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Lisa Wegscheider

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DEDICATED

To

Papa

Who always supported me,

Encouraged me to believe in myself,

Taught me how to become a “Superhenne”.

Thank you for still being my guardian.

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Introduction

“At least for science my brain is valuable”, - a testimony of an autistic individuum, which took part in the current study. This devastating self-perception is thought-provoking, and perfectly indicates the urgent need to raise awareness for differences in human beings. If someone thinks about diversity in people, nowadays quite familiar and widely discussed topics such as skin color, sexual orientation, or handedness may cross the mind. However, as regards to the clinical-psychological field and its vast spectrum, consensus is still far behind. Especially in the clinical context of neurological-neuroscientific knowledge, researchers have a lot to catch up on.

More dissent than consensus is also the case for reward-related, neurodevelopmental conditions like autism. Since autism was first identified by Kanner (1943) and Asperger (1944), a large number of researchers have made countless attempts to discover the main underlying factors of autism.

The current master thesis is part of a bigger study investigating neuronal as well as behavioural differences in wanting and liking of reward between autistic individuals and control participants and tries to support the social motivation hypothesis (Chevallier et al., 2012) as one of the explanatory theories of autism. Focusing on the social reward domain in form of social touch, differences between the two experimental groups have been tested through behavioural data in form of subjective ratings on a visual analogue scale (VAS), as well as through a psychophysiological interactions (PPI) analysis of the acquired data. A significant difference between autistic participants and controls is hypothesized.

Theoretical background

Autism Spectrum Disorder

First and foremost, it is important to particularise how autism spectrum disorder (ASD) is formally defined in the clinical context. According to the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; DSM–5; American Psychiatric Association, 2013), ASD is marked by persistent deficits in social communication and social interaction in various contexts. These include deficits in social reciprocity, nonverbal communication, normal back-and-forth conversation as well as in developing, maintaining, and understanding relationships. Reduced sharing of interests, emotions and affect and absence of interest in peers and making friends are some common behavioural patterns that have been identified. Additionally, a diagnosis of ASD requires restricted and repetitive patterns of behaviour, interests, or activities. A few examples for this diagnostic criterion include stereotyped, repetitive movements and speech, inflexible adherence to routines and abnormal hyper- or hypoactivity to sensory input and aspects of the environment. Symptoms must be present in early childhood, cause clinically significant limitation and impairment of everyday functioning and are not clearly explained by intellectual disability or global developmental delay (American Psychiatric Association, 2013).

Secondly, the question arises how history has led to this term and diagnosis. In his pioneering work Kanner (1943) states:

> Since 1938, there have come to our attention a number of children whose condition differs so markedly and uniquely from anything reported so far, that each case merits – and, I hope, will eventually receive – a detailed consideration of its fascinating peculiarities. (p. 217)

Labeling it “early infantile autism” his most important requirements for autism diagnosis were social aloofness and elaborate repetitive routines (Kanner,1944). Asperger (1944) simultaneously published a very similar description of “autistic psychopaths” with critical social deficits and unusual behaviour. Both pioneers used the term “autistic”, which for the first time was used by Bleuler in 1919, a Swiss psychiatrist, who tried to characterize individuals with schizophrenia. Since Kanner has published his first description of autism in 1943, lot of disagreements about the etiology, nature and clinical criteria for diagnosis occurred. Particularly, the boundaries between autism and other phenomena have been debated a lot. Kanner confidently classified autism being a unique, specific condition. However, Wing (1988) hypothesized that “Kanner´s

syndrome" was part of a continuum of autistic disorders. This was the time when the term "autism spectrum disorder" was born by the psychiatrist and mother of an autistic child. Since then, autism received more and more attention, and was determined as a concept of significant complexity varying widely in type and severity.

In DSM-5, at the present day, the degree of severity is based on restricted, repetitive patterns of behaviour as well as social communication impairments. Severity specifiers are used to briefly define the current symptomatology. Intensity of social communication impairments and restricted, repetitive behaviours are rated individually, recognizing that fluctuations over time and by context likely occur. The evaluation of verbal and nonverbal skills is essential to estimate potential strengths in autistic individuals with limited language. Shortly summarized, severity levels for ASD in DSM-5 reach from "requiring support", to "requiring substantial support" to "requiring very substantial support" (American Psychiatric Association, 2013).

Researchers in the last decades associated the discussion about the degree of severity closely with the question of common IQ levels of ASD, since some autistic individuals showed intellectual disabilities, whereas others had typical intellectual development. Lincoln et al. (1988) started to use the term "high-functioning autism" (HFA) to describe autistic individuals with an IQ above the intellectual disability range (≥70). This embedding to this day helps to better categorize and differentiate the effects of ASD from the effects of intellectual developmental disorder or global developmental delay until today. Nevertheless, intellectual disability and ASD frequently co-exist. For comorbid diagnosis, social communication is predicted to be below the general expected developmental level (American Psychiatric Association, 2013).

In summary, since autism first has been described, a large number of researchers have made countless attempts to discover the main underlying factors, causes and theories of social impairment in ASD. As a result, one of the most influential scientific discourses and theories is the so-called "Theory of Mind Hypothesis".

Theory of Mind Hypothesis

The Theory of Mind (ToM) hypothesis describes the ability of an individuum to impute mental states to one's self and to others to understand and predict behaviours. This includes states such as thinking, guessing, doubting, pretending, or liking (Premack & Woodruff, 1978). Over time, other authors also refer to this theory as "mentalizing" (Frith et al., 1991). In 2005, Frith and Frith again stated that peoples' behaviour is naturally explained based on their mind, which comprises beliefs, desires,

and emotions. Through ToM, an individuum has the possibility to recognize the difference to other peoples' thoughts and knowledge. This ability is fundamental, as in everyday life we regularly explain behaviour in terms of mental states (Frith & Frith, 2005); however, according to ToM, ASD is the result of a lack of social insight and impaired communication (Baron-Cohen et al., 1985). Research on ToM in the first decades has been mainly examined with infants and children in the context of ASD (Baron-Cohen et al., 1985; Mitchell, 1997). Nevertheless, the demand for more sensitive and advanced tasks such as the “Strange Stories Test” (Happé, 1994) or the “Frith-Happé Animations” (Abell et al., 2000) increased over time. These silent animations of geometric shapes, moving around an online screen, can be traced back to Heider and Simmel (1944), who emphasized in their early study that people often attribute human character traits to moving geometric shapes and sometimes even impute mental states (Heider & Simmel 1944). The animations, originally used in the study of Abell et al., represent three types of motion: “random”, “GD” and “ToM”. The “random” animations depict purposeless movements of two triangles, the “GD” animations are intended to show physical interaction, whereas the “ToM” animations illustrate one triangle reacting to the mental state of the other triangle (Abell et al., 2000). Since then, these animations have been increasingly and successfully used in various experiments, asking individuals to watch and evaluate the different interactions of the triangles (Castelli et al., 2002; White et al., 2011). Over the years, the investigation and research on ToM of autistic and non- autistic individuals was expedited through lot of other tasks. The so-called “Sandbox Task” (Begeer et al., 2012; Samuel et al., 2018) or the perspective-taking experiments of Samson et al. (2010) need to be additionally mentioned and appreciated in this regard.

In 2000, Baron-Cohen presented in his “fifteen year review” that a deficit in ToM can be revealed even in the highest-functioning individuals, in whom general comprehension difficulties can be excluded. Admittedly, one might fail for a variety of vague reasons in situations where mentalizing is required. However, this specific deficit can be hypothesized as diagnostic, as individuals with HFA, particularly, don´t have noticeable impairments in any other domain (Baron-Cohen, 2000). Evidence suggests that even individuals with HFA read minds distinctively, as they may experience long delays during mentalizing requirements and as they are more vulnerable to errors on more advanced ToM tasks (Baron-Cohen et al., 2001a; Happé, 1994; Klin, 2000).

To sum up, ToM has attracted a vast number of researchers. Nevertheless, the "Theory of Mind Hypothesis" is not the only attempt to deliver statements and explanations for ASD.

Social Motivation Hypothesis

In 2012, a lack in social motivation as a further explanatory theory of autism was suggested by Chevallier and colleagues. Contrary to the "Theory of Mind Hypothesis", which centres on the core deficit in social cognition, this framework focuses on the negative impact of defective motivational factors on developing social skills and social cognition. Accordingly, deficits in social cognition are interpreted as a result, rather than a cause, of absent interest in social interactions (Chevallier et al., 2012).

The need to belong is a foundational human motivator (Baumeister & Leary, 1995). Frequent interactions within a well-cared relational bond have strong effects on emotional as well as on cognitive processes. Existing evidence support these fundamental statements of Baumeister & Leary (1995) and underline a variety of negative effects on health, behaviour, adjustment, and well-being, if there is absence of attachment. By emphasizing the importance of collaborative activities, such as simply helping each other (Tomasello, 2010), or pooling and sharing volumes of foods (Kaplan et al., 2009), all these authors support the theory of social motivation.

Social motivation represents an evolutionary adaptation to enhance fitness in collaborative environments (Chevallier et al., 2012). More precisely, social motivation refers to a set of psychological dispositions and biological mechanisms, which, on the one hand, lead to "social orienting", and on the other hand, evoke "social maintaining". Therefore, an individuum seeks to orient to the social world and to maintain social bonds. Finally, people do not only try to orient and maintain social interactions, but they also find it rewarding (Chevallier et al., 2012).

To better understand the existing literature on the "Social Motivation Hypothesis", which, in short, postulates that ASDs have deficits in processing the reward value of social stimuli (Bottini, 2018; Clements et al., 2018), it is inevitable to set out and understand meaning and function of reward in human beings.

Reward

In an evolutionary point of view, it is essential to recognize and extract a large variety of stimuli, objects, situations, activities, or events with the possibility to offer an individuum the best way of reproduction, well-being, and survival (Schultz, 2000, 2015). Both the control of vegetative functions as well as the organization of goal-

directed behaviour belong to the elementary functions of reward. Reward can be anything that has the potential to make a person consume, learn, and approach, and it induces subjective, pleasurable feelings and positive emotions. Guiding human beings to drink, eat and couple is the basic function of these so-called primary rewards as “most crucial objects for life” (Schultz, 2000, 2015).

There has been growing interest in the interaction of reward processes and motivational states over the past years in neuroscience. Lot of different reward manipulations have been made in several studies, with monetary reinforcements as secondary rewards leading the way (Thut et al., 1997; Pessiglione et al., 2007; Murayama et al., 2010; Delmonte et al., 2012). This type of reward is not directly connected with reproduction and survival. It gains its motivational value as a product of learned association through earlier mentioned primary rewards. A growing body of research has been investigating similarities and differences in the processing of primary and secondary rewards over the last decades (Schultz, 2000, 2015). In addition to all these uncountable studies, one special reward domain still raises a lot of questions. Especially in the context of ASD, effects and functions of so-called social reward need to be determined and delimited more precisely.

