 95% CI = [3.25 – 4.00]), a difference that remained stable until the end of the experiment (180 min: $b = 3.96$, 95% CI = [3.58 – 4.33]; 240 min: $b = 2.85$, 95% CI = [2.47 – 3.23]; see Figure S1).

Testosterone increases noise, but does not decrease model-based compared to model-free behavior

To model the choice behavior of participants we applied a computational model with three parameters. The parameter ω describes the weight of how much model-based (MB), relative to model-free (MF) subjective values affects trial-by-trial choice. The decision temperature parameter η determines the degree of behavior that is not accounted by the model, with lower values indicating more random behavior. Finally, because it might happen that participants do not see one of the first stage pairs for several trials, we added a discounting factor γ that accounts for the devaluation of unobserved stimulus outcome association across time. In other words, this accounts for how fast participants "forget" the outcomes of previous choices when the stimuli are not observed.

We found no effect of testosterone on the weight of model-based relative to model-free behavior ($d = -0.014$, 95% CrI [-0.339, 0.303], $p(d>0) = 0.464$), neither was there an effect on the discounting parameter ($d = 0.161$, 95% CrI [-0.216, 0.547], $p(d<0) = .198$). We did however observe that testosterone led to a decrease in the decision temperature parameter ($d = -0.343$, 95% CrI [-0.641, -0.047], $p(d>0) = .012$), suggesting higher randomness in choices (Fig. 2).

Testosterone affects staying behavior in same first state trial, but not in different first state trials.

We next examined how the modeling results are reflected in the choice behavior. We analyzed the degree to which previous points affect the choice to stay with the spaceship that flies to the same planet and how this relationship changes with respect to previous first stage states being the same or different and under testosterone vs placebo (Fig. 3). As expected, the higher the number of points in the previous trial the more likely the participants were to stay with their previous choice of planets ($b_{logodds} = 0.48$, 95% CrI [0.424, 0.539], $p(b_{logodds}<0) < .001$). However, when the first state of the trial is different from that of the previous trial, staying with the same planet requires that participants keep the mapping from spaceships to planets online and the slope between previous points. As expected, staying behavior was reduced when the first states of two

consecutive trials were different ($b_{logodds}$ = -0.264, 95% CrI [-0.318, -0.208], $p(b_{logodds}>0)$ < .001).

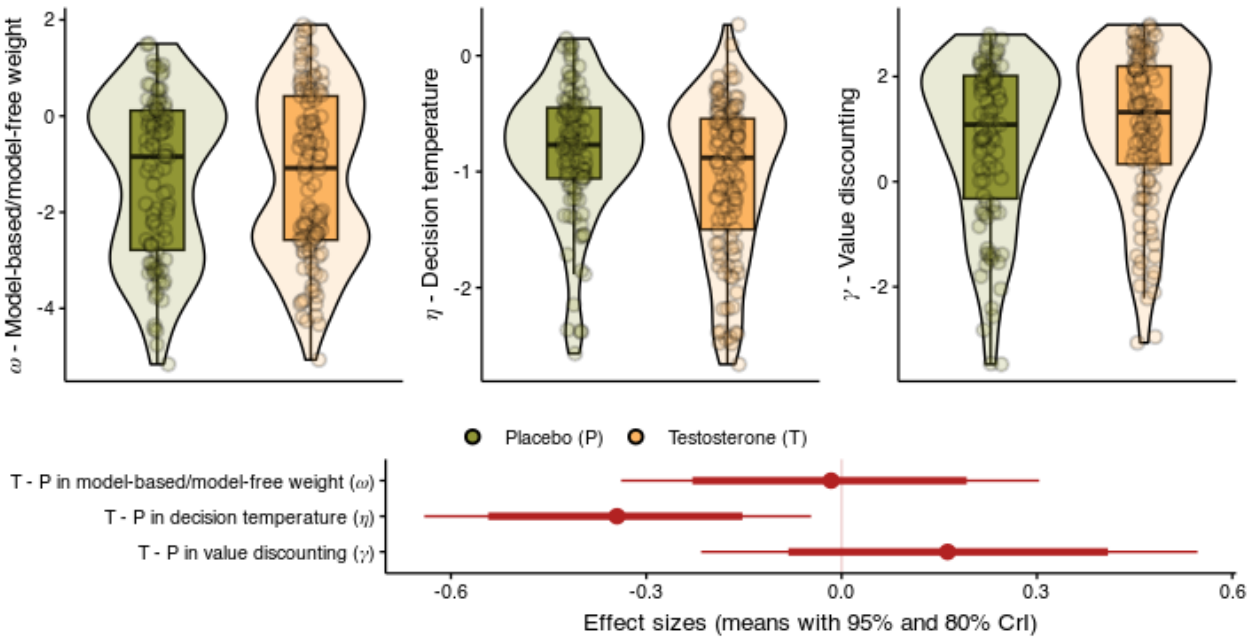


Fig. 2. Computational parameter estimates plotted separately for Placebo and Testosterone. Below, posterior distribution of effect sizes for regression coefficients estimating the difference of testosterone compared to placebo on all three parameters (means with 80% and 95% CrI).

When looking at group differences, we found that under testosterone, the effect of previous points on staying behavior is reduced when the first states are the same ($b_{logodds}$ -0.087, 95% CrI [-0.163, -0.01], $p(b_{logodds}>0)$ = .013) but not when the first states are different ($b_{logodds}$ = -0.014, 95% CrI [-0.088, 0.06], $p(b_{logodds}>0)$ = 0.351). Interestingly, the interaction factor (difference in slopes) was positive ($b_{logodds}$ = 0.073, 95% CrI [-0.001, 0.147], $p(b_{logodds}<0)$ = 0.026), suggesting that participants take rewarding points less into consideration under testosterone than participants under placebo in the same first state trials but do so relatively more in trials that require keeping the task structure online. If testosterone would decrease deliberate behavior, we should expect that participants administered testosterone would be less sensitive to previous points in their choices in trials where the first stage state is different compared to trials where it is the same. In contrast, decreased effects of previous points on choice in general imply that testosterone simply increases choice randomness overall. In support of this, participant-level random slopes representing the effect of previous points on staying behavior in same first state trials correlate strongly with the η parameter (b = 0.837, t(216) = 30.083, p < .001); whereas the slope difference between the same and different first state trials correlate with the ω parameter (b = 0.610, t(216) = 12.575, p < .001) and correlate negatively with the exploration parameter (b =-0.445, t(2016) = -12.522, p < .001).

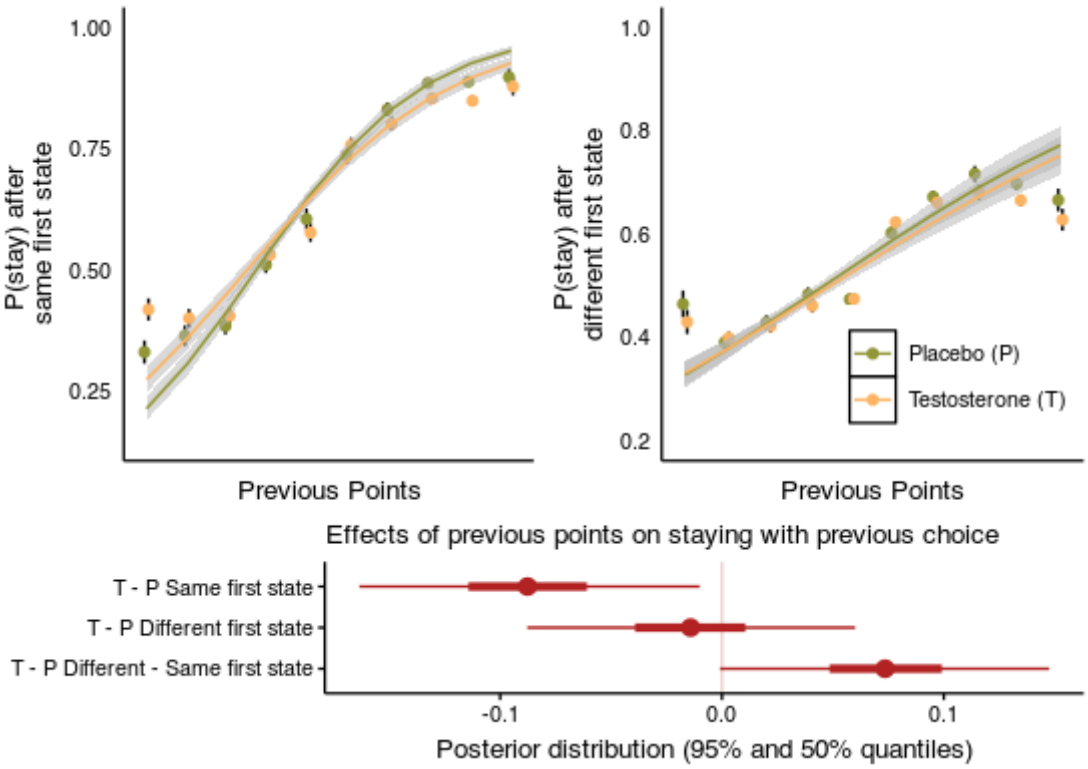


Fig. 3. Goal-directed behavior is measured by the degree to which previous points encourage choice repetition in trials where previous first state was different. Linear analysis of staying behavior showed that participants under testosterone were not less likely to stay with each previous point compared to placebo. Interestingly, they were less influenced by previous points in easier trials, where the first state was the same as in the previous trial. Lines depict means of posterior predictive plots of the logistic regression analysis (shades are 80% percentile intervals of the mean). Points and error-bars are means and standard errors of raw data pooled first within participants and then averaged across participants for each of the ten points (-4 to 5). Below, the posterior distribution of the regression coefficients.

The finding that testosterone was more detrimental to performance in the same first state but not in the different first state trials was confirmed when analyzing points earned (Fig. 4). Participants under testosterone earned fewer points when the first state was the same as in the previous trials (mean difference in points is -0.096, 95% CrI [-0.191, -0.001], $p(b>0)$ = .024, with the effect size d = -0.039, 95% CrI [-0.077, 0.000]), but not when the first state was different (mean difference in points is -0.022, 95% CrI [-0.097, 0.054], $p(b>0)$ = .288, d = -0.009, 95% CrI [-0.039, 0.022]). With a positive (but not significant) difference between the two effects (b = 0.074, 95% CrI [-0.022, 0.173], $p(b<0)$ = 0.069, d = 0.03, 95% CrI [-0.009, 0.07])). We note, however, that the effect sizes of testosterone's effects on overall points earned are very small.

When analyzing reaction time data, we found a trend that testosterone led to faster responding in trials where the first stage state was the same as in the previous trial (d = -0.051, 95% CrI [-0.113, 0.010], $p(d>0)$ = 0.052) as well as in trials where it was different (d = -0.145, 95% CrI [-0.304, 0.013], $p(d>0)$ = 0.034).

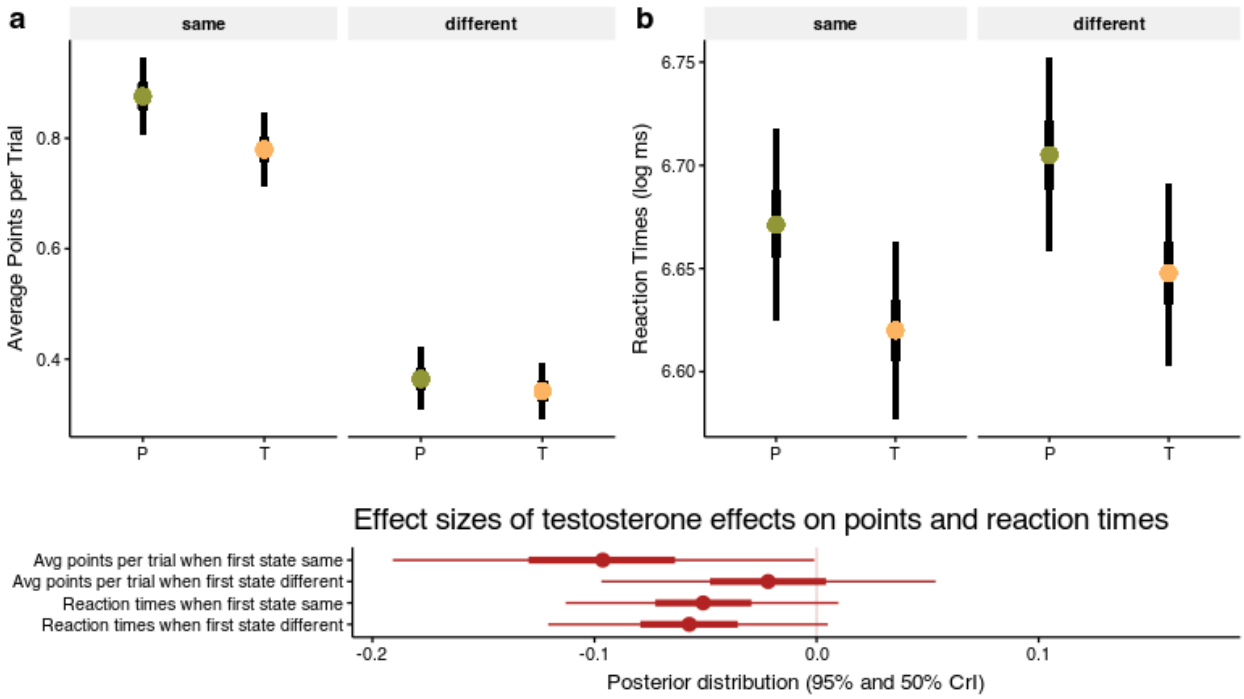


Fig. 4. Points earned on average per trial (**a**) and reaction times (**b**) shown separately for trials where the first state was the *same* and trials where it was *different* than in the previous trials with 50% and 95% posterior predictive intervals of the mean. Reaction times were log-scaled to reduce the skew. Below, the posterior distribution of regression coefficients for the effects of testosterone compared to placebo.

Accounting for baseline variation in genetic polymorphisms related to dopamine and androgen receptors

We then extended the hierarchical computational model with the main effects of genetic variables as well as their interactions with testosterone on all model parameters. We found that including the genetic variables in the model did not affect inference on the main effects of testosterone on the model-based/model-free weight ω (b = -0.076, 95% CrI [-0.561, 0.405], p (b>0) = .379), nor did it change the negative effect of testosterone on the decision temperature parameter η (b = -0.267, 95% CrI [-0.477, -0.056], p (b>0) < .001).

We found no strong support for the interaction of testosterone's effects on model-based/model-free trade-off with the COMT polymorphism (d = 0.352, 95% CrI [-0.115, 0.842], p(d<0) = .07), with the CAG polymorphism (d = 0.338, 95% CrI [-0.133, 0.808], p(d<0) = .083), or the DAT1 polymorphism (d = 0.566, 95% CrI [-0.338, 1.473], p(d<0) = .115).

We did, however, observe a significant interaction of the DAT1 polymorphism and testosterone effects on decision temperature (d = 0.62, 95% CrI [0.033, 1.203], p(d<0) = 0.021), whereas this was not the case for COMT and CAG (Figure S2). Specifically, 9-repeat allele carriers of the DAT1 polymorphisms, associated with increased striatal dopamine levels, showed increased choice stochasticity following testosterone administration (d = -0.692, 95% CrI [-1.128, -0.239],

$p(d>0) < 0.001$), contrary to the 10/10 allele homozygotes with putatively lower striatal dopamine levels (d = -0.069, 95% CrI [-0.481, 0.306], $p(d>0)$ = .358).

We then looked at how genetic variables interact with testosterone's effects on reaction times, points earned and staying behavior (the degree to which points earned on a trial increase the odds of repeating the same choice; full model output in Tables S2, S3, and S4). We observed a significant interaction of DAT1 polymorphism and testosterone on reaction times for same first state trials (b = 0.133, 95% CrI [0, 0.267], $p(b<0)$ = .025) as well as different first state trials (b = 0.146, 95% CrI [0.013, 0.281], $p(b<0)$ = .015), with no significant difference between trial types (b = 0.013, 95% CrI [-0.025, 0.05], $p(b<0)$ = .26). With points earned, the DAT1 x testosterone interaction was significant for the same first state trials (b = 0.209, 95% CrI [0.014, 0.404], p (b<0) = .016), but not different first state trials (b = 0.103, 95% CrI [-0.047, 0.252], p (b<0) = 0.088), with no significant difference between trial types (b = -0.104, 95% CrI [-0.307, 0.094], P(b>0) = .146). For the effect of previous points on staying behavior we found a significant interaction of DAT1 and testosterone in same first state trials (b = 0.172, 95% CrI [0.018, 0.331], p (b<0) = .015), but not on the difference between the same and different first state trials (b = -0.023, 95% CrI [-0.18, 0.127], p (b>0) = .379).

