universität wien

MASTERARBEIT

Titel der Masterarbeit

P3 Topographies Of Different Sensory Modalities:

Testing the Common Pathway Hypothesis of P3 Generation

Verfasser

Daniel Attia, BA

angestrebter akademischer Grad

Master of Science (MSc)

Wien, 2014

Studienkennzahl lt. Studienblatt:	A 066 013
Studienrichtung lt. Studienblatt:	Masterstudium Joint Degree Programme MEi:CogSci – Cognitive Science
Betreuerin / Betreuer:	Prof. Dr. Med. Zvezdan Pirtošek

Contents

0 Foreword

During my studies in Philosophy I mainly focused on the role of body establishing perception and world understanding. Switching from a philosophical investigation to a natural scientific investigation in the field of Cognitive Neuroscience and Cognitive Psychology is a challenging endeavor: a vast amount of new knowledge, a different way of thinking and a new understanding has to be learned, while the interest in such a complex field as human cognition remains the same. Having one eye on the present and one on the future, I was searching for a research question that was elementary enough to get me well acquainted with ERP research, yet also complex enough to build on it for further future investigations. Therefore, I decided to circle my research around the P3 Potential, an ERP component, which is well studied in ERP research and fairly easy to isolate.

The study presented here is a merely descriptive one, where the effects and differences of two different sensory modalities on P3 scalp distribution are analyzed and compared. My aim is to further build on this knowledge for future research on topics such as meditation, where e.g. the P3 of long-term meditators has been found to differ in comparison to novices regarding amplitude and latency (Cranson, Goddard, Orme-Johnson, & Schuster, 1990).

1 Structure of Thesis

I start by introducing the subject of my thesis. A brief explanation of the history, state of the art and theory is given here. Also the research question and the hypothesis are formulated and elaborated here.
Afterwards, a definition of attention and a concise background on relevant and important research in that area will be given to the reader.
In chapter 4, I will provide the most important and basic information on the event-related potentials (ERP) technique to the reader. A brief overview over its history will be given. The advantages and disadvantages of this measurement, basic underlying electrical concepts, neural origins of ERPs and an introduction to the major and relevant ERP components will be elaborated here as well.
Chapter 5 focuses on the P3 component in greater detail. Arguments for the endogenicity of the P3, its subcomponents and neural sources will be discussed in this chapter.
In chapter 6, the study will be presented. Aim of the study, methods, results as well as discussion is given here.
Finally, the thesis and findings will be recapitulated in chapter 6: Conclusion of Thesis.

In the appendix, additional information (paradigm & instructions, abstract, curriculum vitae) can be found.

2 Introduction

In everyday life, the rapid detection of changes in our environment is crucial for survival. For that reason several attentional mechanisms have evolved and several methods developed to study them. One of the best-studied physiological “windows” on attention is the P3 potential (also called P300 or late positive component), first measured by Chapman and Bragdon (1964). It is an event related potential (ERP), with a peak-amplitude timing at roughly 250 - 600ms from stimulus onset depending on the modality, task conditions, age, gender (Katayama & Polich, 1998; Brumback, Arbel, Donchin, & Goldman, 2012; Polich & Kok, 1995) and a multitude of environmental factors, such as ethanol, marijuana and nicotine intake (Polich & Criado, 2006; Evans, Maxfield, Van Rensburg, Oliver, Jentink, & Drobes, 2013). P3 is considered to be an endogenous potential (Donchin, Ritter & McCallum, 1978; Katayama & Polich, 1999), generated irrespectively of the actual sensory modality (visual, auditory, somatosensory). The subject’s reaction is crucial for the generation of the P3 potential, which has been tied to attentional, evaluative, categorization and memory processes (Polich, 2007; Squires, Squires, & Hillyard, 1975; Comerchero & Polich, 1999). Figure 1 shows the currently accepted model for its generation The context update theory proposes that after initial sensory processing, the new incoming stimulus is compared to the previous one, which is stored in the working memory (Polich, 2007). If the stimulus remains the same or similar enough, only exogenous, sensory evoked potentials (N1, P2, N2) are generated. However, if the incoming stimulus is significantly different, the stored neural representation of the environment gets updated, resulting in the generation of the P3 potential (Polich, 2007; Polich, 2003).