Social reward

As already highlighted previously in the context of the “Social Motivation Hypothesis”, the need to belong is a basic human motivator (Baumeister & Leary, 1995). In 1951, Bowlby had already underlined the significant importance of parental care on the future mental health of children. The experience of a warm, intimate, and permanent relationship with the mother or a substitute is therefore vital for a human being and its mental health (Bowlby, 1951). Few years later, Harlow began investigating the maternal bond as well, rearing infant rhesus monkeys with a laboratory constructed mother-substitute. The importance of intimate and frequent body contact was shown, especially through the process of lactation (Harlow, 1958). In 2004, Eisenberger and Lieberman progressed in this field, stating that experiencing “social pain” caused by social separation and rejection may be an adaptive way to survive maternal separation and isolation (Eisenberger & Lieberman, 2004). A good example for possible effects of social isolation is the present pandemic caused by the outbreak of the COVID-19 virus resulting in long standing social distancing measures. There has been a lot of research conducted over the last years and, especially, months, studying the damaging consequences on one’s physical and mental health by

being isolated from one's loved ones (Flores & Berenbaum, 2012; White et al., 2015; Pietrabissa & Simpson, 2020; Brooks et al., 2020).

Social interaction is, indeed, a cornerstone for human beings, and it is an elusively multiplex event, implicating knowledge about the self, perception of others, or interpersonal motivations and states. Coming to a decision dependent on its reward value or perceiving one´s own reputation in the eyes of fellow human beings require highly complex cognitive processes (Amodio & Frith, 2006). Whether one thinks about trying to obtain a good reputation (Izuma, 2012), or about "broken hearts" and "hurt feelings" because of social rejection (Eisenberger & Lieberman, 2004), human behaviour and well-being strongly depend on the existence of and the interaction with other human beings. The presence of others can be seen as positive reinforcement, as it strengthens behaviour that leads to social reward.

In conclusion, social reward can be defined as interaction with fellows, which gives satisfaction and pleasure. Even though this domain of reward does not have a homeostatic and reproductive function, it indirectly increases the chance of survival, well-being, and reproduction (Schultz, 2015). In 1963, Mason et al. conducted a study with chimpanzees, underlining the animals' preference of social play more than of their favourite food. Thus, social reward can be even more pleasurable than non-social primary reward (Mason et al., 1963). Another very good example for social reward is sexual reward and attraction, which is not essential for reproduction and does not have primary reward function in a direct way. However, it generates closeness and attachment. Altruism, random social encounters, friendship, or any social activity which leads to cooperation and cohesiveness can be seen as social reward too (Schultz, 2015).

In the past years, many different types of stimuli have been used as social reward in research (Bhanji & Delgado, 2014). Whether researchers were focusing on eye contact or face processing (Kampe et al., 2001; Dawson et al., 2005; Senju & Johnson, 2009), positive evaluation (Izuma et al., 2008), or social touch (Gazzola et al., 2012; Korb et al., 2020), the variability in using and defining this reward domain leaves many unanswered questions. In this context, the next paragraph is dedicated to (social) touch and its various characteristics and functions.

Touch can, on the one hand, refer to the registration of information by the sensory systems, in short, a feeling-, and on the other hand, to any kind of sensory action on the skin (Hertenstein et al., 2006). As regards its discriminative function, the

primary role of touch is detecting, discriminating, and identifying external stimuli (McGlone et al., 2014). Discriminative touch includes the perception of vibration, texture and provides haptic information during exploratory actions. Affective (social) touch refers to feelings rather than sensing states (McGlone et al., 2014) and it is the one type of touch, which is the focal point of this thesis. Thus, for the sake of convenience, “touch” will be used in the continuing work to represent “social touch”.

Touch is vital for physical and emotional well-being (Harlow, 1958), as it has a major significance and powerful nature in everyday life (Gazzola et al., 2012) and as it is indivisibly connected with the establishment and maintenance of social relationships and structures (Suvilehto et al., 2015). It is, undoubtedly, essential to nonverbally communicate emotional states between individuals and has the power to reduce or enhance every form of social interaction (Argyle,1988). Allowing positive hedonic experience, this tactile sensation occurs in many different forms (Morrison et al., 2010).

The simplest appearance of touch implies brief, intentional contact on the body surface of a receiver during a social interaction. By contrast, holding hands or cuddling are good examples for protracted and mutually executed skin-to-skin contact. Additionally, tickling is mentioned as a good example of a more dynamic form of touch, which combines tactile sensation with playful behaviour. While listing all these different characteristics of touch, Morrison et al. (2010) presented the “skin as a social organ” hypothesis in their work. In 2013, this hypothesis was supported by Gordon et al., who conducted a functional magnetic resonance imaging (fMRI) study, showing that the so-called “social brain” (Brothers, 1990) was involved in processing gentle touch. Thus, certain brain regions, which will be discussed below, were linked to social cognition and, in further consequence, to some major impairments in ASD.

Lack thereof, a sensory processing dysfunction is proven to be common in people with ASD (Kern et al., 2007). In general, individuals with ASD show greater touch aversion since infancy (Baranek, 1999). They may tend to pull away or convulse when being touched (Kern et al., 2007). These findings are consistent with naming “abnormal hyper- or hypoactivity to sensory input and aspects of the environment” as a diagnostic criterion of the American Psychiatric Association (2013), which was stated at the beginning of this thesis.

Any kind of touch has the potential to be either accompanied by positive affective feelings or negative affective feelings expressed through aversion and disgust (Morrison et al., 2010). With all its possible positive and negative consequences and

effects (Fisher et al., 1976) touch is very meaningful to human beings, in shaping social reward, attachment, communication, and emotional regulation, from early childhood throughout the whole life (Cascio et al., 2019).

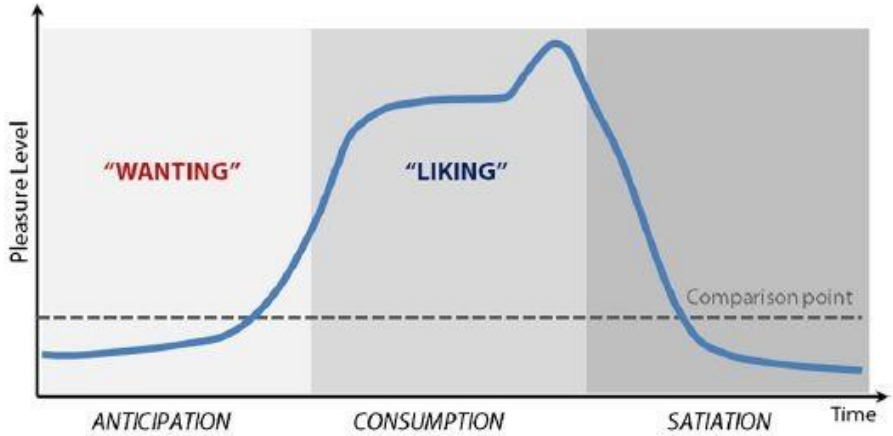
To better understand the relationship between touch and ASD, the psychological components of reward (Berridge & Robinson, 2003) need to be investigated and understood. They are highlighted in the next passage of this thesis.

Wanting and liking framework

Whether a certain stimulus such as touch induces positive or negative feelings of affection is strongly connected with the psychological components of reward (Berridge & Robinson, 2003). One component of reward is “liking”, which is related to the hedonic value and pleasurable effect of the reward stimuli. Berridge and Robinson (2003) defined it as objective affective reaction, supplement to conscious pleasure as subjective affective reaction. The so-called “wanting” component refers to the incentive salience of reward, corresponding to motivational aspects of the reward stimuli. Equally to the liking component, wanting can also be divided into unconscious and conscious processes. Additionally, “learning” needs to be mentioned as third component of reward, referring to Pavlovian or instrumental associations and cognitive representations (Pavlov, 1927; Berridge & Robinson, 2003). These three components can occur at any time during the full reward process, though learning needs to be distinguished from the other two components. Learning happens throughout the entire cycle, whereas wanting and liking, tend to dominate different phases (Berridge & Kringelbach, 2015). Thus, wanting and liking and connected phases and influences have been examined in more detail in the following passage.

Figure 1

Time Course of Reward Processing



Note. This figure gives an overview of the time course of the reward process. It demonstrates that the wanting component comes along with the anticipation of a stimulus, whereas the liking component goes hand in hand with the reward consumption, followed by a satiation phase. This graph is taken from the “Social 'wanting' dysfunction in autism: Neurobiological underpinnings and treatment implications.” by G. Kohls et al., 2012, *Journal of Neurodevelopmental Disorders, 4*(10), p.3 (https://doi.org/10.1186/1866-1955-4-10) copyright 2012 by Gregor Kohls, Coralie Chevallier, Vanessa Troiani and Robert T Schultz.

In general, rewards that are liked are typically also wanted (Berridge et al., 2009; Kohls et al., 2012). However, as shown in Figure 1, reward is not a consistent construct and wanting and liking must be clearly separated (Kohls et al., 2012). Under certain circumstances the wanting component of a reward could change, whereas the liking component remains consistent (Massaccesi et al., 2021). Thus, typically low responsiveness or even aversion to social stimuli in ASD may be affected by the disparate fluctuations of uncoupled wanting and liking (Kohls et al., 2012). In principle, research is consistent with these assumptions regarding the wanting and liking framework. However, the separation of the two components has led to controversial opinions so far (Havermans, 2011; Finlayson & Dalton, 2012). In the context of food reward, research has progressed over the past years, but in terms of social reward, the distinction of wanting and liking still trails behind. However, the social reward domain has been making progress in the recent years (Korb et al., 2020; Ihssen & Wadsley, 2021). Especially in the clinical context, research has yet to examine, whether both wanting and liking of social reward are affected equally. In fact, there is a large gap in our knowledge of reward mechanisms in ASD (Kohls et al., 2012). In the following section of this thesis, the neural correlates of social cognition and reward is been used to investigate the possibilities of bridging this gap.

Neural correlates

As already mentioned above, there are certain brain regions, which have been linked to social cognition (Brothers, 1990). In this context, amygdala, orbitofrontal cortex (OFC) and temporal cortex (TC) are major components of the social brain. The initial research studies were mainly based on studies with monkeys, but with the

invention of brain imaging, research based on the human brain received significant interest and support (Frith, 2007).

The components of the social brain allow us to interact with fellow human beings and to understand their mental states. In short, the social brain enables ToM or mentalizing (Premack & Woodruff, 1978; Frith et al., 1991).