Discussion

Using single-dose hormone administration and computational modeling, we investigated the role of testosterone in the trade-off between deliberate and intuitive decision-making. If testosterone has no effect on the trade-off but impairs decision-making performance not directly related to the arbitration between the two decision-making styles, we expected an overall increase in noise in responding ("sloppy thinking hypothesis"). If testosterone promotes intuitive at the expense of deliberate action, we expected the weight to shift towards intuitive, model-free, and away from deliberate, model-based action ("intuitive thinking hypothesis"). Through computational modeling, we showed that testosterone had no effect on the trade-off between the two systems but did increase overall randomness in participants' choices. This was mirrored in the analysis of choice behavior, which showed that testosterone decreased the effect of previous points on staying behavior in trials that did not require keeping the mapping between stages online (i.e., trials where the first stage state was the same as in the previous trial), but not in trials where remembering the mapping was beneficial (i.e., trials, where the first stage state was different to that of the previous trial). Furthermore, participants under testosterone earned fewer points than the placebo participants, particularly in the same first-stage state trials, and generally tended to respond faster. These data suggest that testosterone does not increase intuitive actions at the expense of deliberate behavior but instead makes the choice behavior noisier.

The lack of testosterone's effects on the trade-off between model-free and model-based decision-making in our study is to some degree in contrast with results from Nave et al. (2017), where a cognitive reflection test (CRT) was used to measure the effects of testosterone on the arbitration between the two decision-making styles. Nave et al. report that testosterone increased answers in the CRT that are considered intuitive (but incorrect and decreased responses that required deliberate cognitive reflection. Because testosterone had no effect on the arithmetic control task, the authors concluded that testosterone did not impair cognitive capacity, rather, it decreased the probability of engaging in effortful cognitive processes associated with impulse control. Indeed, previous work has shown that testosterone increased impulsivity (Wu et al., 2020) as well as decision noise in a reinforcement learning task (Kutlikova et al., 2023). The computational approach together with the task we used in this study, allowed us to dissociate such general effects testosterone might have on decision-making from the effects on the trade-off between intuitive and deliberate behavior. Our finding of higher noisiness in simple model-free processes supports the notion that testosterone does increase impulsive responses. Yet, although testosterone increased noisiness, it had no effect on the trade-off between deliberate and intuitive behavior, meaning it did not make individuals less likely to engage in the effortful deliberate than in the intuitive cognitive processes (Nave et al.2017).

Our findings are in line with other three experiments that also used CRT but found weak and variable effects of testosterone on cognitive reflection (Knight et al., 2020). Moreover, through genetic data analysis, we provide initial evidence that the reported heterogeneity of testosterone effects on cognitive processes might be influenced by differences in genotypes related to the functioning of the brain's dopaminergic circuits that play a crucial role in deliberate and intuitive decision-making (Daw et al., 2011; Frank et al., 2009; Wunderlich et al., 2012). Specifically, our results show that testosterone led to higher noise and faster responding particularly among individuals with 9-repeat (9R) compared to the homozygous 10-repeat (10/10R) variant of DAT1 polymorphism. Previous neurobiological research demonstrated that the 9R variant of the DAT1 polymorphism is associated with a lower density of dopamine transporter in the striatum compared to the 10/10R variant. Hence, 9-repeat carriers are expected to have higher synaptic striatal dopamine availability than 10/10R homozygotes (Heinz et al., 2000). Interestingly, previous studies show that 9R carriers of the DAT1 polymorphism tend to have higher self-reported (Forbes et al., 2009) and behavioral (Kim et al., 2006) impulsivity than 10/10 homozygotes. It is, therefore, possible that testosterone increases noisiness and response speed primarily in individuals with an inherent baseline predisposition for impulsive actions.

In contrast to the observed interaction effect of testosterone administration and dopamine-related genetic polymorphism on choice noisiness, our analysis of the model-based vs. model-free trade-off did not yield compelling evidence for such interactions (COMT: $p = .06$, DAT1: $p = .11$). Previous research has linked higher prefrontal dopamine levels indexed by the Val/Met

substitution in the COMT gene polymorphism to a higher likelihood of deliberate behavior (Doll, Bath, Daw, & Frank, 2016). Similarly, higher tonic striatal dopamine has been associated with an enhanced willingness to exert cognitive effort (Westbrook et al., 2020) and increased deliberate behavior (Kroemer et al., 2019; Wunderlich, Smittenaar, & Dolan, 2012). Given these findings and our inconclusive evidence, a further investigation involving larger sample sizes with genetic prescreening may provide more insights into whether and how the interaction between exogenous testosterone and genetic polymorphism of the dopaminergic system shapes deliberate decision-making. Alternatively, more direct measures of the underlying states of biological circuits, such as neurochemical imaging of dopamine availability, could also shed light on the pathways through which testosterone influences deliberate vs. intuitive cognitive processes.

Lastly, it needs to be noted that due to the sex differences in testosterone metabolism and unknown pharmacokinetics following the topical administration of testosterone in women (Eisenegger et al., 2013), the study included only male participants. Hence, the generalization of these findings to females also requires further investigation.

In sum, using testosterone administration and computational modeling, our study provides novel evidence that the hormone does not promote intuitive behavior at the expense of more deliberate choice options. Rather, our findings show that testosterone increases sloppy decision-making and suggest that this process occurs in interaction with the striatal dopaminergic pathways.

References

Ahn, W.-Y., Haines, N., & Zhang, L. (2017). Revealing Neurocomputational Mechanisms of Reinforcement Learning and Decision-Making With the hBayesDM Package. *Computational Psychiatry (Cambridge, Mass.)*, *1*, 24–57. https://doi.org/10.1162/CPSY_a_00002

Bürkner, P.-C. (2017). brms: An R Package for Bayesian Multilevel Models Using Stan. *Journal of Statistical Software*, *80*, 1–28. https://doi.org/10.18637/jss.v080.i01

Carpenter, B., Gelman, A., Hoffman, M. D., Lee, D., Goodrich, B., Betancourt, M., Brubaker, M., Guo, J., Li, P., & Riddell, A. (2017). Stan: A Probabilistic Programming Language. *Journal of Statistical Software*, *76*, 1–32. https://doi.org/10.18637/jss.v076.i01

Carré, J. M., Geniole, S. N., Ortiz, T. L., Bird, B. M., Videto, A., & Bonin, P. L. (2017). Exogenous Testosterone Rapidly Increases Aggressive Behavior in Dominant and Impulsive Men. *Biological Psychiatry*, *82*(4), 249–256. https://doi.org/10.1016/j.biopsych.2016.06.009

Cotrufo, P., Monteleone, P., d'Istria, M., Fuschino, A., Serino, I., & Maj, M. (2000). Aggressive Behavioral Characteristics and Endogenous Hormones in Women with Bulimia nervosa. *Neuropsychobiology*, *42*(2), 58–61. https://doi.org/10.1159/000026673

Daw, N. D., Gershman, S. J., Seymour, B., Dayan, P., & Dolan, R. J. (2011). Model-based influences on humans' choices and striatal prediction errors. *Neuron*, *69*(6), 1204–1215. https://doi.org/10.1016/j.neuron.2011.02.027

Daw, N. D., Niv, Y., & Dayan, P. (2005). Uncertainty-based competition between prefrontal and dorsolateral striatal systems for behavioral control. *Nature Neuroscience*, *8*(12), 1704–1711. https://doi.org/10.1038/nn1560

Decker, J. H., Otto, A. R., Daw, N. D., & Hartley, C. A. (2016). From Creatures of Habit to Goal-Directed Learners: Tracking the Developmental Emergence of Model-Based Reinforcement Learning. *Psychological Science*, *27*(6), 848–858. https://doi.org/10.1177/0956797616639301

Dickinson, A. (1985). Actions and Habits: The Development of Behavioural Autonomy. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *308*(1135), 67–78. https://www.jstor.org/stable/2396284

Doll, B. B., Bath, K. G., Daw, N. D., & Frank, M. J. (2016). Variability in Dopamine Genes Dissociates Model-Based and Model-Free Reinforcement Learning. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *36*(4), 1211–1222. https://doi.org/10.1523/JNEUROSCI.1901-15.2016

Eisenegger, C., von Eckardstein, A., Fehr, E., & von Eckardstein, S. (2013). Pharmacokinetics of testosterone and estradiol gel preparations in healthy young men. *Psychoneuroendocrinology*, *38*(2), 171–178. https://doi.org/10.1016/j.psyneuen.2012.05.018

Forbes, E., Brown, S., Kimak, M., Ferrell, R., Manuck, S., & Hariri, A. (2009). Genetic variation in components of dopamine neurotransmission impacts ventral striatal reactivity associated with impulsivity. *Molecular Psychiatry*, *14*(1), 60–70. https://doi.org/10.1038/sj.mp.4002086

Frank, M. J., Doll, B. B., Oas-Terpstra, J., & Moreno, F. (2009). Prefrontal and striatal dopaminergic genes predict individual differences in exploration and exploitation. *Nature Neuroscience*, *12*(8), 1062–1068. https://doi.org/10.1038/nn.2342

Frederick, S. (2005). Cognitive Reflection and Decision Making. *Journal of Economic Perspectives*, *19*(4), 25–42. https://doi.org/10.1257/089533005775196732

Gelman, A., & Rubin, D. B. (1992). Inference from Iterative Simulation Using Multiple Sequences. *Statistical Science*, *7*(4), 457–472. https://www.jstor.org/stable/2246093

Geniole, S. N., Procyshyn, T. L., Marley, N., Ortiz, T. L., Bird, B. M., Marcellus, A. L., Welker, K. M., Bonin, P. L., Goldfarb, B., Watson, N. V., & Carré, J. M. (2019). Using a Psychopharmacogenetic Approach To Identify the Pathways Through Which—And the People for Whom—Testosterone Promotes Aggression. *Psychological Science*, *30*(4), 481–494. https://doi.org/10.1177/0956797619826970

Gillan, C. M., Kosinski, M., Whelan, R., Phelps, E. A., & Daw, N. D. (2016). Characterizing a psychiatric symptom dimension related to deficits in goal-directed control. *ELife*, *5*, e11305. https://doi.org/10.7554/eLife.11305

Heinz, A., Goldman, D., Jones, D. W., Palmour, R., Hommer, D., Gorey, J. G., Lee, K. S., Linnoila, M., & Weinberger, D. R. (2000). Genotype Influences In Vivo Dopamine Transporter Availability in Human Striatum. *Neuropsychopharmacology*, *22*(2), 133–139. https://doi.org/10.1016/S0893-133X(99)00099-8

Kahneman, D. (2011). *Thinking, fast and slow* (p. 499). Farrar, Straus and Giroux.

Kim, S. J., Kim, Y. S., Lee, H. S., Kim, S. Y., & Kim, C.-H. (2006). An interaction between the serotonin transporter promoter region and dopamine transporter polymorphisms contributes to harm avoidance and reward dependence traits in normal healthy subjects. *Journal of Neural Transmission*, *113*(7), 877–886. https://doi.org/10.1007/s00702-006-0444-3

Knight, E. L., McShane, B. B., Kutlikova, H. H., Morales, P. J., Christian, C. B., Harbaugh, W. T., Mayr, U., Ortiz, T. L., Gilbert, K., Ma-Kellams, C., Riečanský, I., Watson, N. V., Eisenegger, C., Lamm, C., Mehta, P. H., & Carré, J. M. (2020). Weak and Variable Effects of Exogenous Testosterone on Cognitive Reflection Test Performance in Three Experiments: Commentary on Nave, Nadler, Zava, and Camerer (2017). *Psychological Science*, *31*(7), 890–897. https://doi.org/10.1177/0956797619885607

Kool, W., Cushman, F. A., & Gershman, S. J. (2016). When Does Model-Based Control Pay Off? *PLOS Computational Biology*, *12*(8), e1005090. https://doi.org/10.1371/journal.pcbi.1005090

Kool, W., Gershman, S. J., & Cushman, F. A. (2017). Cost-Benefit Arbitration Between Multiple Reinforcement-Learning Systems. *Psychological Science*, *28*(9), 1321–1333. https://doi.org/10.1177/0956797617708288

Kroemer, N. B., Lee, Y., Pooseh, S., Eppinger, B., Goschke, T., & Smolka, M. N. (2019). L-DOPA reduces model-free control of behavior by attenuating the transfer of value to action. *NeuroImage*, *186*, 113–125. https://doi.org/10.1016/j.neuroimage.2018.10.075

Kutlikova, H. H., Zhang, L., Eisenegger, C., van Honk, J., & Lamm, C. (2023). Testosterone eliminates strategic prosocial behavior through impacting choice consistency in healthy males. *Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology*. https://doi.org/10.1038/s41386-023-01570-y

Lengersdorff, L. L., Wagner, I. C., Lockwood, P. L., & Lamm, C. (2020). When Implicit Prosociality Trumps Selfishness: The Neural Valuation System Underpins More Optimal Choices When Learning to Avoid Harm to Others Than to Oneself. *Journal of Neuroscience*, *40*(38), 7286–7299. https://doi.org/10.1523/JNEUROSCI.0842-20.2020

McElreath, R. (2016). *Statistical Rethinking: A Bayesian Course with Examples in R and Stan*. Chapman and Hall/CRC. https://doi.org/10.1201/9781315372495

Mikus, N., Korb, S., Massaccesi, C., Gausterer, C., Graf, I., Willeit, M., Eisenegger, C., Lamm, C., Silani, G., & Mathys, C. (2022). Effects of dopamine D2/3 and opioid receptor antagonism on the trade-off between model-based and model-free behaviour in healthy volunteers. *ELife*, *11*, e79661. https://doi.org/10.7554/eLife.79661

Nalborczyk, L., Batailler, C., Loevenbruck, H., Vilain, A., & Bürkner, P.-C. (2019). An introduction to Bayesian multilevel models using brms: A case study of gender effects on vowel variability in standard Indonesian. *Journal of Speech, Language, and Hearing Research*, *62*, 1225–1242. https://doi.org/10.1044/2018_JSLHR-S-18-0006

Nave, G., Nadler, A., Zava, D., & Camerer, C. (2017). Single-Dose Testosterone Administration Impairs Cognitive Reflection in Men. *Psychological Science*, *28*(10), 1398–1407. https://doi.org/10.1177/0956797617709592

Otto, A. R., Gershman, S. J., Markman, A. B., & Daw, N. D. (2013). The curse of planning: Dissecting multiple reinforcement-learning systems by taxing the central executive. *Psychological Science*, *24*(5), 751–761. https://doi.org/10.1177/0956797612463080

Patton, J. H., Stanford, M. S., & Barratt, E. S. (1995). Factor structure of the Barratt impulsiveness scale. *Journal of Clinical Psychology*, *51*(6), 768–774. https://doi.org/10.1002/1097-4679(199511)51:6<768::aid-jclp2270510607>3.0.co;2-1

Plymate, S. R., Tenover, J. S., & Bremner, W. J. (1989). Circadian variation in testosterone, sex hormone-binding globulin, and calculated non-sex hormone-binding globulin bound testosterone in healthy young and elderly men. *Journal of Andrology*, *10*(5), 366–371. https://doi.org/10.1002/j.1939-4640.1989.tb00120.x

Reynolds, M. D., Tarter, R., Kirisci, L., Kirillova, G., Brown, S., Clark, D. B., & Gavaler, J. (2007). Testosterone Levels and Sexual Maturation Predict Substance Use Disorders in Adolescent Boys: A Prospective Study. *Biological Psychiatry*, *61*(11), 1223–1227. https://doi.org/10.1016/j.biopsych.2006.07.008

Rodríguez-Nieto, G., Dewitte, M., Sack, A. T., & Schuhmann, T. (2021). Individual Differences in Testosterone and Self-Control Predict Compulsive Sexual Behavior Proneness in Young Males. *Frontiers in Psychology*, *12*, 723449. https://doi.org/10.3389/fpsyg.2021.723449

Schultheiss, O. C., & Mehta, P. H. (2019). *Routledge international handbook of social neuroendocrinology*. Routledge Abingdon.

Sutton, R. S., & Barto, A. G. (2018). *Reinforcement Learning, second edition: An Introduction*. MIT Press.

Svensson, A. I., Åkesson, P., Engel, J. A., & Söderpalm, B. (2003). Testosterone treatment induces behavioral disinhibition in adult male rats. *Pharmacology Biochemistry and Behavior*, *75*(2), 481–490. https://doi.org/10.1016/S0091-3057(03)00137-0

Thorndike, E. L. (1911). *Animal intelligence: Experimental studies* (pp. viii, 297). Macmillan Press. https://doi.org/10.5962/bhl.title.55072

Voon, V., Derbyshire, K., Rück, C., Irvine, M. A., Worbe, Y., Enander, J., Schreiber, L. R. N., Gillan, C., Fineberg, N. A., Sahakian, B. J., Robbins, T. W., Harrison, N. A., Wood, J., Daw, N. D., Dayan, P., Grant, J. E., & Bullmore, E. T. (2015). Disorders of compulsivity: A common bias towards learning habits. *Molecular Psychiatry*, *20*(3), Article 3. https://doi.org/10.1038/mp.2014.44

Voon, V., Reiter, A., Sebold, M., & Groman, S. (2017). Model-Based Control in Dimensional Psychiatry. *Biological Psychiatry*, *82*(6), 391–400. https://doi.org/10.1016/j.biopsych.2017.04.006

World Medical Association. (2001). World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. *Bulletin of the World Health Organization*, *79*(4), 373–374. https://apps.who.int/iris/handle/10665/268312

Wu, Y., Shen, B., Liao, J., Li, Y., Zilioli, S., & Li, H. (2020). Single dose testosterone administration increases impulsivity in the intertemporal choice task among healthy males. *Hormones and Behavior*, *118*, 104634. https://doi.org/10.1016/j.yhbeh.2019.104634

Wunderlich, K., Smittenaar, P., & Dolan, R. J. (2012). Dopamine enhances model-based over model-free choice behavior. *Neuron*, *75*(3), 418–424. https://doi.org/10.1016/j.neuron.2012.03.042

Supplementary Materials for: Thinking Fast Or Slow Under Testosterone - Exploring Variability Through Computational Pharmacogenetics

Hormone analysis

Out of total 216 baseline samples, we noted that 38 contained above-normal testosterone levels, atypical for normal young men (> 2000 pg/mL). The samples with abnormally high testosterone values appeared only in the participants who later received testosterone treatment, not in the placebo group. The levels of dihydrotestosterone, a metabolite of testosterone, were hormonally typical. Previous research described similar abnormally high testosterone levels and attributed it to the testosterone contamination of the common surfaces (e.g., doorknobs, keyboards), excluding the option of the physiological contamination. Based on their recommendation, we implemented a cleaning protocol that included wearing of disposable sterile gloves, cleaning of keyboards, computer mice, tables, and doorknobs with an alcohol-based solution after each session. Although these precautions successfully prevented between-session contamination, we suspect that they still did not reliably impede contamination of the saliva containers. For future studies, we therefore recommend even stricter sanitizing protocols and more careful handling of the saliva collection tubes and boxes before, during, but also after sample collection.
As in our sample, the abnormally high values were present only in the sessions where testosterone was administered, and this notwithstanding, the testosterone group showed a reliable testosterone increase after the drug administration in comparison to the placebo group, we decided to retain the participants with contaminated baseline sample for the analyses, except for the analyses that include baseline testosterone levels.