To bridge gaps between ToM and “neural signatures” of ASD (Kaiser et al., 2010), several studies need to be referenced, which revealed differences in reward structures, including OFC, amygdala, anterior cingulate cortex (ACC) or striatum in ASD (Dichter et al., 2012; Delmonte et al., 2012; Kohls et al., 2013a; Scott-Van Zeeland). Investigating social and monetary reward, an overlapping of the neural correlates of these reward domains was ascertained tendentiously. In their review, Berridge and Kringelbach (2015) stated a “common neural currency”, independently from a certain type of pleasure. The authors refer to pleasure (liking), which is generated by certain hedonic hot spots within limbic structures of the brain. By contrast, the wanting component of reward is related to a more distributed dopaminergic brain system (Berridge and Kringelbach, 2015). To give a more precise description, wanting, or the anticipation of a rewarding stimulus, is predominantly influenced by phasic dopaminergic neural firing in the ventral striatum. Liking, or the consumption of a rewarding stimulus, is more related to the opioid system and the ventromedial prefrontal cortex (vmPFC). Unfortunately, research on liking in the social domain has generated inconclusive data so far, whereas there is substantial evidence of social reward wanting in ASD (Kohls et al., 2012).

In the context of neural correlates of social cognition and reward, the ventral striatum, more precisely, the nucleus accumbens (NAcc) has been in the spotlight lately (e.g., Ikemoto & Panksepp, 1999; Knutson et al., 2001a; Carlezon & Thomas, 2009; Botvinick et al., 2009; Cohen et al., 2009; Salimpoor et al., 2013; Kohls et al., 2013b; Park et al., 2017; Walsh et al., 2018; Richter et al., 2020). As the NAcc is not only one of the main hedonic hotspots of the opioid liking system, but also a crucial part of the dopaminergic wanting system (Berridge & Kringelbach, 2015), this brain region is from extraordinary interest in the (clinical) research field of reward. Therefore, NAcc was nominated as region of interest (ROI) in this thesis.

Region of interest: Nucleus accumbens

In their comprehensive review, Salgado and Kaplitt (2015) emphasized the necessity to understand structural, biological as well as clinical characteristics of the

NAcc, as it is a promising target for future therapeutic studies and interventions in many regards. To better understand key features of the NAcc, it needs be looked into the basal ganglia, a group of interconnected subcortical nuclei consisting of diencephalon, telencephalon, and midbrain (Albin et al., 1989). The main afferent key region of the basal ganglia is the striatum, which is divided into a dorsal sensorimotor part and a ventral region, more specialized in emotions and processing limbic information (Voorn et al., 2004). There are various loops, connecting basal ganglia, frontal cortex (FC), and thalamus, modulating brain activity and, in further consequence, decreasing or increasing certain behaviour. The limbic circuit, a loop responsible for reward-based learning, has its main source in the OFC as well as limbic regions, including amygdala, ACC, crossing thalamus and NAcc, which is described as a key component of the ventral striatum (Alexander & Crutcher, 1990).

As stated above, NAcc has been the key region of the mesocorticolimbic system in the context of reward research over the last few decades. Ikemoto and Panksepp (1999) published a review with the aim to provide an interpretation of the role of NAcc in appetitive behavioural arousal and its role in aversive contexts. 10 years later, Carlezon and Thomas explored the contribution of NAcc in mediating aversive states and reward. Further, Knutson et al. (2001a) investigated its activation during the anticipation of increasing monetary rewards and punishments in healthy participants. As regards to ASD, Park et al. (2017) investigated the clinical outcome of deep brain stimulation (DBS), treating bilateral NAcc of a 14-year-old boy with ASD. In 2018, Walsh et al. conducted research on ASD and the dysfunction of prosocial interactions, studying NAcc in mice. Animas are frequently used in the research field of NAcc (e.g., Lyness et al., 1979; Carelli, 2002; Monroy et al., 2010; Muhammad et al., 2012; Knight et al., 2013). In contrast, research studies about neurobiological substrates of motivational (wanting) as well as hedonic (liking) aspects of reward in autistic human beings is still in the early stages (Kohls et al., 2012). In 2008, Silani et al. implemented an fMRI study with ASD participants and a control group, investigating the neural system underpinning emotional awareness in ASD, with no focus on the neural system underpinning reward mechanisms.

As fMRI has been discussed briefly in this thesis, it should also be discussed the neuroimaging technology, a very powerful approach to investigating brain activity in healthy as well as in clinical contexts (Matthews and Jezzard, 2004). It is important

to note that fMRI is the central underlying methodology of this master thesis and the whole accompanied study.

fMRI: Psychophysiological interaction

In 2011, Friston outlined the extensive impact of neuroimaging over the past decades as predominant technique in neuroscience and emphasized its major future role in investigating the brain´s functional and operational principles. One powerful functional neuroimaging technique that creates images of brain´s functional properties, aspects of cognition and associated information processing, is blood oxygen-level-dependent (BOLD) fMRI (Huettel et al., 2014, p.4). During fMRI investigations, a static magnetic field, which strength is expressed in units of tesla, is used to visualize images of biological tissue. To create images, the fMRI scanner uses a series of changing magnetic gradients and oscillating electromagnetic fields, also known as a “pulse sequence”. Depending on which pulse sequence is used, different tissue properties and types can be detected. The difference between white and gray matter or blood vessel abnormalities can be elicited in this way. Different from structural neuroimaging, functional neuroimaging enables researchers to obtain insights into short-term physiological changes related to active functioning of the brain. In fact, specific parts of the brain, where mental processes occur, as well as certain patterns of brain activation associated with such processes can be identified and characterized with functional neuroimaging (Huettel et al., 2014, p.3).

The question, which certain brain area increases or decreases activity during a behavioural task is quite typical in fMRI research (O'Reilly et al., 2012). In addition, functional imaging allows to study activity in networks of areas simultaneously, more precise, to investigate functional interactions between brain areas. In 1997, Friston et al. for the first time introduced the method of so-called PPIs. PPI needs to be referred to functional connectivity, “a statistical dependence between activity in between brain areas” (O'Reilly et al., 2012). Therefore, PPI is “a statistical approach for identifying the effect of an experimental manipulation on the functional connectivity between two brain regions” (Huettel et al., 2014, p. 433). The basic idea of a PPI analysis is that mental processes modulate the influence of one brain region over another. The time course of activation in one ROI or seed region is used to predict changes in activation in another area of the brain. PPI consists of three regressors: a psychological regressor (experimental variable of interest), a physiological regressor (selected ROI), and a PPI regressor, calculating an interaction term between the psychological and the

physiological regressor. Interactions between mental processes and physiological fluctuations in the connectivity between brain regions are modelled this way (Huettel et al., 2014, p. 433).

To bring the theoretical background of this master thesis full circle, it needs to be referred again to the study of Castelli et al. (2002), who used positron emission tomography (PET), another functional neuroimaging technique, to scan an ASD group and a control group and to investigate connectivity brain mechanisms of mentalizing or ToM during watching animated shapes. The study showed reduced functional connectivity within regions associated with processing of biological motion and mentalizing, a possible physiological cause for the mentalizing dysfunction in autism (Castelli et al., 2002).

“Functional brain imaging has the potential to revolutionize our understanding of the biological basis of rewarding and aversive mood states in animal models and, ultimately, people” (Carlezon & Thomas, 2009). The fact that in vivo investigation of reward related brain structures such as NAcc in humans has been rare yet (Richter et al., 2020), is just another contribution to the enormous relevance and topicality of this master thesis.

Aim of the thesis

First and foremost, it needs to be emphasized that this master thesis is part of a bigger study, analyzing the role and function of social reward (social touch), as well as investigating the role and function of non-social reward in form of food reward. This thesis focuses on the social reward domain, associated with NAcc as a reward related ROI and its hypothesized functional connectivity differences between ASD and control participants. Social reward is separated into three different levels of desirability: high, medium, and low.

Secondly, both anticipation and consumption of social touch are in the spotlight, as literature research called attention to the enormous clinical relevance of the distinction of wanting and liking. With a possibly occurring neuronal as well as behavioural imbalance and difference in wanting and liking between ASD participants and the control group, this thesis supports the social motivation hypothesis (Chevallier et al., 2012) as one of the explanatory theories of ASD.

Better understanding the pathologies related to the reward system is a main objective of this thesis. The extension of knowledge in fMRI research as well as in the clinical context is another important objective. Further, this non-invasive human study

acts contrary to frequently conducted animal studies in this research field. Finally, calling attention to the importance of neurodiversity awareness is another main objective of this master thesis.

Research questions

As a result of comprehensive literature research as well as of the main contributions of this thesis, the main research question reads as follows: “Does social reward processing in ASD differ from neurotypical individuals on the neural and behavioural level?”

Deriving from this general research question, five more detailed research questions are listed below:

1. Are there differences in subjective wanting between ASDs and controls depending on the reward level?
2. Are there differences in subjective liking between ASDs and controls depending on the reward level?
3. Do individuals with ASD show different connectivity patterns of NAcc and other areas of the brain in comparison to controls in the social reward domain?
4. How is the connectivity of NAcc and the rest of the brain changing as soon as during anticipation of social touch there is an increase in wanting compared between both groups?
5. How is the connectivity of NAcc and the rest of the brain changing as soon as during consumption of social touch there is an increase in liking compared between both groups?

Hypotheses

Thus, the hypotheses tested within the context of this thesis are as follows:

H1: There are differences in subjective wanting between the two groups depending on the reward level.

1a. The ASD group will show lower subjective ratings on a VAS for wanting a high incentive social reward than the control group.

1b. The ASD group will show lower subjective ratings on a VAS for wanting a medium incentive social reward than the control group.

H2: There are differences in subjective liking between the two groups depending on the reward level.

2a. The ASD group will show lower subjective ratings on a VAS for liking a high incentive social reward than the control group.

2b. The ASD group will show lower subjective ratings on a VAS for liking a low incentive social reward than the control group.

H3: There is less connectivity of the NAcc with other areas of the brain in the ASD group in comparison to the control group in the social reward domain.

H4: There are differences in connectivity patterns of the NAcc between the two groups in the social reward domain.

4a. Connectivity differences of the NAcc between the two groups are specific for highly wanted social touch.

4b. Connectivity differences of the NAcc between the two groups are specific for highly liked social touch.

Summary

In summary, the study on which this master thesis is based on, includes behavioural data in form of subjective wanting ratings and given objective effort and in form of subjective liking ratings and objective Electromyography (EMG) data. Additionally, fMRI data is examined to support the findings. As for this thesis, only subjective wanting and liking ratings are investigated and the acquired fMRI data is analyzed using PPI analysis (additional methodological insights are discussed below). Therefore, research questions one and two present behavioural data analysis and research questions three, four and five present fMRI data analysis.

In this thesis, a significant difference between ASD participants and the control group´s wanting and liking ratings for social touch depending on the reward type is expected. Additionally, it is hypothesized that the dissimilarity of wanting and liking ratings between the two groups can also be shown as difference in functional connectivity of NAcc, a region specifically linked to the reward system.