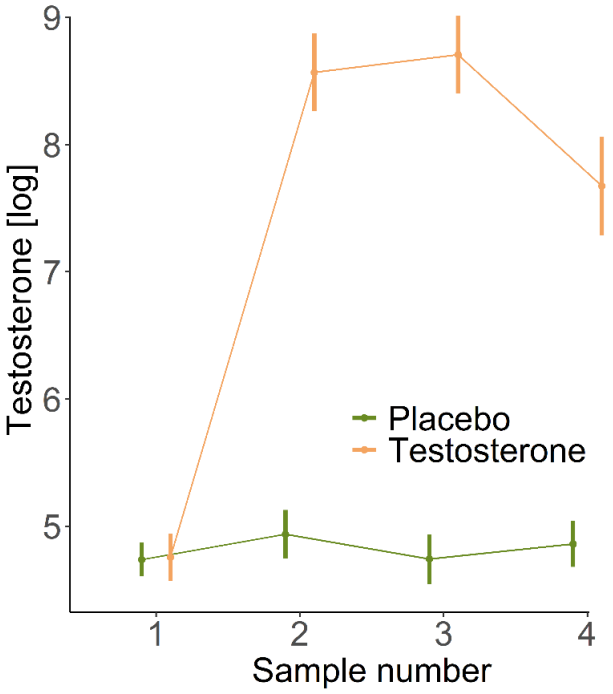


Figure S1. Testosterone levels during the experimental session. Error bars = Mean ± CI.

Genetic analysis

For amplification of the CAG repeat polymorphism in exon 1 of the AR gene primers forward - 5' GCGCGAAGTGATCCAGAAC 3' tagged with 6–carboxyfluorescein and reverse - 5' CTCATCCAGGACCAGGTAGC 3', DAT1-3'UTR VNTR polymorphism primers forward - 5' GTCCTTGTGGTGTAGGGAAC 3' tagged with 6–carboxyfluorescein and reverse - 5' CTGGAGGTCACGGCTCAAG 3' and rs4680 SNP polymorphism primers forward -5' GTTCCCCTCTCTCCACCTGT 3' and reverse - 5' GGGTTTTCAGTGAACGTGGT 3' were used in PCR with 20 µL reaction using 250 nmol/L final primer molarity. As PCR masterrmix 5x Hot FIREPol Blend Mastermix with 7.5 mM MgCl2 (Solis Biodyne, Tartu, Estonia) was used in all amplifications. The following PCR program was used: initial denaturation step at 95°C for 15 min, followed by 30 cycles each consisting of denaturation at 95°C for 30 s, annealing at 60°C for 30 s and polymerization at 72°C for 1 min. The lengths of the final fragments were 214-277 bp, 439-562 bp and 360 bp, respectively. The number of repeats of AR CAG STR and DAT1-3'UTR VNTR were analyzed by fragment anlysis and the rs4680 SNP was genotyped using Sanger sequencing on ABI 3500 Genetic Analyzer (Applied Biosystems, USA).

Detailed results and discussion of the genotype interactions with testosterone

We used the *COMT* single nucleotide polymorphism (SNP) as an indicator of prefrontal dopamine function, the *DAT1* polymorphism, a 40 base-pair variable number tandem repeat polymorphism (VNTR) of the dopamine transporter, as a marker of striatal dopamine function, and the CAG repeats lengths of AR gene as a marker of androgen receptors receptor efficiency. We included genetic data as group-level variables in the hierarchical estimation of the parameters of the computational model. The results of all group-level effects are presented in Figure S2.

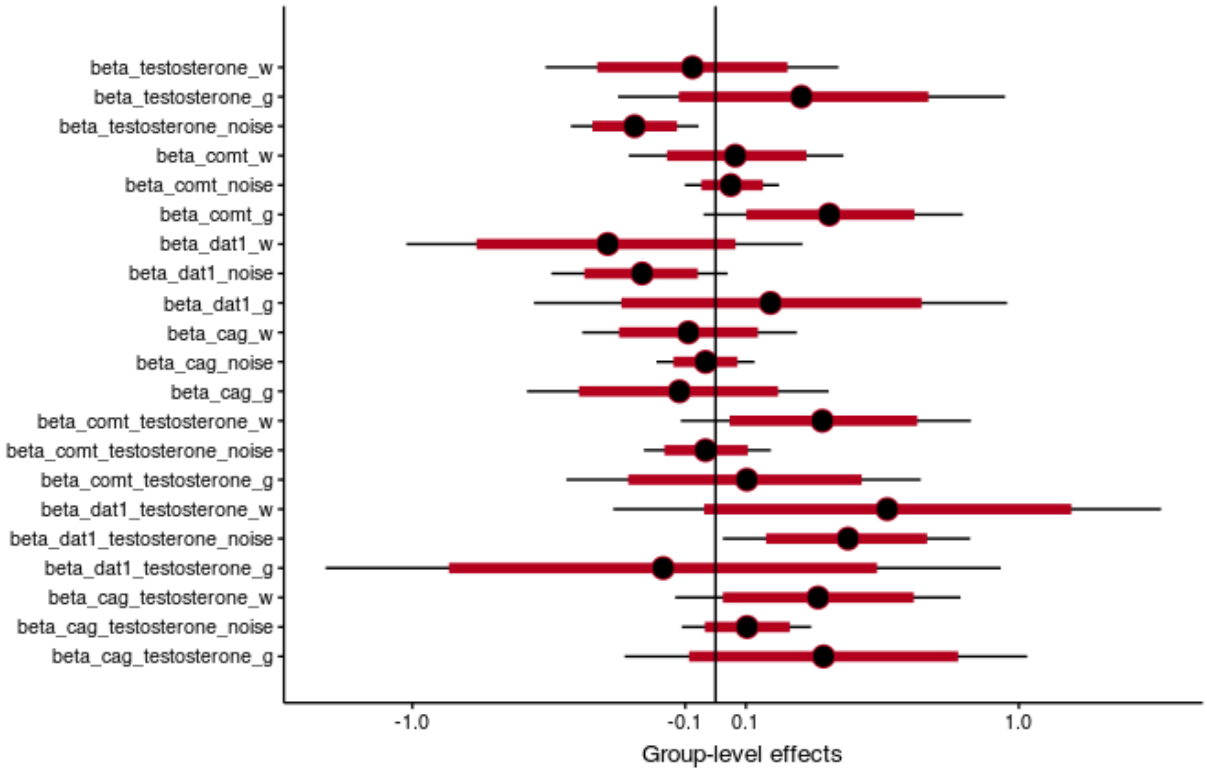


Figure S2. Posterior distributions of group level effects. Hierarchical computational model with effe cts of genotype variables (dat1, cag, and comt) on model-based/model-free weight (w), discounting par ameter (g) and decision temperature (noise). Points are means, with 80% and 95% credibility intervals.

The COMT x testosterone interaction effect on model-based/model-free weight had a moderate effect size on average, but with the 95% CrI not being entirely above 0 (d = 0.352, 95% CrI [-0.115, 0.842], p(d<0) = .07, Figure S2, S3). We found that in the testosterone group a higher number of Met mutations of the COMT polymorphism (related to increased prefrontal dopamine levels) was associated with increased model-based/model-free weight (effect size d = 0.594, 95% CrI [0.131, 1.097], p(d<0) = .004). This effect was not present in the placebo group (d = 0.065, 95% CrI [-0.286, 0.421], p(d<0) = .355).

Interestingly, we also observed that higher Met mutations were associated with increased γ indicating less forgetfulness both in the placebo group (d = 0.375, 95% CrI [-0.04, 0.815], p(d<0) = .036) and even more so in the testosterone group (d = 0.469, 95% CrI [0.06, 0.921], p (d<0) = 0.013), with no significant differences between the two effects (d = 0.103, 95% CrI [-0.492, 0.677], p (d<0) = .364).

For the androgen receptor polymorphism, we found some evidence for the observation that higher CAG repeats, indexing lower receptor efficiency are associated with more model-based behavior in the testosterone group (d = 0.245, 95% CrI [-0.072, 0.576], p (d<0) = .064), but not in the placebo group (d = -0.09, 95% CrI [-0.44, 0.268], p (d>0) = .309), with a positive (but not significant) difference between the effects (d = 0.338, 95% CrI [-0.133, 0.808], p (d<0) = .083).

For the results on DAT1 see main text.

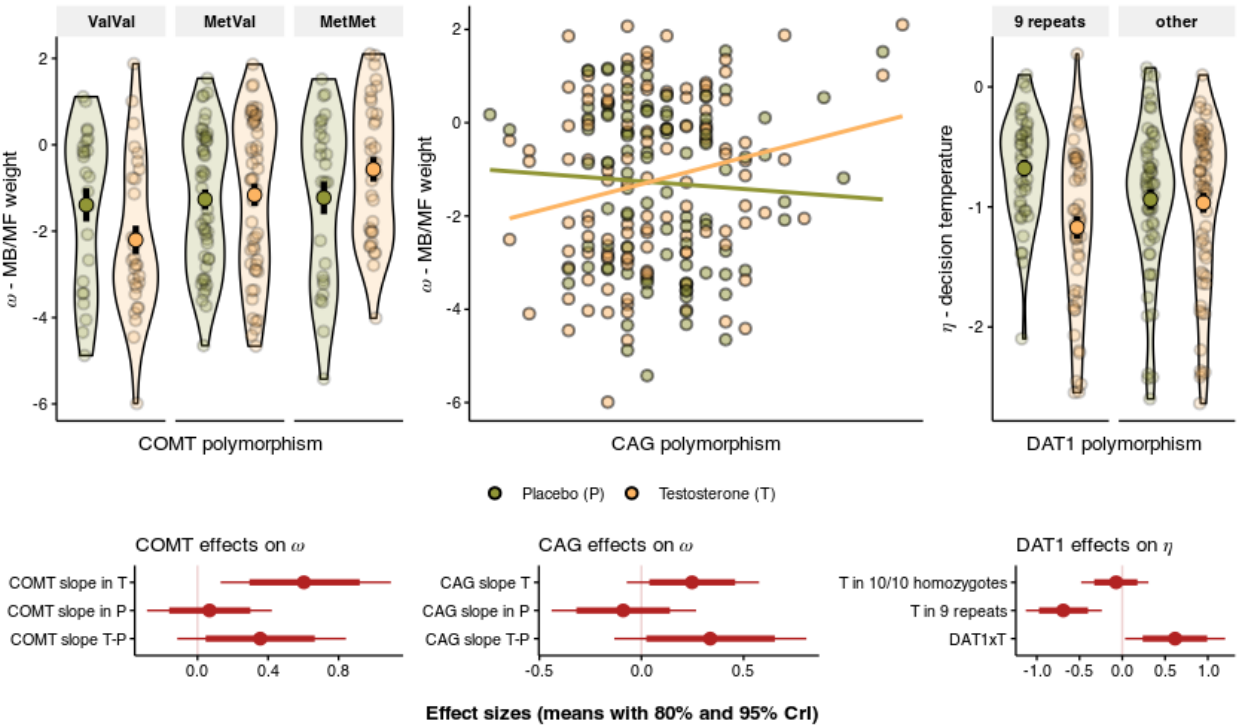


Figure S3. Genotype effects on model parameters. Plotting the MB/MF wright ω across COMT group s, with points as single participants, raw means and standard errors as error bars. Below, selected effect sizes with means, and 80% and 95% credibility intervals.

Supplementary Tables

Table S1. Descriptive statistics: Mean [CI].

Drug treatment	**Placebo**	**Testosterone**
Sample size	99	117
Baseline testosterone [pg/ml]	142.17 [121.63, 162.71]	174.58 [130.63, 218.53]
log	4.74 [4.60, 4.87]	4.79 [4.59, 4.99]
CAG repeat length	19.67 [19.01, 20.31]	19.27[18.63, 19.91]
Impulsivity trait	31.2 [30.13, 32.27]	31.39 [30.29,32.49]

Table S2. Bayesian mixed model predicting log reaction times from administration (admin: placebo=-0.5, testosterone=0.5), previous state (prev_state: same = 0, diff = 1), and genotype variables COMT (scaled), CAG (scaled) and DAT1 (-0.5, 0.5).

log(rt1) ~ (prev_state | ID) + admin * (comt_s + dat1_c + cag_s) * prev_state	**Estimate**	**Est.Error**	**Q2.5**	**Q97.5**
Intercept	6.679	0.024	6.632	6.726
admin	-0.062	0.032	-0.126	0.002
comt_s	-0.004	0.025	-0.053	0.046
dat1_c1	-0.083	0.049	-0.177	0.016
cag_s	-0.015	0.026	-0.063	0.038
prev_state	0.035	0.007	0.021	0.049
admin:comt_s	0.025	0.033	-0.041	0.089
admin:dat1_c1	0.133	0.068	0	0.267
admin:cag_s	0.013	0.033	-0.052	0.077
admin:prev_state	-0.007	0.01	-0.026	0.012
comt_s:prev_state	-0.004	0.007	-0.018	0.01
dat1_c1:prev_state	-0.018	0.014	-0.046	0.01
cag_s:prev_state	0.002	0.008	-0.013	0.017
admin:comt_s:prev_state	-0.005	0.01	-0.024	0.014
admin:dat1_c1:prev_state	0.012	0.019	-0.025	0.05
admin:cag_s:prev_state	0.001	0.01	-0.018	0.021

Table S3. Bayesian mixed model predicting earned points from administration (admin: placebo=-0.5, testosterone=0.5), previous state (prev_state: same = 0, diff = 1) and genotype variables COMT (scaled), CAG (scaled), and DAT1 (-0.5, 0.5).

points ~ (prev_state | ID) + admin * (dat1_c + comt_s + cag_s) * prev_state	**Estimate**	**Est.Error**	**Q2.5**	**Q97.5**
Intercept	0.888	0.036	0.819	0.961
admin	-0.11	0.048	-0.205	-0.016
dat1_c1	-0.133	0.073	-0.273	0.016
comt_s	0.015	0.037	-0.057	0.088
cag_s	-0.021	0.038	-0.094	0.053
prev_state	-0.515	0.038	-0.589	-0.44
admin:dat1_c1	0.209	0.099	0.014	0.404
admin:comt_s	-0.038	0.049	-0.134	0.058
admin:cag_s	0.069	0.05	-0.03	0.167
admin:prev_state	0.079	0.051	-0.023	0.179
dat1_c1:prev_state	0.041	0.076	-0.109	0.187
comt_s:prev_state	-0.028	0.039	-0.105	0.049
cag_s:prev_state	-0.016	0.04	-0.095	0.062
admin:dat1_c1:prev_state	-0.105	0.102	-0.307	0.094
admin:comt_s:prev_state	0.079	0.052	-0.021	0.181
admin:cag_s:prev_state	-0.023	0.052	-0.125	0.081

Table S4. Bayesian logistic mixed model predicting staying behavior from administration (admin: placebo= -0.5, testosterone=0.5), previous state (prev_state: same = 0, diff = 1), previous points, and genotype variables COMT (scaled), CAG (scaled), and DAT1 (-0.5, 0.5).

stay ~ (prev_state*prev_points | ID) + admin * (cag_s + comt_s + dat1_c) * prev_points * prev_state	**Estimate**	**Est.Error**	**Q2.5**	**Q97.5**
Intercept	0.626	0.053	0.522	0.73
admin	-0.018	0.072	-0.157	0.122
cag_s	-0.004	0.056	-0.113	0.104
comt_s	0.042	0.055	-0.064	0.15
dat1_c1	-0.022	0.108	-0.233	0.19
prev_points	0.489	0.03	0.431	0.549
prev_state	-0.474	0.064	-0.596	-0.348
admin:cag_s	0.04	0.072	-0.105	0.182
admin:comt_s	-0.067	0.074	-0.212	0.075
admin:dat1_c1	-0.075	0.144	-0.354	0.212
admin:prev_points	-0.098	0.041	-0.177	-0.018
cag_s:prev_points	-0.012	0.031	-0.071	0.048
comt_s:prev_points	0.013	0.03	-0.045	0.072
dat1_c1:prev_points	-0.099	0.06	-0.216	0.019
admin:prev_state	-0.029	0.088	-0.2	0.141
cag_s:prev_state	-0.039	0.069	-0.175	0.096
comt_s:prev_state	-0.051	0.068	-0.182	0.084
dat1_c1:prev_state	-0.076	0.131	-0.339	0.184
prev_points:prev_state	-0.263	0.029	-0.319	-0.206
admin:cag_s:prev_points	0.041	0.04	-0.038	0.118
admin:comt_s:prev_points	-0.001	0.04	-0.08	0.077
admin:dat1_c1:prev_points	0.173	0.08	0.018	0.331
admin:cag_s:prev_state	0.046	0.09	-0.132	0.22
admin:comt_s:prev_state	0.168	0.091	-0.01	0.347
admin:dat1_c1:prev_state	0.144	0.177	-0.217	0.489
admin:prev_points:prev_state	0.073	0.039	-0.003	0.147
cag_s:prev_points:prev_state	-0.016	0.03	-0.074	0.041
comt_s:prev_points:prev_state	-0.016	0.029	-0.074	0.04
dat1_c1:prev_points:prev_state	-0.002	0.057	-0.113	0.11
admin:cag_s:prev_points:prev_state	0.008	0.039	-0.067	0.085
admin:comt_s:prev_points:prev_state	0.03	0.039	-0.047	0.107
admin:dat1_c1:prev_points:prev_state	-0.024	0.077	-0.18	0.127

Exploratory analysis of estradiol levels

The post-hoc exploratory analyses reported here were conducted after the publication of the above article, in order to examine whether the salivary levels of the hormone estradiol explained more variance than the drug administration factor (see also General Discussion).