Methods

As the present thesis only focuses on (subjective) wanting and liking of social reward, which is associated with NAcc as reward related ROI and its hypothesized functional connectivity differences between ASD and control group, other areas of interest (e.g., food reward, objective wanting and liking, questionnaires) are skipped or only described superficially in the following explanation of the methods. As next step, the participants of this fMRI case-control study with mixed between-within subject design are described.

Sample

The acquired sample counted a total of 49 voluntary participants. The ASD group consisted of 24 subjects with a mean age of 33.21 (*SD* = 12.19), ranged between 18 and 57 years, and the control group consisted of 25 subjects with a mean age of 34.92 (*SD* = 12.13), ranged between 20 and 60 years. As regards gender distribution, 13 male (*M* = 36.3) and 11 female (*M* = 29.2) were part of the ASD group, 12 male (*M* = 28.7) and 13 female (*M* = 30.0) were tested in the control group. Any type of handedness (44 right-handed, two mixed, three left-handed) and any sexual orientation (41 heterosexual, three homosexual, three bisexual, one pansexual, one asexual) was welcomed. To quantify autistic traits in the study sample, the Autism-Spectrum Quotient (AQ; Baron-Cohen et al., 2001b) was used. At a cut-off score of 17, the ASD group significantly differed from the control group ($p < .001$). Groups were matched by age, gender, and IQ. Some of the most important exclusion criteria, valid for possible subjects, are listed subsequently in table 1.

Table 1

Exclusion Criteria

Category	Exclusion
age	younger than 18 years
education	psychology/cognitive sciences
study participation	part of any similar study
abilities, IQ	poor reading ability, IQ too high/low

ASD	no HFA (IQ≤70), no medical diagnosis
physiology, health	pregnancy, lactose intolerance metal implants, cornflour allergy no touch-sensitivity, any other mental disorder, medication, alcohol/drug abuse

Recruitment

For advertising purposes, flyers were handed over to people and distributed in public places (universities, cafes, libraries). Additionally, study announcements were published and posted via social media. As regards recruitment of possible participants with ASD explicitly, contacting took place via an established internal contact database of various institutions and practical psychologists (e.g., Autistenhilfe, Autistenzentrum Arche Noah, Rainman's Home, Ambulatorium Sonnenschein, Barmherzige Brüder Linz). Suitability for participation and exclusion criteria were checked via an online health questionnaire. Moreover, all potential participants received a general information sheet about purpose and procedure of the study, instructions on how to reach the destination and a video clip, summarizing all the relevant information. After the participants received permission, a study appointment was fixed at dental clinic of Medical University of Vienna. An early withdrawal or a refusal to participate did not have any negative consequences for the subjects. Insurance cover, monetary compensation of 30 EUR and reimbursement of possible travel costs were included.

Study procedure

The duration of the laboratory appointment was approximately 3½ hours. After the participants worked through an informed consent, a COVID-19-free confirmation and some more health, clinical and personality paper questionnaires, they were guided into the laboratory by the experimenter. They were prepared for the fMRI scanner and the EMG electrodes for objective liking measurement were fixed. After a final check for fMRI suitability, the participants got free access to the fMRI scanner room, where the experiment was realised. Participants were asked to comfortably lay down on the patient table and to check out all the devices, which were used for subjective and objective wanting and liking measurements. Before the head coil was put on, the participants got some earplugs and additional instructions and the person, doing the touch reward, was introduced. Finally, the fMRI resistant tubes and the pacifier for receiving the food reward were put in the mouth of the subjects and training sessions

started. After training trials were done successfully, the fMRI scanner was turned on and the actual experiment started.

As already mentioned, this thesis used only parts of the whole study procedure and measurements for hypotheses testing. For this reason, the following passages focus more on relevant stimuli and quantifications, whereas other methods are skipped or outlined superficially.

Reward stimuli

As regards the reward tasks, which were performed inside the fMRI scanner, different levels of reward stimuli were employed to investigate and compare wanting and liking of reward processes. Two types of reward were conducted, each hypothesized with high, medium, and low desirability, and implemented in alternating blocks: A food reward, delivered in form of milk (low desirability), chocolate milk (high desirability), or a mixture (medium desirability) and a social reward, operationalized as slow (high desirability), medium (medium desirability) and fast (low desirability) social touch. Each of the altogether four implemented blocks (FTFT/TFTF) consisted of 16 trials. Once more, the food reward is not investigated in this master thesis. The social reward is explained in the following paragraph.

Social touch

Referring to the theoretical background and meaning of touch, it again needs to be underlined that with the function of shaping social reward, attachment, communication, and emotional regulation, touch is enormously meaningful for human beings (Cascio et al., 2019). Any type of touch has the potential to be related to positive affective feelings as well as to negative affective feelings (Morrison et al., 2010).

In the current thesis, slow, medium, and fast touches were performed by a same-sex toucher (social, nonsexual stimulus) on the right forearm (radial bone) of the participants. It had to be strictly sticked to a standardized area of 9 cm, using middle finger and index finger and tracking a standardized rhythm via headphones. The toucher had to administer the social stimulus as constant, comfortable, and rhythmic as possible. Additionally, cornflour was used, trying to ensure a feeling as pleasant and smooth as possible.

Dependent measurements

To give an introductory overview, the dependent variables of the whole study procedure were as follows: subjective stimulus ratings on a VAS for either liking or wanting of the stimulus, as well as objective wanting measurements (effort) and

objective liking measurements (EMG). Objective measurements are not used and investigated within the frame of this thesis. Nevertheless, they are as well described briefly below.

Subjective wanting and liking

VASs and sliders are tools, which allow participants to specify a value within a predefined range (Matejka et al., 2016) by subjectively selecting a spot along a continuous line with two endpoints (Hayes & Patterson, 1921). Participants of the current study were asked to rate by use of a button box, how much they wanted and how much they liked the (slow, medium, fast) social touch. In each trial (see figure 2), a wanting rating was required after the first announcement of the stimulus and a liking rating after consumption and relaxation on a VAS scale, depicted on a screen inside the fMRI scanner. The starting point of the digital slider was randomly picked among -50:10:50 positions (from -50 to 50, at steps of 10).

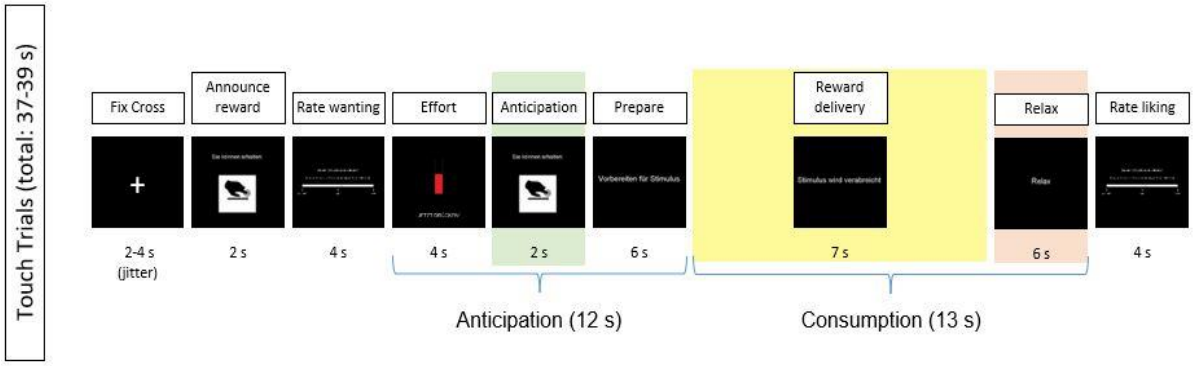
Objective wanting and liking

As “effort may be a valid method for dissociating the ‘liking’ from ‘wanting’ components of reward motivation in humans” (Waugh & Gotlib, 2008), a dynamometer (Vernier Software & Technology) was used to objectively measure wanting of the reward stimulus through effort. During each trial, the participants had to close their right hand as tightly as possible around the dynamometer. Depending on their physical effort, the probability to receive the most desirable touch type increased or decreased. Maximum voluntary contraction (MVC) was measured before and after the reward task.

Previously published studies emphasized advantages of EMG usage during consumption (Mayo et al., 2018; Ree et al., 2019) as well as anticipation (Korb et al., 2020) of social stimuli in adults. For this reason, the measurement of objective liking was done through EMG in the current study too. Trying to detect unconsciously positive as well as negative facial reactions to the given touch stimulus, corrugator supercilii and zygomaticus major were in the spotlight of the investigation.

Figure 2

Timeline of Touch Trial



Note. This figure gives an overview of one single touch trial, which was repeated 16 times, implemented in two sessions, and alternating with the food task. Consisting of nine consecutive conditions, one trial lasted nearly 40s (x16x2).

Data analyses

Behavioural data

The analysis of the behavioural data was conducted with IBM Statistical Package for the Social Sciences (SPSS ®) Statistics, Version 27, and Windows Excel.

As one between-subject factor (ASD group/control group) and one within-subject factor (reward level) were expected to influence the dependent variables (wanting ratings or liking ratings), a mixed-design analysis of variance (ANOVA) was the best fitting model to use for analysis (Field, 2017). In greater detail, a two-way (2x2) mixed ANOVA was used to investigate ratings of wanting and a two-way (2x3) mixed ANOVA was used to investigate ratings of liking.

For more details and further analyses of the behavioural data, see below in the results section of this thesis.

fMRI data

Image acquisition was done in a 3.0 Tesla Siemens Magnetom Skyra Tim Trio magnetic resonance imaging (MRI) scanner with a 20-channel head and neck coil (Siemens, Erlangen, Germany). The whole-brain functional images were acquired with the following parameters: TR = 2500 ms, TE = 36 ms, flip angle = 66°, interleaved acquisition and interleaved multi-slice mode, 44 axial slices, slice thickness = 2.0 mm,

matrix size = 96x96, and voxel size = 2.1x2.1x2.1. Around 250 volumes were collected in each of the two touch blocks.

For the analysis of the acquired fMRI data, the free and open-source software Statistical Parametric Mapping (SPM) was used. Using the latest version of this software (SPM12), the analysis was accompanied by MATLAB (version R2020b), a "matrix laboratory" software developed by MathWorks. Seven MATLAB scripts were generated and used to configurate and run batch pipelines, modified for preprocessing, 1st-level analysis, 2nd-level analysis, and PPI.

Preprocessing of the raw fMRI data was started with slice timing correction, to interpolate all slices of a volume with the middle slice. Subsequently, the field maps, used to unwarp geometrically distorted echo-planar imaging (EPI) data, were calculated. The images were realigned, registering them to the mean image and the voxel displacement map (from field maps) was used for unwarping. Images were warped to standard Montreal Neurological Institute (MNI) brain template. Finally, T1s were co-registered, segmented and normalized and EPI images were smoothed. Smoothing of the normalized images was done by a 6mm FWHM Gaussian kernel. Additionally, there have been no volumes discarded to allow for T1 equilibration effects and no specific realignment parameters were used to exclude certain images from 1st-level contrast specification later.

As regards 1st-level analysis, another batch pipeline was used to specify and generate design matrix and contrasts. The following nine conditions were adapted specifically for both sessions of the touch trials (visualized in figure 2): fixation cross, 1st announcement (+ parametric modulation), wanting ratings, effort, obtained reward, preparation, delivery (+ parametric modulation), relax and liking ratings. Additionally, four t-contrasts were defined: anticipation, linear wanting, delivery and linear liking. With reference to the underlying research questions of the current thesis, parametric wanting and parametric liking were in the spotlight of the analysis. Movement regressors were not considered and therefore excluded.

After the main 1st-level analysis was done, another 1st-level analysis needed to be done for PPI. Indeed, two additional 1st-level analyses were generated as within-subject factor, to avoid concatenation of the sessions. Before the extraction of the underlying ROI (NAcc) was done in this regard, an effect of interest (EOI), which describes any activation in any direction that is above the statistical threshold, needed to be specified. From this F-contrast, NAcc was identified, and representative time

series of the selected brain region were extracted. For consistency reasons both left and right NAcc were investigated in this thesis. Through meta-analysis of prior reward activation studies, two 8mm-radius ROIs, one on the left and one on the right, from the center of activation in the NAcc regions (MNI: (-8,12,0), (11,12,0), were determined (e.g., Knutson et al., 2001b; Manning et al., 2015). Next, the psychological regressor, the physiological regressor and the PPI regressor were created, again focusing on parametric modulation. In total, four PPIs (parametric liking of left NAcc, parametric liking of right NAcc, parametric wanting of left NAcc and parametric wanting of right NAcc) for each session and each participant were generated. Thus, four contrasts, with the level of reward included, were brought to PPI 2nd-level analysis. Unfortunately, the contrast for parametric wanting of right NAcc of one participant needed to be excluded.

To finally figure out, whether there are differences in functional connectivity or whether there are any regions commonly connected to the underlying ROIs between the ASD group and control group, a two-sample t-test for each ROI and each parametric modulation was calculated for 2nd-level analysis.

Results

Behavioural data

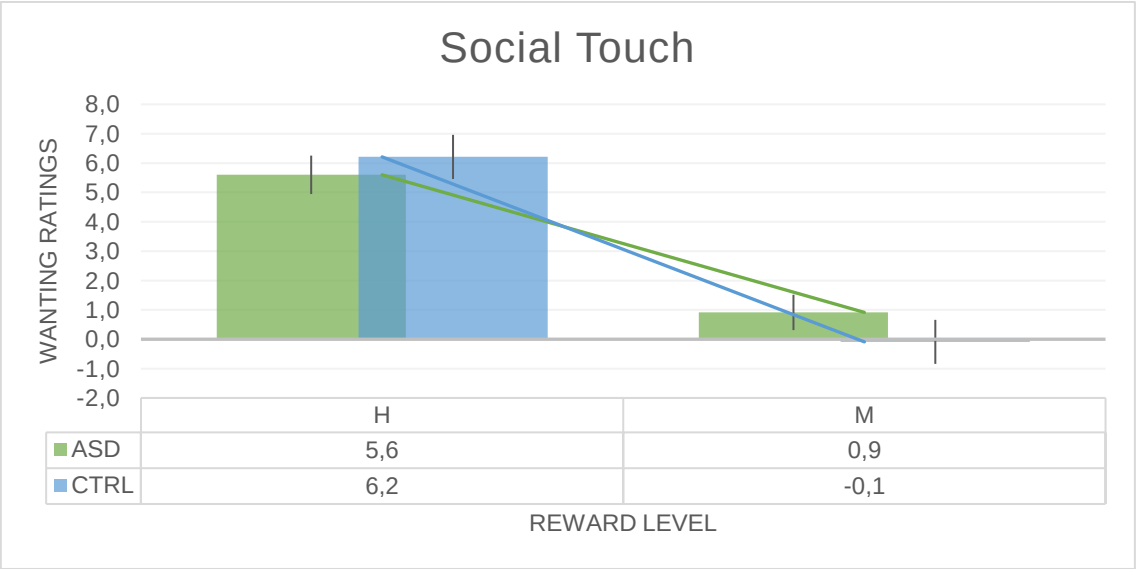
To briefly summarize again, two mixed ANOVAs with reward level being the within-subject factor, with group (ASD/control) being the between-subject factor and either wanting ratings or liking ratings as dependent variable were investigated.

Wanting ratings

A two-way (2x2) mixed ANOVA was used to investigate ratings of wanting regarding high and medium reward desirability. It could be found a significant main effect with F (1,37) = 29.52, p <. 001, which shows a difference in wanting ratings, irrespective group separation. However, the ratings of the ASD group and control group did not significantly differ from each other (F (1,37) = .17, p =. 68). To summarize, there was a significant decrease of subjective wanting within high and medium reward level, but no significant difference between ASD and control group (see figure 3).

Figure 3

Two-Way (2x2) Mixed ANOVA, Wanting Ratings on a VAS

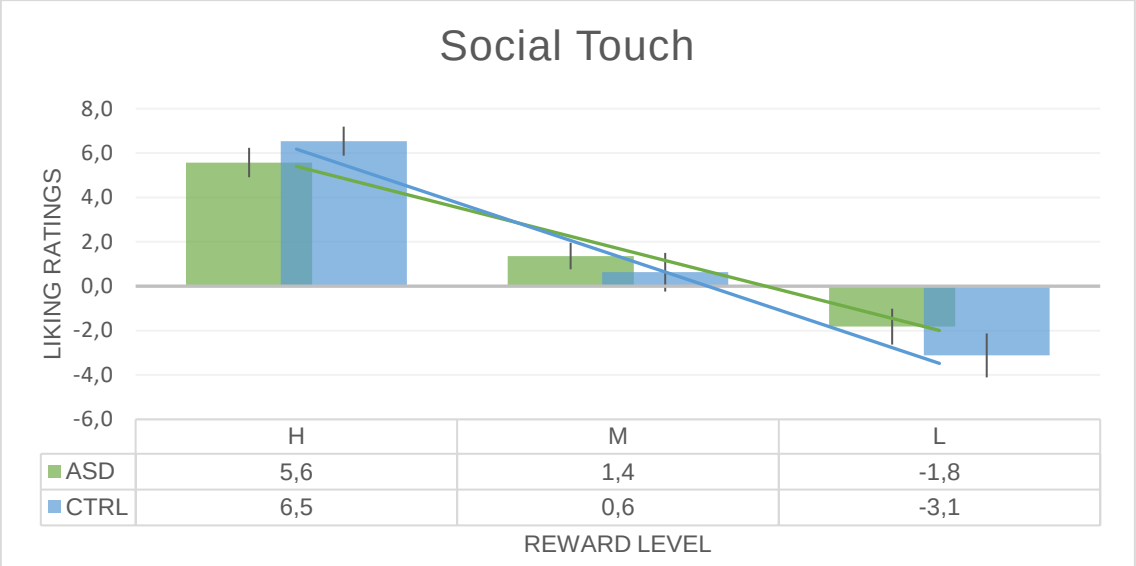


Liking ratings

A two-way (2x3) mixed ANOVA was used to investigate ratings of liking regarding high, medium, and low reward desirability. Same as with the analysis of wanting ratings, there was found a significant decrease within the three different reward levels with F (2,92) = 25.78, p <. 001. Nevertheless, a difference in wanting ratings, respective group separation, could not be detected ((F (1,37) = .01, p =.99). In summary, it could be found a significant main effect, but no significant interaction effect (see figure 4).

Figure 4

Two-Way (2x3) Mixed ANOVA, Liking Ratings on a VAS



fMRI data

To reconnect to the 2nd-level analysis (PPI) of the acquired fMRI data, it needs to be referred again to the implementation of a two-sample t-test for each ROI and each parametric modulation. In reference to the underlying research questions, two additional contrasts were generated for each of the four conducted two-sample t-tests: conASD ([1 -1]; What is more connected in ASDs compared to controls?) and conCTL ([-1 1]; What is more connected in controls compared to ASDs?). With these two contrasts, differences in brain activity correlated with the activity of right and left NAcc during increased wanting or increased liking of the announced or delivered social touch between ASDs and controls, were tried to figure out.

A threshold of $p_{uncorrected} \leq 0.005$ was selected for brain activity representation in SPM. Activated coordinates were inserted and identified through MRIcron, a cross-platform NIfTI format image viewer. For results of the analysis, see table 2 and figures 5 - 9 below.

Table 2

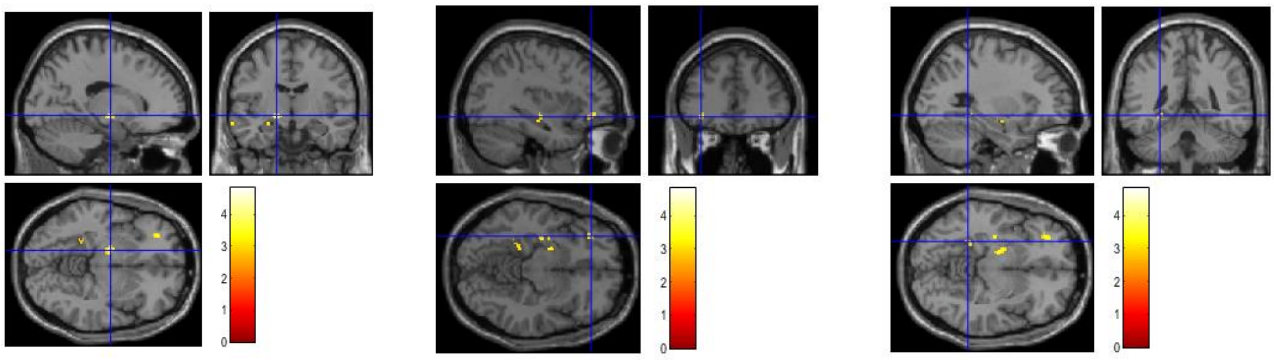
Results of PPI 2nd-Level Analysis

	voxels	*T*	p_{uncorr}	coordinates	brain area
brain areas positively correlated with left NAcc-activity in the context of increased liking, controls compared with ASDs (figure 5)	62	4.84	0.000	-16 -10 -6	Left ventral DC
	34	3.42	0.000	-34 38 -10	Left inferior frontal gyrus, orbital part
	33	3.33	0.001	-28 -44 -8	Left fusiform gyrus
brain areas positively correlated with right NAcc-activity in the context of increased liking, ASDs compared with controls (figure 6)	76	3.97	0.000	16 -80 22	Right cuneus
	31	4.37	0.000	54 0 10	Right rolandic operculum
	27	3.72	0.000	-56 4 16	Left precentral gyrus
	31	3.69	0.000	-52 18 30	Left inferior frontal gyrus, triangular part
	21	3.46	0.001	60 4 40	Right precentral gyrus
	33	3.28	0.001	-2 -62 -24	Lobule VII of vermis, cerebellum

brain area positively correlated with right NAcc-activity in the context of increased liking, controls compared with ASDs (figure 7)	16	3.23	0.001	-2 44 10	Left anterior cingulate gyrus
brain areas positively correlated with left NAcc-activity in the context of increased wanting, ASDs compared with controls (figure 8)	37	4.10	0.000	-46 -28 -16	Left inferior temporal gyrus
	21	3.57	0.000	-36 -64 -32	Left crus I of cerebellar hemisphere
	17	3.06	0.002	-4 -46 -8	Left lobule IV, V of cerebellar hemisphere
brain areas positively correlated with right NAcc-activity in the context of increased wanting, ASDs compared with controls (figure 9)	21	3.20	0.001	20 -16 -10	Right ventral DC
	23	3.08	0.002	40 -82 34	Right middle occipital gyrus
	17	3.04	0.002	46 -6 0	Right insula