The analysis of the change in the estradiol levels across the duration od the experiment did not show a significant interaction between the factors drug administration and time **(**$F(3,409.95) = 2.582$, $p = .077$). Contrary to the drug administration factor (original model, see Method: Behavioral analysis), including the difference in estradiol levels (before task - baseline) in the GzLMM of staying behavior as a continuous predictor did not yield a significant interaction with the other factors ($OR = 1.01$, CI = [0.99 – 1.02], $p = .245$). The estradiol levels had no main effect either ($OR = 1.03$, CI = [0.96 – 1.11], $p = .394$). The original model had lower AIC and BIC values, and log-likelihood value closer to 0. A chi-squared test for model comparison yielded a non-significant result ($\chi2(1) = 4.933$, $p > .05$), indicating that there was no significant difference in model fit between the original model and the model with the predictor estradiol levels instead of drug administration group.

Chapter 7

GENERAL DISCUSSION

How can we best understand the evolved function of endocrine systems in human behavior? Hormones typically exert multiple simultaneous effects distributed throughout the brain and body, which indicates their potential to coordinate diverse outcomes. Such coordinated outputs are likely evolved functional responses to specific eliciting conditions that cause increases or decreases in the release of the respective hormones (Roney, 2016). If we want to characterize their role in complex social behavior, our investigation has to be multifaceted. First, research needs to examine how and why endocrine signaling appeared and was formed during evolution in non-human organisms. Second, we need to study the eliciting conditions of hormonal functioning, in other words, the interaction of the hormone with the surrounding environment. Third, a comprehensive investigation requires studying the biological mechanisms through which the hormones exert their actions, including the hormones' interactions with other regulatory systems of the organism.

In my dissertation, I aimed to contribute to our understanding of the role the hormone testosterone plays in complex human social behavior. While the first chapter summarizes previous research on testosterone's evolution and functioning in non-human animals, the subsequent chapters report five testosterone-administration studies, in which we (A) test testosterone's role in status-seeking behavior (B) study how the social context present in the surrounding environment determines testosterone's effect, and (C) investigate physiological, computational and cognitive pathways whereby testosterone exerts its impact.

In Study 1, we demonstrate that the way testosterone influences physiological responses to stressors crucially depends on the presence or absence of social context. In the situation when an individual faced a biological stressor, testosterone enhanced sympathetic activation. Conversely, when the biological stressor was imbued with social context, and the individual was watched by another person, testosterone dampened the biomarkers of sympathetic arousal. Such findings highlight the flexibility of testosterone's functioning, which may facilitate adaptive forms of status-seeking. Rapid mobilization has benefits when facing a biological threat and preparing for a

fight-flight response. On the other hand, when facing a socio-evaluative challenge, where the aim is to persist rather than to withdraw, calming down may foster a beneficial reaction.

In Study 2, we show that when one's behavior is visible to others, testosterone promotes dominant rather than reputational forms of status-seeking. Although the presence of observers made volunteers in the placebo group act more prosocially, testosterone administration abolished this effect. Using reinforcement-learning drift-diffusion modeling, we sought to uncover whether testosterone exerts its behavioral effect through impacting reward-related processes. We found that testosterone administration influenced the degree to which an individual's behavior aligns with the reward values they learned. In particular, when individuals were observed, testosterone, compared to placebo, increased relative noise in prosocial choices. Together, these findings provide evidence that testosterone boosts dominant status-seeking and support the claim that it does so through mechanisms associated with reward processing.

Besides stress regulation and reward processing, another possible pathway through which testosterone could affect behavior in status-challenging situations is modulating the subjective perception of one's own competence and the competence of the potential opponent. To test this assertion, in Study 3, we experimentally manipulated the control participants perceived over their task performance and showed that the subjectively perceived personal control determines their persistence in competition against a stronger opponent. Crucially, testosterone administration disrupted the link between perceived personal control and competition persistence. Under testosterone, participants with low perceived control kept competing despite incurring substantial monetary costs. The enhanced persistence in the testosterone group was not associated with increased subjective personal competence or blunted perception of the opponent's competence. Such findings indicate that testosterone encourages behavior that may lead to status enhancement in challenging situations, yet it does not do so by altering explicit evaluation of own or opponent's competence.

Finally, in this dissertation, I also investigated whether testosterone biases cognitive functions away from deliberate processes toward reflexive ones, an effect that could potentially serve as a mechanism for promoting fast responses in status-challenging situations. In collaborative Study 4, which pooled together data from three independent experiments, we show that the effects of testosterone administration on cognitive reflection are weak and highly variable. In Study 5, we aimed to bring the investigation further and examine the possible sources of this variability by (A) using Daw's 2-step task (Daw et al., 2011) embedded in a reinforcement-learning framework which allows distinguishing between model-free (reflexive, quick) and a model-based (deliberate, slow) valuation systems, and (B) exploring the potential modulating influence of genetic polymorphisms which account for individual differences in dopaminergic and androgen signaling. In line with Study 4, we did not find a convincing general effect of testosterone on the trade-off

between the deliberate and reflexive processes. Interestingly, similar to Study 2 and Study 3 (see Supplementary Materials A), we found that testosterone decreased choice consistency, suggesting higher noise or exploration in participants' behavior. The exploratory analysis of genetic polymorphisms revealed that the testosterone-induced decrease in choice consistency was driven by participants with a genetic predisposition for higher striatal dopamine (indexed by the DAT1 gene polymorphism, Heinz et al., 2000). The results of these two studies do not support the hypothesis that testosterone generally decreases the probability of engaging in slow and effortful cognitive processes to prioritize reflexive responding (Nave et al., 2017). However, we provide a possible explanation for the reported variability in testosterone effects on cognitive processes by showing that testosterone effects are related to the genetic variability of the dopaminergic system.

Our novel findings open up new avenues for further investigations in the field of psychoneuroendocrinology. The first set of inquiries pertains to the involvement of dopaminergic receptors in the signaling pathway of testosterone. There is some evidence that testosterone can influence the activity of dopamine D2 receptors, although the exact nature is not yet fully understood. For example, D2 mRNA in substantia nigra and striatum increases after testosterone replacement in gonadectomized male rates (Purves-Tyson et al., 2014), and injections of dopamine D2-receptor antagonists to male rats block behavioral effects of testosterone administration (Schroeder & Packard, 2000). Interestingly, dopamine D2 receptors influence the consistency of our actions with the learned reward values, a process influenced by exogenous testosterone in our studies 2, 3, and 5. In particular, dopamine D2-receptor knockout mice show reduced value-dependent action selection, and administration of dopamine D2-receptor antagonists in macaques can lead to both decreased (Kwak et al., 2014) and increased choice consistency (Lee et al., 2015). Similarly, in humans, administration of D2/3 receptor antagonists may lead to noisier choice performance (Eisenegger et al., 2014; Mikus et al., 2022; but see Soutschek & Tobler, 2023). Hence, it is plausible to consider that the results observed in our research might not have been solely influenced by androgen receptors, but rather, the participation of dopamine D2 receptors also had a significant impact. In this regard, it is intriguing that the density of dopamine D2 receptors changes as a function of social dominance and the presence of social challenges. For instance, socially challenging environments and successful assertion of dominance increase the amount or availability of dopamine D2 receptors in monkeys (Morgan et al., 2002; Nader et al., 2012). Similarly, in humans, a PET study found that social status correlates with D2/3 receptor binding (Martinez et al., 2010). Together with the evidence that testosterone's status-seeking effects are enhanced in those with high dominance (Study 2, and Carré et al., 2017), these findings indicate how dopamine D2 receptors and testosterone interact to promote status-seeking and maintenance behaviors. This possible mechanism, however, still needs to be tested in future research, preferably by a double placebo-controlled administration of testosterone and dopamine D2 antagonists such as sulpiride or haloperidol.

Another way to shed light on the testosterone signaling pathway is to include in testosterone administration studies the analysis of TaqI A polymorphism of the dopamine D_2 receptor gene. Studies using post-mortem brains showed that the subjects with one or two A1 alleles of this polymorphism had lower D2 receptor density in the striatum (Thompson et al., 1997) and caudate nuclei (Noble, 1998) than those without the A1 allele, and these results have been confirmed in vivo with positron emission tomography (Jönsson et al., 1999). Relevant to our research, impairments in choice performance (an effect similar to the one reported in our Studies 2, 3, 5) induced by sulpiride were greater in volunteers carrying at least one copy of the A1 allele of the Taq1A polymorphism (Eisenegger et al., 2014). If we assume that testosterone impacts decision-making also through acting on dopamine D2 receptors, it is plausible to expect that its effect will depend on the polymorphic variant of the dopamine D2 receptor gene.

The list of the genetic polymorphisms that influence the functioning of dopamine D2 receptors, and may consequently also impact testosterone's effects, is indeed much longer. Of these, the C957T polymorphism was found to exert opposite influences on frontally mediated reflective learning and striatally mediated reflexive learning (Xie et al., 2015), making it a suitable candidate for deeper examination in relationship to testosterone's effects.

Besides dopamine receptors, other components of the dopaminergic signaling pathway may interact with testosterone effects. Our studies show some evidence that testosterone administration interacts with the polymorphism of the dopamine transporter gene, DAT1. Although in Study 2 we did not find a significant interaction effect, Study 5 showed that testosterone increased choice randomness in the 9-repeat allele carriers assumed to have reduced dopamine transport activity, thus higher striatal dopamine (Heinz et al., 2000; Ito et al., 2008). Such a finding may be interpreted in the context of theoretical and empirical accounts suggesting an inverted-U-shaped relationship between dopaminergic activity and choice performance (Cools & D'Esposito, 2011; Eisenegger et al., 2013). Yet, to reliably characterize the role of DAT1 polymorphisms in testosterone behavioral effects, future studies with larger sample sizes will be required. Larger sample sizes and genetic pre-screenings will also be necessary to address our inconclusive evidence of whether COMT polymorphism modulates testosterone's impact on deliberate cognitive processes. The pre-screening measures are especially important as COMT polymorphism has an uneven trimodal distribution in European populations (Klebe et al., 2013; McLeod et al., 1998).

In the introduction chapter of this dissertation, I point out that in the course of evolution, the testosterone molecule appeared earlier than the androgen receptor. Hence, testosterone might have been initially an inactive component of estradiol synthesis. In the process of estradiol synthesis, testosterone is metabolized by the enzyme aromatase to estradiol, which activates its own receptor system: estrogen receptors alpha and beta (Litwack, 2022). There is evidence that repeated

testosterone administration increases estradiol levels in a dose-dependent manner (Lakshman et al., 2010). Furthermore, in rodents, some testosterone effects can be blocked by administering an aromatase inhibitor, which prevents testosterone's conversion to estradiol (Nathan et al., 2001). However, the evidence from single-dose testosterone administration studies in humans is scarce, and no study has directly tested the hypothesis that testosterone behavioral effects occur through estradiol pathways. Although our studies were not originally designed to test this hypothesis, we have conducted exploratory post-hoc analyses to address the issue. The additional analyses of the available estradiol measurements (Studies 2, 3, 5) did not show a reliable increase in estradiol levels following testosterone administration. Including estradiol as a predictor in our primary analyses did not considerably improve the fit of the models. These results indicate that the observed testosterone effects were not consequences of testosterone conversion to estradiol. However, if we want to claim more reliably that testosterone effects are not, in fact, the effects of estradiol binding to estrogen receptors, future testosterone administration studies should also include placebo-controlled administration of aromatase and 5-alpha-reductase inhibitors (Ishikawa et al., 2006)

Another intriguing research avenue is the investigation of brain regions and networks implicated in the testosterone effects we observed in our studies. Although identifying the corresponding brain regions was not a goal of our studies, the findings suggest potential areas for further investigation. Given the possible involvements of dopamine signaling pathways, it is highly probable that striatal regions are involved in the effects observed in our studies 2, 3, 4, and 5. Their involvement is likely regardless of whether the effects are subserved by dopamine receptors or androgen receptors, which are also expressed in high density in striatal regions (Tobiansky et al., 2018) and on dopaminergic neurons projecting to the ventral striatum (Creutz & Kritzer, 2004).

Testosterone's impact on the physiological stress response (Study 1) likely recruits diverse brain regions. Testosterone might influence the response to stressor via the arginine vasopressin (AVP) system, which is essential for regulating blood pressure (Pittman et al., 1982; Zhang et al., 1999). It has been shown that testosterone upregulates vasopressin gene expression in rat medial amygdala (Szot & Dorsa, 1994) and also increases AVP receptor binding in rodent hypothalamus (Delville et al., 1996). However, studies of short-term interactions between testosterone and the AVP system in the amygdala and hypothalamus are lacking. Furthermore, given that the testosterone effects observed in our studies were determined by the surrounding social context, it is likely that the effects also require the involvement of the cortical regions that regulate higher-order behavior. A candidate region that may be implicated in the observed outcomes that has previously shown sensitivity to testosterone administration is the orbitofrontal cortex (Mehta & Beer, 2010). Importantly, testosterone administration was shown to reduce amygdala–orbitofrontal cortex coupling (e.g., Bos et al., 2012; van Wingen et al., 2010), a mechanism essential for

processes such as self-regulation (Coccaro et al., 2007; S. Peters et al., 2015) and acute threat response (Heany et al., 2018; for a review and neural framework see also Terburg & van Honk, 2013). Future insights into the mechanisms of context-dependent testosterone effect may be thus brought by studying testosterone's influence on the functional crosstalk between cortical and subcortical brain regions.

Finally, it needs to be mentioned that our studies examined the effects of testosterone administration only in male participants. In general, single-dose testosterone administration studies conducted in men appear to be more common than the studies in women. For instance, a PubMed® search using the keyword combination ("single dose"[Title/Abstract]) AND (testosterone[Title]) AND (men[Title/Abstract]) provided 42 items, while the search using the keywords ("single dose"[Title/Abstract]) AND (testosterone[Title]) AND (women[Title/Abstract]) provided 23 items. Interestingly, although a different metabolism of the testosterone hormone in men and women is emphasized (Gurvich et al., 2018; Nieschlag & Behre, 1998), the outcomes of testosterone administration studies in men and women are often summarized in a mixed fashion without acknowledging the differences in the studied samples (e.g., Eisenegger et al., 2011; Knight et al., 2017; Losecaat Vermeer et al., 2020). While some independently conducted studies show comparable results in male and female samples (e.g., Goetz et al., 2014; Hermans et al., 2008; van Wingen et al., 2009), others show different effects (Dreher et al., 2016; Eisenegger et al., 2010; Zak et al., 2009). Based on the empirical evidence presented in this dissertation, it is not possible to predict whether implementing an identical research design in a female sample would yield similar results. Importantly, our research findings consistently demonstrate that the effects of testosterone depend on the social context, a factor likely to exert distinct modulatory influences in males and females. Future research is therefore required to test whether the outcomes of our research can be generalized to women. Of note, the forthcoming studies are expected to be impacted by the latest developments in administration paradigms (Luberti et al., 2021) that may facilitate the inclusion of mixed study samples.