Figure 5

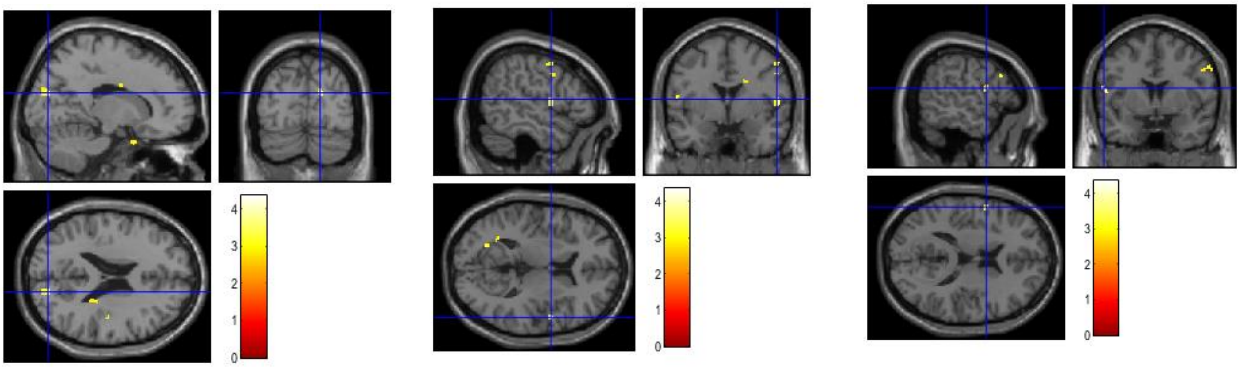
Heat Maps of Brain Areas positively correlated with left NAcc-activity in the context of Increased Liking, Controls compared with ASDs



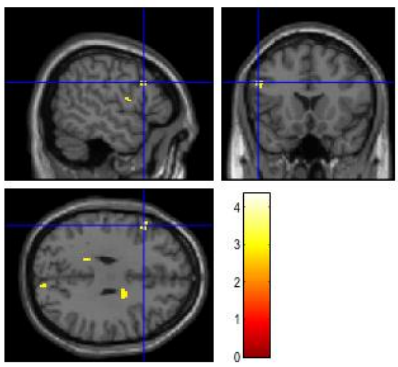
Ventral DC Inferior Frontal Gyrus Fusiform Gyrus

Figure 6

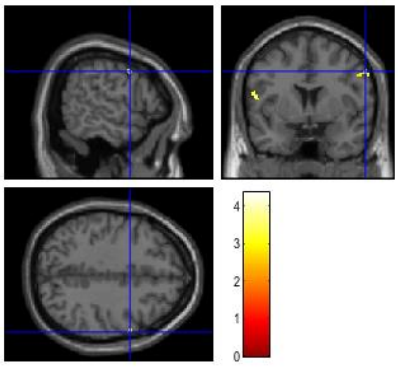
Heat Maps of Brain Areas positively correlated with right NAcc-activity in the context of Increased Liking, ASDs compared with Controls



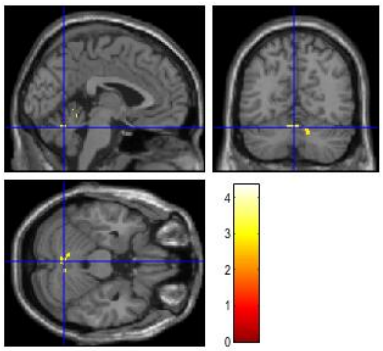
Cuneus Rolandic Operculum Left Precentral Gyrus



Inferior Frontal Gyrus



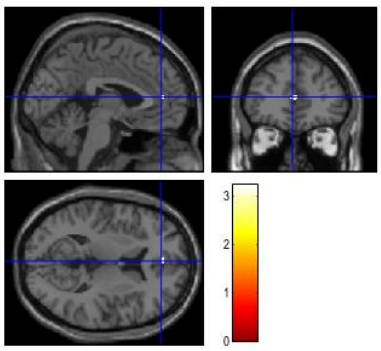
Right Precentral Gyrus



Lobule VII of Vermis

Figure 7

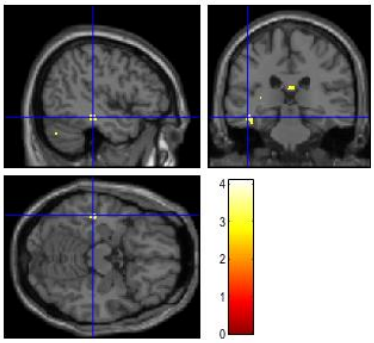
Heat Map of Brain Area positively correlated with right NAcc-activity in the context of Increased Liking, Controls compared with ASDs



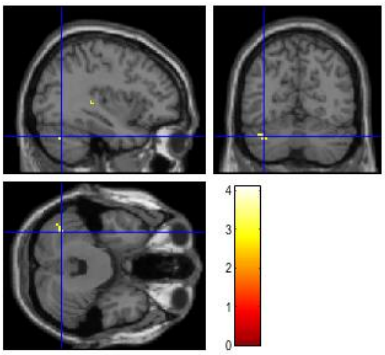
Anterior Cingulate Gyrus

Figure 8

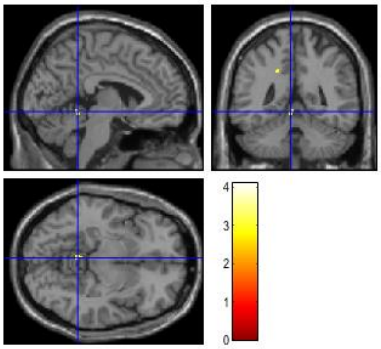
Heat Maps of Brain Areas positively correlated with left NAcc-activity in the context of Increased Wanting, ASDs compared with Controls



Inferior Temporal gyrus



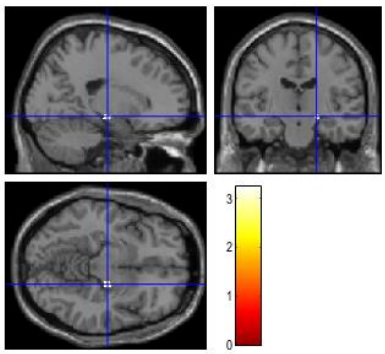
Left crus I, cerebellar



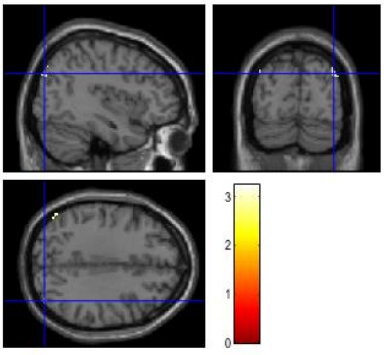
Left lobule IV, V, cerebellar

Figure 9

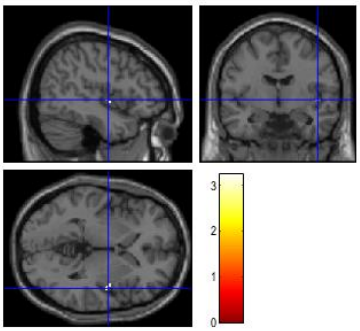
Heat Maps of Brain Areas positively correlated with right NAcc-activity in the context of Increased Wanting, ASDs compared with Controls



Ventral DC



Middle Occipital Gyrus



Insula

In summary, left ventral DC, left inferior frontal gyrus, and left fusiform gyrus were found to significantly increase positive correlation with the activity of left NAcc during increased liking of the delivered social touch in the control group compared with the ASD group. As regards conASD in the context of increased liking of the delivered social touch, no brain areas were detected to significantly increase positive correlation with the activity of left NAcc. Right cuneus, right rolandic operculum, left precentral gyrus, left inferior frontal gyrus, right precentral gyrus and lobule VII of vermis were found to significantly increase positive correlation with the activity of right NAcc during increased liking of the delivered social touch in the ASD group compared with the control group. Left anterior cingulate gyrus was the one brain area, which significantly increased positive correlation with the activity of right NAcc in the control group compared with the ASD group during increased liking of the delivered social touch.

Concerning parametric wanting of left and right NAcc, a few brain areas were detected when comparing ASDs with controls: Left inferior temporal gyrus, left crus I of cerebellar hemisphere and left lobule IV, V of cerebellar hemisphere significantly increased their positive correlations with the activity of left NAcc during increased wanting of the announced social touch. Right insula, right ventral DC, and right middle occipital gyrus significantly increased their positive correlations with the activity of right NAcc during increased wanting of the announced social touch. No brain areas were found when comparing controls with autistic individuals.

Discussion

Summary

The goal of this master thesis is to contribute to a bigger study of a research group, instructed by Assoz. Prof. Giorgia Silani, Privatdoz. PhD, focusing on “the investigation of the opiate system and dopamine system during the modulation of wanting and liking of primary and social rewards”.

The current study is focused on social reward in form of social touch, investigating meaningful processing differences between autistic individuals and control participants. Identifying differences not only through behavioural data in form of subjective wanting ratings and liking ratings on a VAS, but also through the PPI analysis of the acquired fMRI data was the main focus of this thesis. Therefore, it was hypothesized that a significant difference existed between ASD participants and the control group regarding VAS ratings depending on different reward levels. Additionally, the hypothesis that a difference of subjective ratings can also be shown as difference in functional connectivity was constructed.

Bilateral NAcc, a brain region, which in former research was specifically linked to the reward system, was determined as ROI of the PPI analysis. 24 autistic individuals and 25 control participants were inspected and matched by age, gender, and IQ, after fulfilling requirements, questionnaires, and inclusion criteria. While being positioned inside a 3.0 Tesla fMRI scanner, the acquired sample was gently touched by a same-sex person on the right forearm.

The experimental procedure, methods, and hypotheses of this thesis were based on literature, focusing on ASD, reward and fMRI research. Summarizing and weighing all possible explanations for ASD, the research questions of this thesis were mainly supporting the social motivation hypothesis, an explanatory theory of ASD, stated by Chevallier et al. in 2012. Both wanting and liking of social touch were studied, as literature research emphasizes the urgency to consider both, especially in the clinical context.