In summary, the novel findings presented in this PhD thesis contribute to our comprehension of testosterone's role in status-seeking and uncover a variety of mechanisms by which testosterone exerts its complex effects. This research highlights the diversity of testosterone effects across various domains, including social behaviors, cognitive processes, and the autonomic nervous system. Moreover, it emphasizes the crucial role of social context in determining the final form and direction of the hormone's effects. Such variability likely enables testosterone, in concert with other regulating systems of the organism, to orchestrate adaptive responses to challenges faced in the individual's environment. We argue that one of the essential mechanisms underlying testosterone's impact on human social behavior and decision-making includes the modulation of reward-related processes, specifically the translation of the learned reward information into actual behavior. Overall, I am convinced that this work deepens our understanding of how testosterone

shapes human lives, and I hope it inspires future research to elucidate the remaining many intricacies of the hormone's effects.

References

Archer, J. (2006). Testosterone and human aggression: An evaluation of the challenge hypothesis. *Neuroscience and Biobehavioral Reviews*, *30*(3), 319–345. https://doi.org/10.1016/j.neubiorev.2004.12.007

Art, S. H. M. B. (2000). Population structure and breeding system of the sex-role reversed, polyandrous Bronze-winged Jacana Metopidius indicus. *Ibis*, *142*(1), 93–102. https://doi.org/10.1111/j.1474-919X.2000.tb07688.x

Aubele, T., & Kritzer, M. F. (2012). Androgen Influence on Prefrontal Dopamine Systems in Adult Male Rats: Localization of Cognate Intracellular Receptors in Medial Prefrontal Projections to the Ventral Tegmental Area and Effects of Gonadectomy and Hormone Replacement on Glutamate-Stimulated Extracellular Dopamine Level. *Cerebral Cortex (New York, NY)*, *22*(8), 1799–1812. https://doi.org/10.1093/cercor/bhr258

Auyeung, B., Lombardo, M. V., & Baron-Cohen, S. (2013). Prenatal and postnatal hormone effects on the human brain and cognition. *Pflugers Archiv: European Journal of Physiology*, *465*(5), 557–571. https://doi.org/10.1007/s00424-013-1268-2

Avise, J. C., Jones, A. G., Walker, D., & DeWoody, J. A. (2002). Genetic Mating Systems and Reproductive Natural Histories of Fishes: Lessons for Ecology and Evolution. *Annual Review of Genetics*, *36*(1), 19–45. https://doi.org/10.1146/annurev.genet.36.030602.090831

Baker, M. E. (2005). Xenobiotics and the Evolution of Multicellular Animals: Emergence and Diversification of Ligand-Activated Transcription Factors1. *Integrative and Comparative Biology*, *45*(1), 172–178. https://doi.org/10.1093/icb/45.1.172

Barkus, C., Korn, C., Stumpenhorst, K., Laatikainen, L. M., Ballard, D., Lee, S., Sharp, T., Harrison, P. J., Bannerman, D. M., Weinberger, D. R., Chen, J., & Tunbridge, E. M. (2016). Genotype-Dependent Effects of COMT Inhibition on Cognitive Function in a Highly Specific, Novel Mouse Model of Altered COMT Activity. *Neuropsychopharmacology*, *41*(13), Article 13. https://doi.org/10.1038/npp.2016.119

Boksem, M. A. S., Mehta, P. H., Van den Bergh, B., van Son, V., Trautmann, S. T., Roelofs, K., Smidts, A., & Sanfey, A. G. (2013). Testosterone inhibits trust but promotes reciprocity. *Psychological Science*, *24*(11), 2306–2314. https://doi.org/10.1177/0956797613495063

Bos, P. A., Hermans, E. J., Ramsey, N. F., & van Honk, J. (2012). The neural mechanisms by which testosterone acts on interpersonal trust. *NeuroImage*, *61*(3), 730–737. https://doi.org/10.1016/j.neuroimage.2012.04.002

Breed, M. D. (2017). Chapter 64—1990 The Challenge Hypothesis. In M. D. Breed (Ed.), *Conceptual Breakthroughs in Ethology and Animal Behavior* (pp. 195–196). Academic Press. https://doi.org/10.1016/B978-0-12-809265-1.00064-2

Buskbjerg, C. R., Amidi, A., Buus, S., Gravholt, C. H., Hadi Hosseini, S. M., & Zachariae, R. (2022). Androgen deprivation therapy and cognitive decline—Associations with brain connectomes, endocrine status, and risk genotypes. *Prostate Cancer and Prostatic Diseases*, *25*(2), Article 2. https://doi.org/10.1038/s41391-021-00398-1

Butenandt, A., & Hanisch, G. (1935). *Über Testosteron. Umwandlung des Dehydro-androsterons in Androstendiol und Testosteron; ein Weg zur Darstellung des Testosterons aus Cholesterin. 237*(1–3), 89–97. https://doi.org/10.1515/bchm2.1935.237.1-3.89

Campbell, B. C., Dreber, A., Apicella, C. L., Eisenberg, D. T. A., Gray, P. B., Little, A. C., Garcia, J. R., Zamore, R. S., & Lum, J. K. (2010). Testosterone exposure, dopaminergic reward, and sensation-seeking in young men. *Physiology & Behavior*, *99*(4), 451–456. https://doi.org/10.1016/j.physbeh.2009.12.011

Carré, J. M., Geniole, S. N., Ortiz, T. L., Bird, B. M., Videto, A., & Bonin, P. L. (2017). Exogenous Testosterone Rapidly Increases Aggressive Behavior in Dominant and Impulsive Men. *Biological Psychiatry*, *82*(4), 249–256. https://doi.org/10.1016/j.biopsych.2016.06.009

Chamberlain, N. L., Driver, E. D., & Miesfeld, R. L. (1994). The length and location of CAG trinucleotide repeats in the androgen receptor N-terminal domain affect transactivation function. *Nucleic Acids Research*, *22*(15), 3181–3186. https://doi.org/10.1093/nar/22.15.3181

Chen, J., Lipska, B. K., Halim, N., Ma, Q. D., Matsumoto, M., Melhem, S., Kolachana, B. S., Hyde, T. M., Herman, M. M., Apud, J., Egan, M. F., Kleinman, J. E., & Weinberger, D. R. (2004). Functional Analysis of Genetic Variation in Catechol-O-Methyltransferase (COMT): Effects on mRNA, Protein, and Enzyme Activity in Postmortem Human Brain. *The American Journal of Human Genetics*, *75*(5), 807–821. https://doi.org/10.1086/425589

Chichinadze, K., & Chichinadze, N. (2008). Stress-induced increase of testosterone: Contributions of social status and sympathetic reactivity. *Physiology & Behavior*, *94*(4), 595–603. https://doi.org/10.1016/j.physbeh.2008.03.020

Choong, C. S., Kemppainen, J. A., & Wilson, E. M. (1998). Evolution of the primate androgen receptor: A structural basis for disease. *Journal of Molecular Evolution*, *47*(3), 334–342. https://doi.org/10.1007/pl00006391

Coates, J. M., & Herbert, J. (2008). Endogenous steroids and financial risk taking on a London trading floor. *Proceedings of the National Academy of Sciences*, *105*(16), 6167–6172. https://doi.org/10.1073/pnas.0704025105

Coccaro, E. F., McCloskey, M. S., Fitzgerald, D. A., & Phan, K. L. (2007). Amygdala and Orbitofrontal Reactivity to Social Threat in Individuals with Impulsive Aggression. *Biological Psychiatry*, *62*(2), 168–178. https://doi.org/10.1016/j.biopsych.2006.08.024

Cohen, J. Y., Haesler, S., Vong, L., Lowell, B. B., & Uchida, N. (2012). Neuron-type-specific signals for reward and punishment in the ventral tegmental area. *Nature*, *482*(7383), 85–88. https://doi.org/10.1038/nature10754

Collaer, M. L., & Hines, M. (1995). Human behavioral sex differences: A role for gonadal hormones during early development? *Psychological Bulletin*, *118*(1), 55–107. https://doi.org/10.1037/0033-2909.118.1.55

Cools, R., & D'Esposito, M. (2011). Inverted-U–Shaped Dopamine Actions on Human Working Memory and Cognitive Control. *Biological Psychiatry*, *69*(12), e113–e125. https://doi.org/10.1016/j.biopsych.2011.03.028

Cox, R. M., Stenquist, D. S., & Calsbeek, R. (2009). Testosterone, growth and the evolution of sexual size dimorphism. *Journal of Evolutionary Biology*, *22*(8), 1586–1598. https://doi.org/10.1111/j.1420-9101.2009.01772.x

Creutz, L. M., & Kritzer, M. F. (2004). Mesostriatal and mesolimbic projections of midbrain neurons immunoreactive for estrogen receptor beta or androgen receptors in rats. *Journal of Comparative Neurology*, *476*(4), 348–362. https://doi.org/10.1002/cne.20229

Cunningham, G. R., Stephens-Shields, A. J., Rosen, R. C., Wang, C., Bhasin, S., Matsumoto, A. M., Parsons, J. K., Gill, T. M., Molitch, M. E., Farrar, J. T., Cella, D., Barrett-Connor, E., Cauley, J. A., Cifelli, D., Crandall, J. P., Ensrud, K. E., Gallagher, L., Zeldow, B., Lewis, C. E., … Snyder, P. J. (2016). Testosterone Treatment and Sexual Function in Older Men With Low Testosterone Levels. *The Journal of Clinical Endocrinology and Metabolism*, *101*(8), 3096–3104. https://doi.org/10.1210/jc.2016-1645

Dabbs, J. M., Carr, T. S., Frady, R. L., & Riad, J. K. (1995). Testosterone, crime, and misbehavior among 692 male prison inmates. *Personality and Individual Differences*, *18*(5), 627–633. https://doi.org/10.1016/0191-8869(94)00177-T

Davey, R. A., & Grossmann, M. (2016). Androgen Receptor Structure, Function and Biology: From Bench to Bedside. *The Clinical Biochemist Reviews*, *37*(1), 3–15. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4810760/

David, K., Dingemanse, E., Freud, J., & Laqueur, E. (1935). Über krystallinisches männliches Hormon aus Hoden (Testosteron), wirksamer als aus Harn oder aus Cholesterin bereitetes Androsteron. *Hoppe-Seyler´s Zeitschrift Für Physiologische Chemie*, *233*(5–6), 281–283. https://doi.org/10.1515/bchm2.1935.233.5-6.281

Daw, N. D., Gershman, S. J., Seymour, B., Dayan, P., & Dolan, R. J. (2011). Model-based influences on humans' choices and striatal prediction errors. *Neuron*, *69*(6), 1204–1215. https://doi.org/10.1016/j.neuron.2011.02.027

Daw, N. D., Niv, Y., & Dayan, P. (2005). Uncertainty-based competition between prefrontal and dorsolateral striatal systems for behavioral control. *Nature Neuroscience*, *8*(12), 1704–1711. https://doi.org/10.1038/nn1560

De Gendt, K., Swinnen, J. V., Saunders, P. T. K., Schoonjans, L., Dewerchin, M., Devos, A., Tan, K., Atanassova, N., Claessens, F., Lécureuil, C., Heyns, W., Carmeliet, P., Guillou, F., Sharpe, R. M., & Verhoeven, G. (2004). A Sertoli cell-selective knockout of the androgen receptor causes spermatogenic arrest in meiosis. *Proceedings of the National Academy of Sciences of the United States of America*, *101*(5), 1327–1332. https://doi.org/10.1073/pnas.0308114100

de Souza Silva, M. A., Mattern, C., Topic, B., Buddenberg, T. E., & Huston, J. P. (2009). Dopaminergic and serotonergic activity in neostriatum and nucleus accumbens enhanced by intranasal administration of testosterone. *European Neuropsychopharmacology*, *19*(1), 53–63. https://doi.org/10.1016/j.euroneuro.2008.08.003

Delville, Y., Mansour, K. M., & Ferris, C. F. (1996). Testosterone facilitates aggression by modulating vasopressin receptors in the hypothalamus. *Physiology & Behavior*, *60*(1), 25–29. https://doi.org/10.1016/0031-9384(95)02246-5

Desjardins, J. K., Hazelden, M. R., Van der Kraak, G. J., & Balshine, S. (2006). Male and female cooperatively breeding fish provide support for the "Challenge Hypothesis." *Behavioral Ecology*, *17*(2), 149–154. https://doi.org/10.1093/beheco/arj018

DeVries, M. S., Winters, C. P., & Jawor, J. M. (2012). Testosterone elevation and response to gonadotropin-releasing hormone challenge by male northern cardinals (Cardinalis cardinalis) following aggressive behavior. *Hormones and Behavior*, *62*(1), 99–105. https://doi.org/10.1016/j.yhbeh.2012.05.008

Diederen, K. M. J., Spencer, T., Vestergaard, M. D., Fletcher, P. C., & Schultz, W. (2016). Adaptive Prediction Error Coding in the Human Midbrain and Striatum Facilitates Behavioral Adaptation and Learning Efficiency. *Neuron*, *90*(5), 1127–1138. https://doi.org/10.1016/j.neuron.2016.04.019

Dreher, J.-C., Dunne, S., Pazderska, A., Frodl, T., Nolan, J. J., & O'Doherty, J. P. (2016). Testosterone causes both prosocial and antisocial status-enhancing behaviors in human males. *Proceedings of the National Academy of Sciences*, *113*(41), 11633–11638. https://doi.org/10.1073/pnas.1608085113

Edwards, A., Hammond, H. A., Jin, L., Caskey, C. T., & Chakraborty, R. (1992). Genetic variation at five trimeric and tetrameric tandem repeat loci in four human population groups. *Genomics*, *12*(2), 241–253. https://doi.org/10.1016/0888-7543(92)90371-x

Eisenegger, C., Haushofer, J., & Fehr, E. (2011). The role of testosterone in social interaction. *Trends in Cognitive Sciences*, *15*(6), 263–271. https://doi.org/10.1016/j.tics.2011.04.008

Eisenegger, C., Naef, M., Linssen, A., Clark, L., Gandamaneni, P. K., Müller, U., & Robbins, T. W. (2014). Role of Dopamine D2 Receptors in Human Reinforcement Learning. *Neuropsychopharmacology*, *39*(10), 2366–2375. https://doi.org/10.1038/npp.2014.84

Eisenegger, C., Naef, M., Snozzi, R., Heinrichs, M., & Fehr, E. (2010). Prejudice and truth about the effect of testosterone on human bargaining behaviour. *Nature*, *463*(7279), 356–359. https://doi.org/10.1038/nature08711

Eisenegger, C., Pedroni, A., Rieskamp, J., Zehnder, C., Ebstein, R., Fehr, E., & Knoch, D. (2013). DAT1 Polymorphism Determines L-DOPA Effects on Learning about Others' Prosociality. *PLoS ONE*, *8*(7), e67820. https://doi.org/10.1371/journal.pone.0067820

Enter, D., Spinhoven, P., & Roelofs, K. (2014). Alleviating social avoidance: Effects of single dose testosterone administration on approach–avoidance action. *Hormones and Behavior*, *65*(4), 351–354. https://doi.org/10.1016/j.yhbeh.2014.02.001

Enter, D., Spinhoven, P., & Roelofs, K. (2016). Dare to approach: Single dose testosterone administration promotes threat approach in patients with social anxiety disorder. *Clinical Psychological Science*, *4*, 1073–1079. https://doi.org/10.1177/2167702616631499

Fernández-Guasti, A., & Martínez-Mota, L. (2005). Anxiolytic-like actions of testosterone in the burying behavior test: Role of androgen and GABA-benzodiazepine receptors. *Psychoneuroendocrinology*, *30*(8), 762–770. https://doi.org/10.1016/j.psyneuen.2005.03.006

Fontanesi, L., Gluth, S., Spektor, M. S., & Rieskamp, J. (2019). A reinforcement learning diffusion decision model for value-based decisions. *Psychonomic Bulletin & Review*, *26*(4), 1099–1121. https://doi.org/10.3758/s13423-018-1554-2

Foradori, C. D., Weiser, M. J., & Handa, R. J. (2008). Non-genomic Actions of Androgens. *Frontiers in Neuroendocrinology*, *29*(2), 169–181. https://doi.org/10.1016/j.yfrne.2007.10.005

Frederick, S. (2005). Cognitive Reflection and Decision Making. *Journal of Economic Perspectives*, *19*(4), 25–42. https://doi.org/10.1257/089533005775196732

Fusani, L. (2008). Testosterone control of male courtship in birds. *Hormones and Behavior*, *54*(2), 227–233. https://doi.org/10.1016/j.yhbeh.2008.04.004

Gaysina, D., Xu, M. K., Barnett, J. H., Croudace, T. J., Wong, A., Richards, M., & Jones, P. B. (2013). The catechol-O-methyltransferase gene (COMT) and cognitive function from childhood through adolescence. *Biological Psychology*, *92*(2), 359–364. https://doi.org/10.1016/j.biopsycho.2012.11.007

Geniole, S. N., Bird, B. M., McVittie, J. S., Purcell, R. B., Archer, J., & Carré, J. M. (2020). Is testosterone linked to human aggression? A meta-analytic examination of the relationship between baseline, dynamic, and manipulated testosterone on human aggression. *Hormones and Behavior*, *123*, 104644. https://doi.org/10.1016/j.yhbeh.2019.104644

Geniole, S. N., Procyshyn, T. L., Marley, N., Ortiz, T. L., Bird, B. M., Marcellus, A. L., Welker, K. M., Bonin, P. L., Goldfarb, B., Watson, N. V., & Carré, J. M. (2019). Using a Psychopharmacogenetic Approach To Identify the Pathways Through Which—And the People for Whom—Testosterone Promotes Aggression. *Psychological Science*, *30*(4), 481–494. https://doi.org/10.1177/0956797619826970

Geniole, S. N., Proietti, V., Bird, B. M., Ortiz, T. L., Bonin, P. L., Goldfarb, B., Watson, N. V., & Carré, J. M. (2019). Testosterone reduces the threat premium in competitive resource division. *Proceedings. Biological Sciences*, *286*(1903), 20190720. https://doi.org/10.1098/rspb.2019.0720

Goel, N., & Bale, T. L. (2008). Organizational and Activational Effects of Testosterone on Masculinization of Female Physiological and Behavioral Stress Responses. *Endocrinology*, *149*(12), 6399–6405. https://doi.org/10.1210/en.2008-0433

Goetz, S. M. M., Tang, L., Thomason, M. E., Diamond, M. P., Hariri, A. R., & Carré, J. M. (2014). Testosterone Rapidly Increases Neural Reactivity to Threat in Healthy Men: A Novel Two-Step Pharmacological Challenge Paradigm. *Biological Psychiatry*, *76*(4), 324–331. https://doi.org/10.1016/j.biopsych.2014.01.016

Goymann, W. (2009). Social modulation of androgens in male birds. *General and Comparative Endocrinology*, *163*(1–2), 149–157. https://doi.org/10.1016/j.ygcen.2008.11.027

Goymann, W., Moore, I. T., & Oliveira, R. F. (2019). Challenge Hypothesis 2.0: A Fresh Look at an Established Idea. *BioScience*, *69*(6), 432–442. https://www.jstor.org/stable/26732562

Gray, P. B., & Campbell, B. C. (2009). Human male testosterone, pair-bonding, and fatherhood. In *Endocrinology of social relationships* (pp. 270–293). Harvard University Press.