Interpretation of behavioural results

Unfortunately, differences in wanting ratings and liking ratings on a VAS, respective group separation, were not significant. Thus, hypotheses H1 (1a, 1b) and H2 (2a, 2b) could not be confirmed in the context of research question 1 (Are there differences in subjective wanting between ASDs and controls depending on the reward level?) and research question 2 (Are there differences in subjective liking between

ASDs and controls depending on the reward level?). The ASD group did neither show significantly lower subjective ratings on a VAS for wanting or liking a high incentive social reward than the control group, nor it showed significantly lower subjective ratings on a VAS for wanting or liking a medium or low incentive social reward than the control group. In summary, ASDs did not show significantly decreased wanting and liking of social touch in comparison to neurotypical participants.

As regards the interpretation of the above-mentioned results, it once again needs to be mentioned that implemented objective wanting and liking measurements as part of the whole accompanied study were not evaluated within the context of this thesis. Admittedly, both anticipation and consumption of social touch were investigated to differentiate between wanting and liking. Nevertheless, additional objective measurements would come in useful, as in the underlying research field's commonly conducted animal studies, subjective measurements, and therefore comparisons and common trends between subjective and objective methods, are not possible to draw.

It could be found a significant main effect regarding the subjective ratings of both reward components, which means a significant variation within the different reward levels. However, these results need to be interpreted carefully, as there is the risk of influence and priming through the instructions of the experimenter at the beginning of the study.

Interpretation of fMRI results

The aim of the fMRI analysis in the context of this study was to figure out if increased wanting and increased liking of social touch is positively correlated with the functional connectivity between both right and left NAcc and other brain areas in autistic individuals and neurotypical participants and if functional connectivity is significantly reduced in ASDs compared to the control group. A PPI analysis with NAcc as ROI was implemented, trying to define brain regions, which increase positive correlation with NAcc during increased wanting and increased liking of the announced and delivered gentle touches.

Incompatible with H3 and H4 (4a, 4b), significantly less connectivity of bilateral NAcc with other brain areas in the ASD group compared with the controls could not be confirmed. Moreover, functional connectivity differences between the ASD group and the control group did turn out to be neither specific for highly wanted social touch, nor specific for highly liked social touch. Nevertheless, various brain areas were found to increase connectivity with bilateral NAcc during increased wanting and liking of the

announced and delivered social touch when comparing ASDs with controls, and vice versa. These brain regions are examined and linked to existing literature in the following passages, subdivided into the wanting and liking component of reward.

Parametric liking

To briefly refer to the results chapter, ipsilateral ventral DC, inferior frontal gyrus, and fusiform gyrus were found to significantly increase positive correlation with the activity of left NAcc during increased liking of the delivered social touch when comparing control group with the ASD group. When comparing the control group with the ASD group in context of the right NAcc, contralateral anterior cingulate gyrus was found to significantly increase positive correlation with the activity of left NAcc during increased liking of the delivered reward. Additionally, right cuneus, right rolandic operculum, left precentral gyrus, left inferior frontal gyrus, right precentral gyrus and lobule VII of vermis were detected to significantly increase positive correlation with the activity of right NAcc during increased liking of the delivered social touch as regards comparison of the ASD group with the control group.

Looking backward to the theoretical background of this thesis and bridging the gap, it again needs to be referred to the “neural signatures” of ASD (Kaiser et al., 2010) and to several studies, which disclosed differences in reward structures, including OFC, amygdala, ACC, or striatum in ASD (Dichter et al., 2012; Delmonte et al., 2012; Kohls et al., 2013a; Scott-Van Zeeland).

With reference to possible functions of ACC, Apps et al. in 2016 referred to a subregion of the ACC, the gyrus (ACCg), which was suggested to play an important role in processing social information. It is only recently that Smith et al. (2021) mentioned ACC appearing to encode affective states of others in both humans and rodents. In their study, social interaction was followed by ACC activation as well as activity in several downstream regions such as NAcc (Smith et a., 2021). ACC is mostly related to the anticipation of reward in the current literature (Lorenz et al., 2014; Vassena et al., 2014; Gorka et al., 2015; Kerr et al., 2015).

What is more, Zhou et al. (2016) discovered an autism-related decrease in functional connectivity between ACC and, among others, right rolandic operculum. Right rolandic operculum was found to be connected to right NAcc in the context of liking when comparing ASDs with controls in the current thesis.

All these facts and findings point out meaningful results of the current thesis in the context of ACCg, as left ACCg was found to significantly increase positive

correlation with the activity of left NAcc during increased liking of the delivered reward only. Thus, one can argue, that the existing literature about ACC is supplemented by this study and the importance to carefully distinguish between all components of reward processing is underlined once again. Furthermore, findings point to the cingulo-opercular network (CON) consisting of, among others, operculum and ACC, a control network, responsible for various cognitive processes that has been found to be impaired under certain circumstances (Redcay et al., 2013; Vaden et al., 2013; Sestieri et al., 2014). Further research across multiple networks such as CON in the context of autism is therefore highly recommended.

Another very interesting and meaningful brain region in the context of the investigation of parametric liking of left and right NAcc in this study is the inferior frontal gyrus (IFG). As regards this brain region, it needs to be referred to the study of Du et al. (2020), which aim was to subdivide OFC, ACC and IFG into different subregions based on resting-state functional connectivity with other areas of the brain. Very interestingly, the authors stated that IFG areas, especially on the left, which were also found to significantly increase positive correlation with the activity of right NAcc in the current thesis, are mainly implicated in language and are quite close to OFC areas. Therefore, a meaningful relationship between OFC functions and language is underlined with these findings (Du et al., 2020). Moreover, these assumptions are consistent with findings of several other researchers, who argued that cognitive processes at language level can bias reward representations and subjective desirability of reward stimuli such as flavour, somatosensory stimuli, taste, and odour in the OFC (e.g., de Araujo et al., 2005; Grabenhorst et al., 2010).

Cuneus, found to significantly increase positive correlation with the activity of right NAcc during increased liking of the delivered reward when comparing autistic individuals with control participants, was mentioned in a study of Wittmann et al. (2007), who conducted a delay discounting task. Participants were asked to choose between immediate and delayed rewards, which, again, points to a meaningful connection between a brain region, which attracted attention within the framework of this thesis, and reward processing. When investigating reward-circuit biomarkers of risk and resilience in adolescent depression, Fischer et al. (2019) linked cuneus to reward processing in their study too.

Very impressively, three years after they published their study in 2007, Wittmann et al. (2010) conducted another neuroimaging study on a delay discounting

task, yielding, among others, the following findings: Not only striatum but also bilateral anterior insulae were significantly activated in the context of both the immediate and delayed options. Additionally, both anterior and posterior insulae were activated during collecting not only immediate but also delayed rewards. These findings point out meaningful results of the current thesis, as insula was detected to significantly increase positive correlation with the activity of right NAcc during increased wanting of the delivered reward when comparing autistic individuals with controls. More insights regarding the investigation of parametric wanting, see below.

A brain region, which needs to be examined carefully too, is bilateral precentral gyrus (PCG), a key element of the motor control network. As an example, Nebel et al. (2014) investigated connections between autism trait severity, which was discussed within the first pages of this thesis, and connectivity of PCG. They detected that connectivity between and within functional subregions of the PCG was related to ASD diagnosis, which underpins not only a connection between social and motor abilities of ASDs, but also meaningful results of this thesis.

An additional very interesting and in literature much discussed area is the fusiform gyrus. There is a big body of research, which has tried to investigate face processing in autistic individuals so far (e.g., de Gelder et al., 1991; Boucher et al., 1992; Adolphs et al., 2001; Dawson et al., 2005), ascertaining impaired recognition of facial expressions and emotions. Therefore, the fact that left fusiform gyrus was detected to be connected to left NAcc in the context of liking when comparing controls with ASDs within the framework of the current study, seems to have a meaningful tendency, worth looking into it more deeply.

Very interestingly, the activation of fusiform face area (FFA), a subregion of fusiform gyrus, was found to be correlated not only with the perception of faces, but also when imagining them (e.g., O'Craven, 2000; Ishai, 2000). As the acquired sample of this study only got demonstrated non-facial words and symbols (see figure 2), while being positioned inside the scanner, the imagination of familiar, beloved people and faces during the consumption of social touch is assumed in this regard.

Parametric wanting

As regards parametric wanting of the announced social touch, the following brain regions were found to significantly increase positive correlation with either right or left NAcc when comparing ASDs with controls: Ipsilateral inferior temporal gyrus,

crus I of cerebellar hemisphere and lobule IV, V of cerebellar hemisphere with left NAcc, and ipsilateral insula, ventral DC, and middle occipital gyrus with right NAcc.

One brain region, which is prominent in the listing above and needs to be mentioned not only in the context of wanting but also with hindsight to liking, is the cerebellum. As regards this brain region, a vast amount of scientific knowledge concerning its role in the etiopathogenesis of ASD (e.g., Fatemi et al., 2012; Wang et al., 2014) as well as its role in reward processing (e.g., Thoma et al., 2008; Carta et al., 2019) is available. In fact, developmental differences at multiple levels of function and structure of cerebellum have been suggested in the context of anatomical, clinical and neuroimaging studies so far. In 2012, Becker and Stoodley emphasized the importance of cerebellum in motor learning and coordination. The authors underlined the role of cerebellum in affective regulation, language, and executive functioning, underpinning that it is an important player in the context of ASD (Becker & Stoodley, 2012). These findings are even more interesting, as lobule VII of vermis, crus I of cerebellar hemisphere and lobule IV, V of cerebellar hemisphere were found to be connected to NAcc in the context of the current thesis.

Finally, there are few more brain areas, which remain unresolved in the context of this thesis, and which were found to be connected to NAcc: Inferior temporal gyrus, ventral DC, and middle occipital gyrus.

The recently conducted study of Dubey et al. (2020) seems to be an excellent indication to determine relevance of these regions. Comparable with the methodology of the current thesis, the authors invited their participants to rate their motivation for seeking social reward and to directly assess the effort required to receive it. Participants were asked to either choose a social or a non-social video in the context of different levels of effort. Very interestingly, significantly more activation in cuneus, precuneus, and OFC was found when participants made social compared to object choices. Significantly increased neural activation was found, among others, in the lingual and fusiform gyri as well as in the middle occipital gyri when deciding for object compared to social choices. On top of the findings outlined above, the authors investigated neural correlates of parametric modulation by effort as well, again identifying increased neural activation in the middle occipital gyrus extending into the inferior temporal gyrus, insula, and thalamus (Dubey et al., 2020).

Very encouragingly, these findings once more underline meaningful results of the current thesis, this time in the context of the activation of inferior temporal gyrus, middle occipital gyrus, and ventral DC.