Gurvich, C., Hoy, K., Thomas, N., & Kulkarni, J. (2018). Sex Differences and the Influence of Sex Hormones on Cognition through Adulthood and the Aging Process. *Brain Sciences*, *8*(9), 163. https://doi.org/10.3390/brainsci8090163

Handa, R. J., & Weiser, M. J. (2014). Gonadal steroid hormones and the hypothalamo–pituitary–adrenal axis. *Frontiers in Neuroendocrinology*, *35*(2), 197–220. https://doi.org/10.1016/j.yfrne.2013.11.001

Hau, M., Gill, S. A., & Goymann, W. (2008). Tropical field endocrinology: Ecology and evolution of testosterone concentrations in male birds. *General and Comparative Endocrinology*, *157*(3), 241–248. https://doi.org/10.1016/j.ygcen.2008.05.008

Heany, S. J., Bethlehem, R. A. I., van Honk, J., Bos, P. A., Stein, D. J., & Terburg, D. (2018). Effects of testosterone administration on threat and escape anticipation in the orbitofrontal cortex. *Psychoneuroendocrinology*, *96*, 42–51. https://doi.org/10.1016/j.psyneuen.2018.05.038

Heinz, A., Goldman, D., Jones, D. W., Palmour, R., Hommer, D., Gorey, J. G., Lee, K. S., Linnoila, M., & Weinberger, D. R. (2000). Genotype Influences In Vivo Dopamine Transporter Availability in Human Striatum. *Neuropsychopharmacology*, *22*(2), 133–139. https://doi.org/10.1016/S0893-133X(99)00099-8

Hermans, E. J., Bos, P. A., Ossewaarde, L., Ramsey, N. F., Fernández, G., & van Honk, J. (2010). Effects of exogenous testosterone on the ventral striatal BOLD response during reward

anticipation in healthy women. *NeuroImage*, *52*(1), 277–283. https://doi.org/10.1016/j.neuroimage.2010.04.019
Hermans, E. J., Putman, P., Baas, J. M., Koppeschaar, H. P., & van Honk, J. (2006). A single administration of testosterone reduces fear-potentiated startle in humans. *Biological Psychiatry*, *59*(9), 872–874. https://doi.org/10.1016/j.biopsych.2005.11.015
Hermans, E. J., Ramsey, N. F., & van Honk, J. (2008). Exogenous testosterone enhances responsiveness to social threat in the neural circuitry of social aggression in humans. *Biological Psychiatry*, *63*(3), 263–270. https://doi.org/10.1016/j.biopsych.2007.05.013
Higham, J. P., Heistermann, M., & Maestripieri, D. (2013). The endocrinology of male rhesus macaque social and reproductive status: A test of the challenge and social stress hypotheses. *Behavioral Ecology and Sociobiology*, *67*(1), 19–30. https://doi.org/10.1007/s00265-012-1420-6
Hirschenhauser, K., & Oliveira, R. F. (2006). Social modulation of androgens in male vertebrates: Meta-analyses of the challenge hypothesis. *Animal Behaviour*, *71*(2), 265–277. https://doi.org/10.1016/j.anbehav.2005.04.014
Igarashi, S., Tanno, Y., Onodera, O., Yamazaki, M., Sato, S., Ishikawa, A., Miyatani, N., Nagashima, M., Ishikawa, Y., & Sahashi, K. (1992). Strong correlation between the number of CAG repeats in androgen receptor genes and the clinical onset of features of spinal and bulbar muscular atrophy. *Neurology*, *42*(12), 2300–2302. https://doi.org/10.1212/wnl.42.12.2300
Ishikawa, T., Glidewell-Kenney, C., & Jameson, J. L. (2006). Aromatase-independent testosterone conversion into estrogenic steroids is inhibited by a 5 alpha-reductase inhibitor. *The Journal of Steroid Biochemistry and Molecular Biology*, *98*(2–3), 133–138. https://doi.org/10.1016/j.jsbmb.2005.09.004
Ito, H., Takahashi, H., Arakawa, R., Takano, H., & Suhara, T. (2008). Normal database of dopaminergic neurotransmission system in human brain measured by positron emission tomography. *NeuroImage*, *39*(2), 555–565. https://doi.org/10.1016/j.neuroimage.2007.09.011
Janvier, P. (2007). Living Primitive Fishes and Fishes From Deep Time. In *Fish Physiology* (Vol. 26, pp. 1–51). Academic Press. https://doi.org/10.1016/S1546-5098(07)26001-7
John-Alder, H. B., & Cox, R. M. (2007). 195Development of sexual size dimorphism in lizards: Testosterone as a bipotential growth regulator. In *Sex, Size and Gender Roles: Evolutionary Studies of Sexual Size Dimorphism*. Oxford University Press. https://doi.org/10.1093/acprof:oso/9780199208784.003.0022
Johnson, L. R., & Wood, R. I. (2001). Oral testosterone self-administration in male hamsters. *Neuroendocrinology*, *73*(4), 285–292. https://doi.org/10.1159/000054645
Johnson, M. A., Kircher, B. K., & Castro, D. J. (2018). The evolution of androgen receptor expression and behavior in Anolis lizard forelimb muscles. *Journal of Comparative Physiology A*, *204*(1), 71–79. https://doi.org/10.1007/s00359-017-1228-y
Jönsson, E. G., Nöthen, M. M., Grünhage, F., Farde, L., Nakashima, Y., Propping, P., & Sedvall, G. C. (1999). Polymorphisms in the dopamine D2 receptor gene and their relationships to striatal dopamine receptor density of healthy volunteers. *Molecular Psychiatry*, *4*(3), Article 3. https://doi.org/10.1038/sj.mp.4000532
Josephs, R. A., Newman, M. L., Brown, R. P., & Beer, J. M. (2003). Status, testosterone, and human intellectual performance: Stereotype threat as status concern. *Psychological Science*, *14*(2), 158–163. https://doi.org/10.1111/1467-9280.t01-1-01435
Käenmäki, M., Tammimäki, A., Myöhänen, T., Pakarinen, K., Amberg, C., Karayiorgou, M., Gogos, J. A., & Männistö, P. T. (2010). Quantitative role of COMT in dopamine clearance in the prefrontal cortex of freely moving mice. *Journal of Neurochemistry*, *114*(6), 1745–1755. https://doi.org/10.1111/j.1471-4159.2010.06889.x
Kahneman, D. (2011). *Thinking, fast and slow* (p. 499). Farrar, Straus and Giroux.
Kaldewaij, R., Koch, S. B. J., Zhang, W., Hashemi, M. M., Klumpers, F., & Roelofs, K. (2019). High Endogenous Testosterone Levels Are Associated With Diminished Neural Emotional Control in Aggressive Police Recruits. *Psychological Science*, *30*(8), 1161–1173. https://doi.org/10.1177/0956797619851753

Ketterson, E. D., & Nolan, V. (1992). Hormones and life histories: An integrative approach. *The American Naturalist*, *140 Suppl 1*, S33-62. https://doi.org/10.1086/285396

Klebe, S., Golmard, J.-L., Nalls, M. A., Saad, M., Singleton, A. B., Bras, J. M., Hardy, J., Simon-Sanchez, J., Heutink, P., Kuhlenbäumer, G., Charfi, R., Klein, C., Hagenah, J., Gasser, T., Wurster, I., Lesage, S., Lorenz, D., Deuschl, G., Durif, F., … Corvol, J.-C. (2013). The Val158Met COMT polymorphism is a modifier of the age at onset in Parkinson's disease with a sexual dimorphism. *Journal of Neurology, Neurosurgery, and Psychiatry*, *84*(6), 666–673. https://doi.org/10.1136/jnnp-2012-304475

Knight, E. L., Christian, C. B., Morales, P. J., Harbaugh, W. T., Mayr, U., & Mehta, P. H. (2017a). Exogenous testosterone enhances cortisol and affective responses to social-evaluative stress in dominant men. *Psychoneuroendocrinology*, *85*, 151–157. https://doi.org/10.1016/j.psyneuen.2017.08.014

Knight, E. L., Christian, C. B., Morales, P. J., Harbaugh, W. T., Mayr, U., & Mehta, P. H. (2017b). Exogenous testosterone enhances cortisol and affective responses to social-evaluative stress in dominant men. *Psychoneuroendocrinology*, *85*, 151–157. https://doi.org/10.1016/j.psyneuen.2017.08.014

Kool, W., Cushman, F. A., & Gershman, S. J. (2016). When Does Model-Based Control Pay Off? *PLOS Computational Biology*, *12*(8), e1005090. https://doi.org/10.1371/journal.pcbi.1005090

Kwak, S., Huh, N., Seo, J.-S., Lee, J.-E., Han, P.-L., & Jung, M. W. (2014). Role of dopamine D2 receptors in optimizing choice strategy in a dynamic and uncertain environment. *Frontiers in Behavioral Neuroscience*, *8*. https://www.frontiersin.org/articles/10.3389/fnbeh.2014.00368

La Spada, A. R., Wilson, E. M., Lubahn, D. B., Harding, A. E., & Fischbeck, K. H. (1991). Androgen receptor gene mutations in X-linked spinal and bulbar muscular atrophy. *Nature*, *352*(6330), 77–79. https://doi.org/10.1038/352077a0

Lakshman, K. M., Kaplan, B., Travison, T. G., Basaria, S., Knapp, P. E., Singh, A. B., LaValley, M. P., Mazer, N. A., & Bhasin, S. (2010). The Effects of Injected Testosterone Dose and Age on the Conversion of Testosterone to Estradiol and Dihydrotestosterone in Young and Older Men. *The Journal of Clinical Endocrinology and Metabolism*, *95*(8), 3955–3964. https://doi.org/10.1210/jc.2010-0102

Landys, M. M., Goymann, W., Raess, M., & Slagsvold, T. (2007). Hormonal responses to male-male social challenge in the blue tit Cyanistes caeruleus: Single-broodedness as an explanatory variable. *Physiological and Biochemical Zoology: PBZ*, *80*(2), 228–240. https://doi.org/10.1086/510564

Lee, E., Seo, M., Dal Monte, O., & Averbeck, B. B. (2015). Injection of a Dopamine Type 2 Receptor Antagonist into the Dorsal Striatum Disrupts Choices Driven by Previous Outcomes, But Not Perceptual Inference. *The Journal of Neuroscience*, *35*(16), 6298–6306. https://doi.org/10.1523/JNEUROSCI.4561-14.2015

Lieberman, A. P., Harmison, G., Strand, A. D., Olson, J. M., & Fischbeck, K. H. (2002). Altered transcriptional regulation in cells expressing the expanded polyglutamine androgen receptor. *Human Molecular Genetics*, *11*(17), 1967–1976. https://doi.org/10.1093/hmg/11.17.1967

Litwack, G. (2022). Chapter 12—Androgens. In G. Litwack (Ed.), *Hormones (Fourth Edition)* (pp. 287–311). Academic Press. https://doi.org/10.1016/B978-0-323-90262-5.00004-4

Lombardo, M. V., Ashwin, E., Auyeung, B., Chakrabarti, B., Taylor, K., Hackett, G., Bullmore, E. T., & Baron-Cohen, S. (2012). Fetal Testosterone Influences Sexually Dimorphic Gray Matter in the Human Brain. *The Journal of Neuroscience*, *32*(2), 674–680. https://doi.org/10.1523/JNEUROSCI.4389-11.2012

Losecaat Vermeer, A. B., Krol, I., Gausterer, C., Wagner, B., Eisenegger, C., & Lamm, C. (2020). Exogenous testosterone increases status-seeking motivation in men with unstable low social status. *Psychoneuroendocrinology*, *113*, 104552. https://doi.org/10.1016/j.psyneuen.2019.104552

Luberti, F. R., Reside, T.-L., Bonin, P. L., & Carré, J. M. (2021). Development of a single-dose intranasal testosterone administration paradigm for use in men and women. *Hormones and Behavior*, *136*, 105046. https://doi.org/10.1016/j.yhbeh.2021.105046

Mariotti, C., Castellotti, B., Pareyson, D., Testa, D., Eoli, M., Antozzi, C., Silani, V., Marconi, R., Tezzon, F., Siciliano, G., Marchini, C., Gellera, C., & Donato, S. D. (2000). Phenotypic manifestations associated with CAG-repeat expansion in the androgen receptor gene in male patients and heterozygous females: A clinical and molecular study of 30 families. *Neuromuscular Disorders: NMD*, *10*(6), 391–397. https://doi.org/10.1016/s0960-8966(99)00132-7

Markov, G. V., Gutierrez-Mazariegos, J., Pitrat, D., Billas, I. M. L., Bonneton, F., Moras, D., Hasserodt, J., Lecointre, G., & Laudet, V. (2017). Origin of an ancient hormone/receptor couple revealed by resurrection of an ancestral estrogen. *Science Advances*, *3*(3), e1601778. https://doi.org/10.1126/sciadv.1601778

Markov, G. V., Tavares, R., Dauphin-Villemant, C., Demeneix, B. A., Baker, M. E., & Laudet, V. (2009). Independent elaboration of steroid hormone signaling pathways in metazoans. *Proceedings of the National Academy of Sciences*, *106*(29), 11913–11918. https://doi.org/10.1073/pnas.0812138106

Marler, C. A., & Moore, M. C. (1988). Evolutionary costs of aggression revealed by testosterone manipulations in free-living male lizards. *Behavioral Ecology and Sociobiology*, *23*(1), 21–26. https://doi.org/10.1007/BF00303053

Martinez, D., Orlowska, D., Narendran, R., Slifstein, M., Liu, F., Kumar, D., Broft, A., Van Heertum, R., & Kleber, H. D. (2010). D2/3 receptor availability in the striatum and social status in human volunteers. *Biological Psychiatry*, *67*(3), 275–278. https://doi.org/10.1016/j.biopsych.2009.07.037

Mazur, A. (1985). A biosocial model of status in face-to-face primate groups. *Social Forces*, *64*, 377–402. https://doi.org/10.2307/2578647

Mazur, A. (2005). *Biosociology of Dominance and Deference*. Rowman & Littlefield Publishers.

Mazur, A. (2017). Testosterone in biosociology: A memoir. *Hormones and Behavior*, *92*, 3–8. https://doi.org/10.1016/j.yhbeh.2015.12.004

Mazur, A., & Booth, A. (1998). Testosterone and dominance in men. *The Behavioral and Brain Sciences*, *21*(3), 353–363; discussion 363-397.

McDonald, P. G., Buttemer, W. A., & Astheimer, L. B. (2001). The influence of testosterone on territorial defence and parental behavior in male free-living rufous whistlers, Pachycephala rufiventris. *Hormones and Behavior*, *39*(3), 185–194. https://doi.org/10.1006/hbeh.2001.1644

McEwen, B. S. (1992). Steroid hormones: Effect on brain development and function. *Hormone Research*, *37 Suppl 3*, 1–10. https://doi.org/10.1159/000182393

McLeod, H. L., Syvänen, A. C., Githang'a, J., Indalo, A., Ismail, D., Dewar, K., Ulmanen, I., & Sludden, J. (1998). Ethnic differences in catechol O-methyltransferase pharmacogenetics: Frequency of the codon 108/158 low activity allele is lower in Kenyan than Caucasian or South-west Asian individuals. *Pharmacogenetics*, *8*(3), 195–199.