Limitations

First and foremost, it needs to be emphasized that in the past years of research, many different types of stimuli have been used as social reward (Bhanji & Delgado, 2014). Thus, the variability in using and defining this reward domain keeps many questions unanswered and the specific selection of social touch reduces external validity of the current thesis.

Secondly, the chosen sample needs to be thoroughly examined, as the small number of participants makes it difficult to generalize the results of the present study. Additionally, the applicability to real life is debatable, as the laboratory setting presents an uncomfortable and unfamiliar environment for the participants.

Moreover, fMRI is just one out of many other neuroimaging techniques, though. This technique is one of the most popular and advanced techniques used for the investigation of brain function in the present day. However, the BOLD signal for instance, consists of different neuronal, metabolic, and vascular processes and therefore exclusively acts as an indirect measure of neuronal activity. In fact, the fMRI signal tends to be very noisy and movement-related effects, instrumental drifts and artefacts are very common (Caballero-Gaudes & Reynolds, 2017). Nevertheless, it is undeniable that fMRI will progress to have an incredible impact on future cognitive neuroscience research.

It additionally should be noted that NAcc is anatomically divided into separate core and shell subregion, areas, which differ from each other in cytoarchitectonic criteria, afferent and efferent projections as well as in function. As regards to the reward system, both core and shell of NAcc are key regions in the processing. Especially in the clinical context the specific targeting of core and shell regions is of utmost importance (e.g., Voorn et al., 2004; Van der Plasse et al., 2012). The specific projections of these two regions underline the necessity for a functional differentiation in future research, which, in the current thesis, was ignored due to time constraints.

Finally, it needs to be emphasized that there are many controversies about the etiology, nature and clinical criteria of ASD. Since Kanner has published a first possible description almost 80 years ago, a large number of researchers conducted several studies of impairments, autistic individuals must encounter. One prominent researcher,

who in his “fifteen year review” presented very interesting ideas and assumptions, focusing on impairments and deficits in ASD (Baron-Cohen, 2000), but over the years shifting his focus from deficits to differences, falling more and more in line with the neurodiversity movement (Baron-Cohen, 2017).

Conclusion

So, “does social reward processing in ASD differ from neurotypical individuals on the neural and behavioural level?” In fact, it needs to be admitted that within the framework of the current study this main research question as well as the five additional research questions cannot be confirmed.

Nevertheless, it is interesting to understand that various brain regions were detected to significantly increase positive correlation with the activity of either right or left NAcc during increased wanting or liking of the announced or delivered social reward when comparing autistic individuals with controls, and vice versa. Additionally, these specific brain regions can be linked to functions relevant in the context of ASD, with processing of reward, social information, social interaction, language, facial expressions, emotions, affective regulation, or coordination leading the way.

With the selected research domain and topic:”Social reward in autism: an fMRI study of differences in functional connectivity”, this master thesis raises awareness for the framework of neurodiversity, no longer labelling ASD as a pathological condition, but accepting and being open for differences and otherness in humanity.

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Appendices

- Abstract (English)
- Abstract (German)
- Abbreviations
- Tables
- Figures
- Flyer (ASDs)
- Flyer (controls)

Abstract (English)

The exploration of the reward system is fundamental to better understand pathologies driven by modified motivational factors on developing social skills and social cognition. There is a large amount of literature which links reward processing to autism. However, there is still a big knowledge gap in this research field. The current study brings into focus differences in sensitivity of social reward between autistic and neurotypical individuals and strictly separates reward in its components of wanting and liking. To investigate the role and function of anticipation and consumption of social touch, subjective wanting and liking ratings on a visual analogue scale as well as an analysis of the psychophysiological interaction of the acquired fMRI data were used. A sample size of 49 voluntary participants were tested in this fMRI case-control study with mixed between-within subject design. Participants were placed inside the fMRI scanner while slow, medium, and fast paced touches were administered on their right radial bone. Overall, results could not confirm any significant differences between the two groups, neither in functional connectivity nor in subjective ratings. Nevertheless, several brain areas were detected to increase connectivity with both left and right nucleus accumbens when comparing the two groups during increased wanting and liking of the announced and delivered touch. This study is a new milestone in a research field, where lot of discussions and controversies still dominate. A better understanding of autistic individuals' differences related to the reward system is inevitable to enable a life without stigmatisation and with the naturalness of neurodiversity.

Keywords: autism, social reward, wanting, liking, functional connectivity, nucleus accumbens, fMRI, neurodiversity

Abstract (German)

Die Erforschung des Belohnungssystems ist grundlegend für das Verständnis von Pathologien, die von Motivationsfaktoren bezüglich sozialer Fähigkeiten und sozialer Kognition angetrieben werden. Es gibt bereits viel Literatur, die das Belohnungssystem mit Autismus in Zusammenhang bringt. Die Wissenslücke in diesem Forschungsfeld ist jedoch immer noch sehr groß. Die vorliegende Studie rückt die Unterschiede in der Sensibilität von sozialer Belohnung zwischen Menschen mit einer Diagnose aus dem Autismusspektrum und neurotypischen Personen in den Fokus und trennt das Belohnungssystem in seine Komponenten Wollen und Mögen. Um Rolle und Funktion der Antizipation und des Konsums sozialer Berührung zu untersuchen, wurden subjektive Bewertungen auf einer visuellen Analogskala erfragt, sowie eine PPI-Analyse der erfassten fMRT-Daten durchgeführt. Eine Stichprobe von 49 freiwilligen Teilnehmenden wurde in dieser fMRT-Fall-Kontroll-Studie mit gemischtem between-within Design getestet. Langsame, mittlere und schnelle Berührungen wurden an der rechten Speiche der Teilnehmenden vollzogen, welche so bequem wie möglich im fMRT-Scanner Platz nahmen. Insgesamt konnten die Ergebnisse keine signifikanten Unterschiede zwischen den beiden Gruppen bestätigen, weder die funktionelle Konnektivität noch die subjektiven Bewertungen betreffend. Nichtsdestotrotz konnte beim Vergleich der beiden Gruppen beobachtet werden, dass mehrere Hirnareale die Konnektivität sowohl mit dem linken als auch mit dem rechten Nucleus accumbens erhöhten. Diese Studie stellt einen neuen Meilenstein in einem Forschungsfeld dar, in welchem noch viele kontroverse Diskussionen und Ungewissheiten dominieren. Ein besseres Verständnis der Besonderheiten von Menschen mit einer Diagnose aus dem Autismusspektrum ist unumgänglich, um ein Leben weg von Stigmatisierung hin zu Inklusion und Neurodiversität zu ermöglichen.

Schlagworte: Autismus, soziale Belohnung, wollen, mögen, funktionelle Konnektivität, Nucleus accumbens, fMRT, Neurodiversität

Abbreviations

VAS	visual analogue scale
PPI	psychophysiological interaction
ASD	autism spectrum disorder
DSM-5	Diagnostic and Statistical Manual of Mental Disorders (5th ed.)
HFA	high-functioning autism
ToM	theory of mind
fMRI	functional magnetic resonance imaging
OFC	orbital frontal cortex
TC	temporal cortex
ACC	anterior cingulate cortex
vmPFC	ventromedial prefrontal cortex
NAcc	nucleus accumbens
ROI	region of interest
FC	frontal cortex
DBS	deep brain stimulation
BOLD	blood oxygen-level-dependent
PET	positron emission tomography
EMG	Electromyography
AQ	Autism-Spectrum Quotient
MVC	maximum voluntary contraction
SPSS	Statistical Package for the Social Sciences
ANOVA	analysis of variance
MRI	magnetic resonance imaging
SPM	Statistical Parametric Mapping
EPI	echo-planar imaging
MNI	Montreal Neurological Institute
EOI	effect of interest
CON	cingulo-opercular network
IFG	inferior frontal gyrus
PCG	precentral gyrus
FFA	fusiform face area

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Flyer (ASDs)

TEILNEHMER_INNEN FÜR STUDIE GESUCHT

Sie sind zwischen **18 und 65 Jahre** alt, haben eine klinische Diagnose aus dem **Autismusspektrum** und mögen **Kakaomilch** sowie **sanfte Berührungen**?

Dann melden Sie sich, um bei unserer Studie mitzumachen und dafür eine **finanzielle Entschädigung** sowie **Bilder Ihres Gehirns** zu erhalten.

In dieser Studie versuchen wir herauszufinden, wie Essens- und Berührungsreize wahrgenommen werden und welche Rolle Motivation für (das „Wollen“) und die Reaktion auf (das „Mögen“) diese Reize spielt.

Nachdem wir mit einem Onlinefragebogen geprüft haben, dass Sie für die Teilnahme geeignet sind, wird ein Termin mit Ihnen ausgemacht um unser Labor zu besuchen.

In unserem Labor werden Sie einige Aufgaben ausführen, die Berührungsreize am Unterarm und das Trinken von Kakaomilch beinhalten. Außerdem wird während dieser Aufgaben Ihre Gehirnaktivität mit funktioneller Magnetresonanztomographie (fMRT) gemessen.

Dauer: Die Studie dauert maximal **3 Stunden**.

Ort: Die Studie findet an der **Universitätszahnklinik der Medizinischen Universität Wien**, Sensengasse 2a, 1090 Wien statt.

Bei Interesse schreiben Sie bitte eine E-Mail an
reward.univie@gmail.com

Flyer (Controls)

TEILNEHMER_INNEN FÜR STUDIE GESUCHT

Sie sind ca. **zwischen 35 und 65 Jahre** alt, **gesund**, und mögen **Kakaomilch** sowie **sanfte Berührungen**? Außerdem sind Sie **Rechtshänder** und studieren **nicht Psychologie**?

Dann melden Sie sich, um bei unserer Studie mitzumachen und dafür eine **finanzielle Entschädigung** sowie **Bilder Ihres Gehirns** zu erhalten.

In dieser Studie versuchen wir herauszufinden, wie Essens- und Berührungsreize wahrgenommen werden und welche Rolle Motivation für (das „Wollen“) und die Reaktion auf (das „Mögen“) diese Reize spielt.

Nachdem wir mit einem Onlinefragebogen geprüft haben, dass Sie für die Teilnahme geeignet sind, wird ein Termin mit Ihnen ausgemacht um unser Labor zu besuchen.

In unserem Labor werden Sie einige Aufgaben ausführen, die Berührungsreize am Unterarm und das Trinken von Kakaomilch beinhalten. Außerdem wird während dieser Aufgaben Ihre Gehirnaktivität mit funktioneller Magnetresonanztomographie (fMRT) gemessen.

Dauer: Die Studie dauert maximal **3 Stunden**.

Ort: Die Studie findet an der **Universitätszahnklinik der Medizinischen Universität Wien**, Sensengasse 2a, 1090 Wien statt.

Bei Interesse schreiben Sie bitte eine E-Mail an
reward.univie@gmail.com