Mehta, P. H., & Beer, J. (2010). Neural Mechanisms of the Testosterone–Aggression Relation: The Role of Orbitofrontal Cortex. *Journal of Cognitive Neuroscience*, *22*(10), 2357–2368. https://doi.org/10.1162/jocn.2009.21389

Mendonça-Furtado, O., Edaes, M., Palme, R., Rodrigues, A., Siqueira, J., & Izar, P. (2014). Does hierarchy stability influence testosterone and cortisol levels of bearded capuchin monkeys (Sapajus libidinosus) adult males? A comparison between two wild groups. *Behavioural Processes*, *109 Pt A*, 79–88. https://doi.org/10.1016/j.beproc.2014.09.010

Michels, G., & Hoppe, U. C. (2008). Rapid actions of androgens. *Frontiers in Neuroendocrinology*, *29*(2), 182–198. https://doi.org/10.1016/j.yfrne.2007.08.004

Mikus, N., Korb, S., Massaccesi, C., Gausterer, C., Graf, I., Willeit, M., Eisenegger, C., Lamm, C., Silani, G., & Mathys, C. (2022). *Effects of dopamine D2 and opioid receptor antagonism on the trade-off between model-based and model-free behavior in healthy volunteers* (p. 2022.03.03.482871). bioRxiv. https://doi.org/10.1101/2022.03.03.482871

Moore, I. T., Hernandez, J., & Goymann, W. (2020). Who rises to the challenge? Testing the Challenge Hypothesis in fish, amphibians, reptiles, and mammals. *Hormones and Behavior*, *123*, 104537. https://doi.org/10.1016/j.yhbeh.2019.06.001

Morgan, D., Grant, K. A., Gage, H. D., Mach, R. H., Kaplan, J. R., Prioleau, O., Nader, S. H., Buchheimer, N., Ehrenkaufer, R. L., & Nader, M. A. (2002). Social dominance in

monkeys: Dopamine D2 receptors and cocaine self-administration. *Nature Neuroscience*, *5*(2), 169–174. https://doi.org/10.1038/nn798
Muehlenbein, M. P., & Watts, D. P. (2010). The costs of dominance: Testosterone, cortisol and intestinal parasites in wild male chimpanzees. *Biopsychosocial Medicine*, *4*, 21. https://doi.org/10.1186/1751-0759-4-21
Muller, M. N. (2017). Testosterone and reproductive effort in male primates. *Hormones and Behavior*, *91*, 36–51. https://doi.org/10.1016/j.yhbeh.2016.09.001
Nader, M. A., Nader, S. H., Czoty, P. W., Riddick, N. V., Gage, H. D., Gould, R. W., Blaylock, B. L., Kaplan, J. R., Garg, P. K., Davies, H. M., Morton, D., Garg, S., & Reboussin, B. A. (2012). SOCIAL DOMINANCE IN FEMALE MONKEYS: DOPAMINE RECEPTOR FUNCTION AND COCAINE REINFORCEMENT. *Biological Psychiatry*, *72*(5), 414–421. https://doi.org/10.1016/j.biopsych.2012.03.002
Naessén, S., Söderqvist, G., & Carlström, K. (2019). So similar and so different: Circulating androgens and androgen origin in bulimic women. *The Journal of Steroid Biochemistry and Molecular Biology*, *185*, 184–188. https://doi.org/10.1016/j.jsbmb.2018.08.013
Nathan, L., Shi, W., Dinh, H., Mukherjee, T. K., Wang, X., Lusis, A. J., & Chaudhuri, G. (2001). Testosterone inhibits early atherogenesis by conversion to estradiol: Critical role of aromatase. *Proceedings of the National Academy of Sciences*, *98*(6), 3589–3593. https://doi.org/10.1073/pnas.051003698
Nave, G., Nadler, A., Zava, D., & Camerer, C. (2017). Single-Dose Testosterone Administration Impairs Cognitive Reflection in Men. *Psychological Science*, *28*(10), 1398–1407. https://doi.org/10.1177/0956797617709592
Newman, M. L., Sellers, J. G., & Josephs, R. A. (2005). Testosterone, cognition, and social status. *Hormones and Behavior*, *47*(2), 205–211. https://doi.org/10.1016/j.yhbeh.2004.09.008
Nieschlag, E., & Behre, H. M. (Eds.). (1998). *Testosterone*. Springer. https://doi.org/10.1007/978-3-642-72185-4
Noble, E. P. (1998). The D2 Dopamine Receptor Gene: A Review of Association Studies in Alcoholism and Phenotypes. *Alcohol*, *16*(1), 33–45. https://doi.org/10.1016/S0741-8329(97)00175-4
Ogino, Y., Katoh, H., Kuraku, S., & Yamada, G. (2009). Evolutionary History and Functional Characterization of Androgen Receptor Genes in Jawed Vertebrates. *Endocrinology*, *150*(12), 5415–5427. https://doi.org/10.1210/en.2009-0523
Ogino, Y., Yamada, G., & Iguchi, T. (2018). Diversified Sex Characteristics Developments in Teleost Fishes: Implication for Evolution of Androgen Receptor (AR) Gene Function. In H. Hirata & A. Iida (Eds.), *Zebrafish, Medaka, and Other Small Fishes: New Model Animals in Biology, Medicine, and Beyond* (pp. 113–126). Springer. https://doi.org/10.1007/978-981-13-1879-5_7
Op de Macks, Z. A., Moor, B. G., Overgaauw, S., Güroğlu, B., Dahl, R. E., & Crone, E. A. (2011). Testosterone levels correspond with increased ventral striatum activation in response to monetary rewards in adolescents. *Developmental Cognitive Neuroscience*, *1*(4), 506–516. https://doi.org/10.1016/j.dcn.2011.06.003
Packard, M. G., Schroeder, J. P., & Alexander, G. M. (1998). Expression of Testosterone Conditioned Place Preference Is Blocked by Peripheral or Intra-accumbens Injection of α-Flupenthixol. *Hormones and Behavior*, *34*(1), 39–47. https://doi.org/10.1006/hbeh.1998.1461
Peters, M., Simmons, L. W., & Rhodes, G. (2008). Testosterone is associated with mating success but not attractiveness or masculinity in human males. *Animal Behaviour*, *76*(2), 297–303. https://doi.org/10.1016/j.anbehav.2008.02.008
Peters, S., Jolles, D. J., Duijvenvoorde, A. C. K. V., Crone, E. A., & Peper, J. S. (2015). The link between testosterone and amygdala–orbitofrontal cortex connectivity in adolescent alcohol use. *Psychoneuroendocrinology*, *53*, 117–126. https://doi.org/10.1016/j.psyneuen.2015.01.004
Pinxten, R., de Ridder, E., & Eens, M. (2003). Female presence affects male behavior and testosterone levels in the European starling (Sturnus vulgaris). *Hormones and Behavior*, *44*(2), 103–109. https://doi.org/10.1016/s0018-506x(03)00120-x

Pittman, Q. J., Lawrance, D., & McLean, L. (1982). Central effects of argininge vasipressin on blood pressure in rats. *Endocrinology*, *110*(3), 1058–1060. https://doi.org/10.1210/endo-110-3-1058

Purves-Tyson, T. D., Owens, S. J., Double, K. L., Desai, R., Handelsman, D. J., & Weickert, C. S. (2014). Testosterone Induces Molecular Changes in Dopamine Signaling Pathway Molecules in the Adolescent Male Rat Nigrostriatal Pathway. *PLoS ONE*, *9*(3), e91151. https://doi.org/10.1371/journal.pone.0091151

Ratcliff, R., & McKoon, G. (2008). The Diffusion Decision Model: Theory and Data for Two-Choice Decision Tasks. *Neural Computation*, *20*(4), 873–922. https://doi.org/10.1162/neco.2008.12-06-420

Rausch, J., Gäbel, A., Nagy, K., Kleindienst, N., Herpertz, S. C., & Bertsch, K. (2015). Increased testosterone levels and cortisol awakening responses in patients with borderline personality disorder: Gender and trait aggressiveness matter. *Psychoneuroendocrinology*, *55*, 116–127. https://doi.org/10.1016/j.psyneuen.2015.02.002

Robbins, T. W., & Everitt, B. J. (1996). Neurobehavioural mechanisms of reward and motivation. *Current Opinion in Neurobiology*, *6*(2), 228–236. https://doi.org/10.1016/s0959-4388(96)80077-8

Roney, J. R. (2016). Theoretical frameworks for human behavioral endocrinology. *Hormones and Behavior*, *84*, 97–110. https://doi.org/10.1016/j.yhbeh.2016.06.004

Rubinow, D. R., Roca, C. A., Schmidt, P. J., Danaceau, M. A., Putnam, K., Cizza, G., Chrousos, G., & Nieman, L. (2005). Testosterone Suppression of CRH-Stimulated Cortisol in Men. *Neuropsychopharmacology*, *30*(10), Article 10. https://doi.org/10.1038/sj.npp.1300742

Ruzicka, L., & Wettstein, A. (1935). Sexualhormone VII. Über die künstliche Herstellung des Testikelhormons Testosteron (Androsten-3-on-17-ol). *Helvetica Chimica Acta*, *18*(1), 1264–1275. https://doi.org/10.1002/hlca.193501801176

Sapolsky, R. M. (2017). Behave: The biology of humans at our best and worst. In *Behave: The biology of humans at our best and worst*. Penguin Press, an imprint of Penguin Random House LLC.

Satterfield, B. C., Hinson, J. M., Whitney, P., Schmidt, M. A., Wisor, J. P., & Van Dongen, H. P. A. (2018). Catechol-O-methyltransferase (COMT) genotype affects cognitive control during total sleep deprivation. *Cortex*, *99*, 179–186. https://doi.org/10.1016/j.cortex.2017.11.012

Schroeder, J. P., & Packard, M. G. (2000). Role of dopamine receptor subtypes in the acquisition of a testosterone conditioned place preference in rats. *Neuroscience Letters*, *282*(1), 17–20. https://doi.org/10.1016/S0304-3940(00)00839-9

Schuppe, E. R., Miles, M. C., & Fuxjager, M. J. (2020). Evolution of the androgen receptor: Perspectives from human health to dancing birds. *Molecular and Cellular Endocrinology*, *499*, 110577. https://doi.org/10.1016/j.mce.2019.110577

Simoncini, T., & Genazzani, A. R. (2003). Non-genomic actions of sex steroid hormones. *European Journal of Endocrinology*, *148*(3), 281–292. https://doi.org/10.1530/eje.0.1480281

Sockman, K. W., Weiss, J., Webster, M. S., Talbott, V., & Schwabl, H. (2008). Sex-specific effects of yolk-androgens on growth of nestling American kestrels. *Behavioral Ecology and Sociobiology*, *62*(4), 617–625. https://doi.org/10.1007/s00265-007-0486-z

Soto-Gamboa, M., Villalón, M., & Bozinovic, F. (2005). Social cues and hormone levels in male Octodon degus (Rodentia): A field test of the Challenge Hypothesis. *Hormones and Behavior*, *47*(3), 311–318. https://doi.org/10.1016/j.yhbeh.2004.11.010

Soutschek, A., & Tobler, P. N. (2023). A process model account of the role of dopamine in intertemporal choice. *ELife*, *12*, e83734. https://doi.org/10.7554/eLife.83734

Spielberg, J. M., Forbes, E. E., Ladouceur, C. D., Worthman, C. M., Olino, T. M., Ryan, N. D., & Dahl, R. E. (2015). Pubertal testosterone influences threat-related amygdala–orbitofrontal cortex coupling. *Social Cognitive and Affective Neuroscience*, *10*(3), 408–415. https://doi.org/10.1093/scan/nsu062

Stephens, M. A. C., Mahon, P. B., McCaul, M. E., & Wand, G. S. (2016). Hypothalamic–pituitary–adrenal axis response to acute psychosocial stress: Effects of biological sex and

circulating sex hormones. *Psychoneuroendocrinology*, *66*, 47–55. https://doi.org/10.1016/j.psyneuen.2015.12.021
Sutton, R. S., & Barto, A. G. (2018). *Reinforcement Learning, second edition: An Introduction*. MIT Press.
Szot, P., & Dorsa, D. M. (1994). Expression of cytoplasmic and nuclear vasopressin RNA following castration and testosterone replacement: Evidence for transcriptional regulation. *Molecular and Cellular Neurosciences*, *5*(1), 1–10. https://doi.org/10.1006/mcne.1994.1001
Taylor, C. J. (2014). Physiological stress response to loss of social influence and threats to masculinity. *Social Science & Medicine (1982)*, *103*, 51–59. https://doi.org/10.1016/j.socscimed.2013.07.036
Terburg, D., Aarts, H., & van Honk, J. (2012). Testosterone Affects Gaze Aversion From Angry Faces Outside of Conscious Awareness. *Psychological Science*, *23*(5), 459–463. https://doi.org/10.1177/0956797611433336
Terburg, D., Syal, S., Rosenberger, L. A., Heany, S. J., Stein, D. J., & Honk, J. van. (2016). Testosterone abolishes implicit subordination in social anxiety. *Psychoneuroendocrinology*, *72*, 205–211. https://doi.org/10.1016/j.psyneuen.2016.07.203
Terburg, D., & van Honk, J. (2013). Approach–Avoidance versus Dominance–Submissiveness: A Multilevel Neural Framework on How Testosterone Promotes Social Status. *Emotion Review*, *5*(3), 296–302. https://doi.org/10.1177/1754073913477510
Thomas, P. (2019). Membrane Androgen Receptors Unrelated to Nuclear Steroid Receptors. *Endocrinology*, *160*(4), 772–781. https://doi.org/10.1210/en.2018-00987
Thompson, J., Thomas, N., Singleton, A., Piggott, M., Lloyd, S., Perry, E. K., Morris, C. M., Perry, R. H., Ferrier, I. N., & Court, J. A. (1997). D2 dopamine receptor gene (DRD2) Taq1 A polymorphism: Reduced dopamine D2 receptor binding in the human striatum associated with the A1 allele. *Pharmacogenetics*, *7*(6), 479–484. https://doi.org/10.1097/00008571-199712000-00006
Thornton, J. W. (2001). Evolution of vertebrate steroid receptors from an ancestral estrogen receptor by ligand exploitation and serial genome expansions. *Proceedings of the National Academy of Sciences*, *98*(10), 5671–5676. https://doi.org/10.1073/pnas.091553298
Tinbergen, N. (1963). On aims and methods of Ethology. *Zeitschrift Für Tierpsychologie*, *20*(4), 410–433. https://doi.org/10.1111/j.1439-0310.1963.tb01161.x
Tobiansky, D. J., Wallin-Miller, K. G., Floresco, S. B., Wood, R. I., & Soma, K. K. (2018). Androgen Regulation of the Mesocorticolimbic System and Executive Function. *Frontiers in Endocrinology*, *9*, 279. https://doi.org/10.3389/fendo.2018.00279
Torre, S. D., Benedusi, V., Fontana, R., & Maggi, A. (2014). Energy metabolism and fertility—A balance preserved for female health. *Nature Reviews Endocrinology*, *10*(1), 13–23. https://doi.org/10.1038/nrendo.2013.203
Toufexis, D., Rivarola, M. A., Lara, H., & Viau, V. (2014). Stress and the Reproductive Axis. *Journal of Neuroendocrinology*, *26*(9), 573–586. https://doi.org/10.1111/jne.12179
Trainor, B. C., & Marler, C. A. (2001). Testosterone, paternal behavior, and aggression in the monogamous California mouse (Peromyscus californicus). *Hormones and Behavior*, *40*(1), 32–42. https://doi.org/10.1006/hbeh.2001.1652
Turan, B., Tackett, J. L., Lechtreck, M. T., & Browning, W. R. (2015). Coordination of the cortisol and testosterone responses: A dual axis approach to understanding the response to social status threats. *Psychoneuroendocrinology*, *62*, 59–68. https://doi.org/10.1016/j.psyneuen.2015.07.166
van Honk, J., Montoya, E. R., Bos, P. A., van Vugt, M., & Terburg, D. (2012). New evidence on testosterone and cooperation. *Nature*, *485*(7399), E4–E5. https://doi.org/10.1038/nature11136
van Honk, J., Peper, J. S., & Schutter, D. J. L. G. (2005). Testosterone reduces unconscious fear but not consciously experienced anxiety: Implications for the disorders of fear and anxiety. *Biological Psychiatry*, *58*(3), 218–225. https://doi.org/10.1016/j.biopsych.2005.04.003
van Wingen, G. A., Zylicz, S. A., Pieters, S., Mattern, C., Verkes, R. J., Buitelaar, J. K., & Fernández, G. (2009). Testosterone Increases Amygdala Reactivity in Middle-Aged

Women to a Young Adulthood Level. *Neuropsychopharmacology*, *34*(3), Article 3. https://doi.org/10.1038/npp.2008.2
van Wingen, G., Mattern, C., Verkes, R. J., Buitelaar, J., & Fernández, G. (2010). Testosterone reduces amygdala–orbitofrontal cortex coupling. *Psychoneuroendocrinology*, *35*(1), 105–113. https://doi.org/10.1016/j.psyneuen.2009.09.007
Vandenbergh, D. J., Persico, A. M., Hawkins, A. L., Griffin, C. A., Li, X., Jabs, E. W., & Uhl, G. R. (1992). Human dopamine transporter gene (DAT1) maps to chromosome 5p15.3 and displays a VNTR. *Genomics*, *14*(4), 1104–1106. https://doi.org/10.1016/s0888-7543(05)80138-7
Viau, V., & Meaney, M. J. (2004). Testosterone-dependent variations in plasma and intrapituitary corticosteroid binding globulin and stress hypothalamic-pituitary-adrenal activity in the male rat. *Journal of Endocrinology*, *181*(2), 223–231. https://doi.org/10.1677/joe.0.1810223
Villavicencio, C. P., Apfelbeck, B., & Goymann, W. (2013). Experimental induction of social instability during early breeding does not alter testosterone levels in male black redstarts, a socially monogamous songbird. *Hormones and Behavior*, *64*(3), 461–467. https://doi.org/10.1016/j.yhbeh.2013.08.005
Volman, I., von Borries, A. K. L., Bulten, B. H., Verkes, R. J., Toni, I., & Roelofs, K. (2016). Testosterone Modulates Altered Prefrontal Control of Emotional Actions in Psychopathic Offenders. *ENeuro*, *3*(1), ENEURO.0107-15.2016. https://doi.org/10.1523/ENEURO.0107-15.2016
Welling, L. L. M., Moreau, B. J. P., Bird, B. M., Hansen, S., & Carré, J. M. (2016). Exogenous testosterone increases men's perceptions of their own physical dominance. *Psychoneuroendocrinology*, *64*, 136–142. https://doi.org/10.1016/j.psyneuen.2015.11.016
Wingfield, J. C. (1994). Regulation of Territorial Behavior in the Sedentary Song Sparrow, Melospiza melodia morphna. *Hormones and Behavior*, *28*(1), 1–15. https://doi.org/10.1006/hbeh.1994.1001
Wingfield, J. C., & Farner, D. S. (1978). The Endocrinology of a Natural Breeding Population of the White-Crowned Sparrow (Zonotrichia leucophrys pugetensis). *Physiological Zoology*, *51*(2), 188–205. https://www.jstor.org/stable/30157866
Wingfield, J. C., Hegner, R. E., Dufty, A. M., & Ball, G. F. (1990). The "Challenge Hypothesis": Theoretical Implications for Patterns of Testosterone Secretion, Mating Systems, and Breeding Strategies. *The American Naturalist*, *136*(6), 829–846. https://www.jstor.org/stable/2462170
Wingfield, J. C., Ramenofsky, M., Hegner, R. E., & Ball, G. F. (2020). Whither the challenge hypothesis? *Hormones and Behavior*, *123*, 104588. https://doi.org/10.1016/j.yhbeh.2019.104588
Wu, Y., Ou, J., Wang, X., Zilioli, S., Tobler, P. N., & Li, Y. (2022). Exogeneous testosterone increases sexual impulsivity in heterosexual men. *Psychoneuroendocrinology*, *145*, 105914. https://doi.org/10.1016/j.psyneuen.2022.105914
Wu, Y., Shen, B., Liao, J., Li, Y., Zilioli, S., & Li, H. (2020). Single dose testosterone administration increases impulsivity in the intertemporal choice task among healthy males. *Hormones and Behavior*, *118*, 104634. https://doi.org/10.1016/j.yhbeh.2019.104634
Xie, Z., Maddox, W. T., McGeary, J. E., & Chandrasekaran, B. (2015). The C957T polymorphism in the dopamine receptor D2 gene modulates domain-general category learning. *Journal of Neurophysiology*, *113*(9), 3281–3290. https://doi.org/10.1152/jn.01005.2014
Zak, P. J., Kurzban, R., Ahmadi, S., Swerdloff, R. S., Park, J., Efremidze, L., Redwine, K., Morgan, K., & Matzner, W. (2009). Testosterone Administration Decreases Generosity in the Ultimatum Game. *PLOS ONE*, *4*(12), e8330. https://doi.org/10.1371/journal.pone.0008330
Zhang, X., Hense, H.-W., Riegger, G. A. J., & Schunkert, H. (1999). Association of arginine vasopressin and arterial blood pressure in a population-based sample. *Journal of Hypertension*, *17*(3), 319. https://journals.lww.com/jhypertension/Abstract/1999/17030/Association_of_arginine_vasopressin_and_arterial.3.aspx

Zhao, X., Fuxjager, M. J., McLamore, Q., & Marler, C. A. (2019). Rapid effects of testosterone on social decision-making in a monogamous California mice (Peromyscus californicus). *Hormones and Behavior*, *115*, 104544. https://doi.org/10.1016/j.yhbeh.2019.06.008

Zhao, X., & Marler, C. A. (2016). Social and physical environments as a source of individual variation in the rewarding effects of testosterone in male California mice (Peromyscus californicus). *Hormones and Behavior*, *85*, 30–35. https://doi.org/10.1016/j.yhbeh.2016.07.007

Zirkin, B. R., & Chen, H. (2000). Regulation of Leydig Cell Steroidogenic Function During Aging1. *Biology of Reproduction*, *63*(4), 977–981. https://doi.org/10.1095/biolreprod63.4.977

Zitzmann, M., & Nieschlag, E. (2003). The CAG repeat polymorphism within the androgen receptor gene and maleness1. *International Journal of Andrology*, *26*(2), 76–83. https://doi.org/10.1046/j.1365-2605.2003.00393.x

ANNEXES

Abstract

While the steroid hormone testosterone has been traditionally associated with male aggression, recent research indicates that it influences a larger variety of behaviors that may be better understood in terms of social status-seeking. The present dissertation reports five placebo-controlled testosterone-administration studies aimed at advancing our understanding of the role of testosterone in male human behavior and uncovering the psychological and physiological mechanisms through which testosterone exerts its effects. Study 1 investigated whether testosterone's effect on physiological stress responses depends on the social context. We found that testosterone enhanced sympathetic arousal when an individual faced a biological stressor while dampened such arousal when the biological stressor was embedded in a social evaluative context. Study 2 tested whether testosterone promotes dominant or reputational status-seeking strategies. Here, testosterone administration abolished strategic prosociality present in the placebo group. Reinforcement-learning drift-diffusion modeling revealed that the hormone diminishes reputational strategies by impacting choice consistency, i.e., the degree to which participants' choices align with the learned reward values. Study 3 examined if testosterone promotes competitive persistence depending on perceived personal control. The results show that testosterone disrupts the link between perceived control and competition persistence, making individuals with low control persist for as long as those with high perceived control. Studies 4 and 5 investigated whether testosterone biases cognitive functions away from deliberate processes toward reflexive ones. Both studies show that the effects of testosterone on deliberate cognitive processes are weak and highly variable. Study 5 provides initial evidence that such a variance is associated with the VNTR polymorphism of the dopamine transporter gene DAT1. Together, this dissertation highlights the diversity and flexibility of testosterone's effects on social behaviors and cognitive functions. It demonstrates that the social context crucially interacts with testosterone to shape physiological responses, strategic prosocial and competitive behavior, as well as associated reward processes. We argue that such variability enables testosterone to promote status-seeking behaviors and adaptively respond to diverse challenges the individuals encounter.

Zuzammenfassung

Das Steroidhormon Testosteron wird traditionell mit männlicher Aggression in Verbindung gebracht, jedoch deutet neuere Forschung daraufhin, dass es eine größere Vielfalt an Verhaltensweisen beeinflusst, die besser im Zusammenhang mit dem Streben nach sozialem Status verstanden werden können. Die vorliegende Dissertation berichtet über fünf placebokontrollierte Testosteron (T) -Verabreichungsstudien, mit dem Ziel unser Verständnis der Rolle von T im männlichen menschlichen Verhalten zu verbessern und die psychologischen und physiologischen Mechanismen aufzudecken, durch die T seine Wirkung entfaltet. Studie 1 untersuchte, ob die Wirkung von T auf physiologische Stressreaktionen vom sozialen Kontext abhängt. Wir fanden heraus, dass T die sympathische Erregung verstärkte, wenn eine Person mit einem biologischen Stressor konfrontiert wurde, während es diese Erregung dämpfte, wenn der biologische Stressor in einen sozialen Evaluierungskontext eingebettet war. Studie 2 untersuchte, ob T dominante oder reputative Statussuchstrategien fördert. Hierbei wurde die strategische Prosozialität, die in der Placebo-Gruppe vorhanden war, durch T-Verabreichung aufgehoben. Ein Verstärkungslernen-Drift-Diffusions-Modell zeigte, dass das Hormon reputative Strategien verringert, indem es die Wahlkonsistenz beeinflusst, d.h. den Grad, in dem die Entscheidungen der Teilnehmer mit den erlernten Belohnungswerten übereinstimmen. Studie 3 untersuchte, ob T wettbewerbsfähige Ausdauer, abhängig von der wahrgenommenen persönlichen Kontrolle, fördert. Die Ergebnisse zeigen, dass T den Zusammenhang zwischen wahrgenommener Kontrolle und Wettbewerbsausdauer unterbricht, Personen mit geringer Kontrolle hielten genauso lange durch wie jene mit hoher wahrgenommener Kontrolle. Studien 4 und 5 untersuchten, ob T kognitive Funktionen von bewussten zu reflexiven Prozessen lenkt. Beide Studien zeigen, dass die Wirkung von T auf bewusste kognitive Prozesse schwach und stark variabel ist. Studie 5 liefert erste Hinweise darauf, dass diese Varianz mit dem VNTR-Polymorphismus des Dopamintransporter-Gens DAT1 zusammenhängt. Zusammenfassend zeigt diese Dissertation die Vielfalt und Flexibilität der Wirkungen von T auf soziale Verhaltensweisen und kognitive Funktionen. Es zeigt, dass der soziale Kontext mit Testosteron interagiert, um physiologische Reaktionen, strategisches Prosozial- und Wettbewerbsverhalten sowie damit verbundene Belohnungsprozesse zu gestalten. Wir argumentieren, dass diese Variabilität es Testosteron ermöglicht, nach Status strebende Verhaltensweisen zu fördern und sich adaptiv an unterschiedliche Herausforderungen anzupassen, denen Individuen begegnen.

CURRICULUM VITAE

HANA HOLLA KUTLIKOVA

EDUCATION

10/2015 – to date **University of Vienna, Austria**
PhD student in Psychology
Supervisors: Prof. Claus Lamm, Christoph Eisenegger, PhD
Thesis:

09/2011 – 02/2014 **University of Geneva, Switzerland**
MSc in Neuroscience
Supervisors: Prof. David Sander, PhD and Prof. Tobias Brosch, PhD
Thesis: Role of the Human Amygdala in Processing of Goal-Relevance: fMRI Study (Grade 6.0/6.0, Overall GPA 5.6/6.0)

09/2008 – 06/2011 **Comenius University in Bratislava, Slovakia**
BSc in Psychology
Thesis title: Developmental Effects of Self-Evaluation on Selectivity of Memory Processes (Dean's Award)

WORK EXPERIENCE

02/2022 – 01/2023 **Utrecht University, the Netherlands**
Department of Experimental Psychology
Visiting researcher

10/2015 – to date **University of Vienna, Austria**
Neuropsychopharmacology & Biopsychology Unit
Doctoral student, lecturer
Neuropsychopharmacology research, teaching

10/2014 – 12/2015 **Slovak Academy of Sciences, Slovakia**
Institute of Normal and Pathological Physiology,
Research assistant
EEG research

06/2014 – 09/2015 **University of Oxford, UK**
Social and Evolutionary Neuroscience Research Group
Long-distance research assistant
Collection of observational data on human social bonding in cooperation with Tamas David-Barrett, PhD

03/2014 – 11/2015 **National Institute for Certified Educational Measurements, Slovakia**
Psychometric statistician for the national and international educational and psychometric assessments (OECD PISA, IEA PIRLS)

01/2013 – 12/2013 Geneva University Hospitals - National Center of Competence in Research SYNAPSY: Synaptic Bases of Mental Diseases, Switzerland
Research assistant and fMRI operator

PUBLICATIONS

Peer-reviewed articles

Murray, R., **Kutlikova, H.H.,** Brosch, T., & Sander, D., (2023). The amygdala and appraised concern-relevance: initial evidence that intrinsic motivation modulates amygdala response to otherwise neutral stimuli. Motivation Science. https://doi.org/10.1037/mot0000293

Kutlikova, H. H., Zhang, L., Eisenegger, C., van Honk, J., & Lamm, C. (2023). Testosterone eliminates strategic prosocial behavior through impacting choice consistency in healthy males. Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology. https://doi.org/10.1038/s41386-023-01570-y

Kutlikova, H. H., Geniole, S. N., Eisenegger, C., Lamm, C., Jocham, G., & Studer, B. (2021). Not giving up: Testosterone promotes persistence against a stronger opponent. *Psychoneuroendocrinology*, *128*. https://doi.org/10.1016/j.psyneuen.2021.105214

Kutlikova, H. H., Durdiaková, J. B., Wagner, B., Vlček, M., Eisenegger, C., Lamm, C., & Riečanský, I. (2020). The effects of testosterone on the physiological response to social and somatic stressors. *Psychoneuroendocrinology*, *117*, 104693. https://doi.org/10.1016/j.psyneuen.2020.104693

Knight, E. L., McShane, B. B., **Kutlikova, H.H.,** … , Eisenegger, C., Lamm, C., Mehta, P. H., & Carré, J. M. (2020). Weak and Variable Effects of Exogenous Testosterone on Cognitive Reflection Test Performance in Three Experiments: Commentary on Nave, Nadler, Zava, and Camerer (2017). *Psychological Science*, *31*(7), 890–897. https://doi.org/10.1177/0956797619885607

Lauring, J. O., Ishizu, T., **Kutlikova, H. H.**, Dörflinger, F., Haugbøl, S., Leder, H., Kupers, R., & Pelowski, M. (2019). Why would Parkinson's disease lead to sudden changes in creativity, motivation, or style with visual art?: A review of case evidence and new neurobiological, contextual, and genetic hypotheses. *Neuroscience & Biobehavioral Reviews*, *100*, 129–165. https://doi.org/10.1016/j.neubiorev.2018.12.016

Moser, D.A., Aue, T., Suardi, F., **Kutlikova, H.**, Cordero, M.I., Rossignol, A.S., Favez, N., Rusconi Serpa, S., & Schechter, D.S. (2015). Violence-related PTSD and neural activation when seeing emotionally charged male-female interactions. *Social Cognitive and Affective Neuroscience*, *10, 5, 645-53.* https://doi.org/10.1093/scan/nsu099

Conference presentations

Kutlikova, H. H., et al. Testosterone across Social Contexts. *The Neurobiological Basis of Human Social Behavior.* Vienna, Austria, June 19, 2022.

Kutlikova, H. H., et al. The effects of testosterone on control perception and persistence. *Hengstberger Symposium on Neurobiological Reward Systems and their Role in Mental Health.* Heidelberg, Germany, May 6-8, 2019.

Kutlikova, H.H., et al. The effect of testosterone on the physiological stress response. *International Society of Psychoneuroendocrinology*, Irvine, CA, USA, September 6-8, 2018.

Kutlikova, H.H., et al. The Effect of Testosterone on the Public and Private Prosociality. *World Meeting of the International Society for Research on Aggression*. Paris, France, July 10 - 14, 2018.

Kutlikova, H. H., et al. Testosterone and biological stress jointly impair analytic cognitive processing. *Symposium on Biology of Decision Making.* Bordeaux. France, May 14-16, 2017.

Kutlikova, H., et al. The amygdala and dorsal striatum detect individual concern-relevance. *Decision Neuroscience in Humans.* Delmenhorst, Germany, June 6 – 8, 2016.

Kutlikova, H., et al. Analysis of the Relationship between Social, Economic and Cultural Status and Achievement in Education. Identifying Gender-Based DIF Items in High Stakes Tests. *Association for Educational Assessment – Europe Conference.* Glasgow, UK, November 5 – 7, 2015.

Kutlikova, H., et al. Identifying Gender-Based DIF Items in High Stakes Tests. *Association for Educational Assessment – Europe Conference*. Tallinn, Estonia, November 6 – 8, 2014.

FELLOWSHIPS AND AWARDS

2022 Marietta Blau Grant OeAD for research stay abroad (18 480€)
2020 – 2021 Action Austria – Slovakia: Science and Education Cooperation (6 300 €)
2015 – 2018 Uni:docs Fellowship for PhD studies, University of Vienna (99 000€)
2012 – 2013 Student Fellowship for excellent results at the University of Geneva
2011 Smart Head Scholarship SPP Foundation
2011 Chance for Talents Grant Orange Foundation
2010 Dean´s award for excellent scientific contribution, Comenius University

PROFESSIONAL MEMBERSHIPS

The International Society for Psychoneuroendocrinology, The American Psychological Association, The International Association for Educational Assessment
Board member of the grants committee at the Vienna Doctoral School for Cognition, Behaviour, and Neuroscience

TEACHING EXPERIENCE

2016 – 2020	Faculty of Psychology, University of Vienna: Special Topics from Cognitive Psychology and Neuroscience, Mind and Brain Seminar, Middle European interdisciplinary master´s program in Cognitive Sciences lecture series
2016 – 2019	Co-supervision of the undergraduate students, Faculty of Psychology, University of Vienna, Austria

LANGUAGE SKILLS

Slovak language	Native proficiency
English language	Full professional proficiency
French language	Professional working proficiency
German language	Limited working proficiency