CONTEXT UPDATING THEORY OF P300

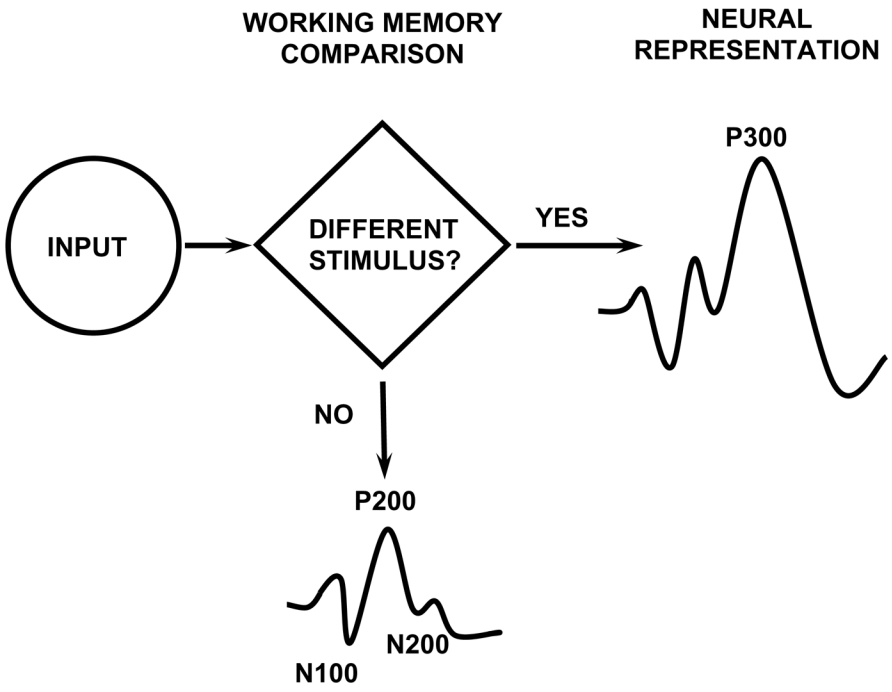

Figure 1: Schematic illustration of the P3 context-updating model. After initial sensory processing, the new incoming stimulus is compared with the previous neural representation of the stimulus environment, which is stored in the working memory (Polich, 2007). If the stimulus remains the same or similar enough, only sensory evoked potentials (N1, P2, N2) are generated. However, if the incoming stimulus is significantly different, the stored neural representation of the environment gets updated, resulting in the generation of P3 potential. (Copyright Polich, 2003)

Subjects instructed to ignore a target tone exhibit a decreased P3 signal (Polich, 2007). This finding led to the hypothesis that P3 consists of separable subcomponents. In the study conducted by Squires et al. (1975) P3 signals between subjects who paid active attention to the stimuli were compared with P3 signals where they had to pay no attention to them. Their results showed that the P3 potentials obtained in these two conditions differed both in latency and scalp topography. In conditions where subjects ignored the rare tones, a positive-going potential occurred 220ms - 280ms poststimulus. This component was termed P3a in contrast to the positive-going potential P3b that occurred when subjects paid attention to infrequent tones. The P3a has its maximum

amplitude over fronto-central electrode sites and is associated with attention-related processing as well as with the processing of novelty stimuli and can be observed during orienting and involuntary shifts to changes in the environment (Polich, 2003). The P3b is associated with attention and seems to be related to memory processing (Polich, 2007) and was generated 310ms - 380ms after stimulus onset with a maximum latency over temporal-parietal electrode sites.

2.1 Research Question

In many studies the P3 potential is usually evoked via the so-called Oddball paradigm, where usually two or three different kinds of stimuli are presented with different probabilities in a random order. The subject is required to discriminate an infrequent target stimulus from a frequent standard stimulus by noting the occurrence of the target, typically by pressing a button or mentally counting. (Comerchero & Polich, 1999) (for more details see chapter 6.2.1., Figure 4, p.37).

The research question of my master thesis is whether the scalp topography evoked via the Oddball paradigm varies across two stimulus modalities, the visual and the auditory. Previous research indicates that the underlying neural generators may well be identical (see Table 2, p.34).

2.2 Hypothesis

The null-hypothesis (H_0) of our research question is, that there are no reliable differences in scalp topography of the P3 across the visual and auditory stimulus modalities.

1. Previous literature (Table 2, p.34) suggests that there may be no significant differences in scalp topography across different stimulus modalities. Among others, Katayama and Polich (1999) tested for differences across different

modalities (i.e. auditory and visual) and found that the scalp topography was identical for both. Therefore, it can be concluded that the underlying neural generators of the P3 potential are endogenous and identical across different sensory modalities.

If H_0 is true and the topography is indeed the same, this would strongly suggest the same underlying neural sources and processing for the P3 potential, supporting also its purely endogenous property and independency of the physical attributes of the stimuli for its generation.

2. One possible explanation why previous studies did not detect significant differences in scalp topography across stimulus modalities could be due to their methodological approach and a too small array of electrodes to account for minute differences. Therefore it would be quite possible that small differences that haven't been found so far would be detectable with high-resolution EEG and a whole-scalp assessment of the topography. In case of different scalp topography, at least partially different neural underpinnings would be reasonable to assume. Therefore, a rejection of H_0 would, in contrast, mean that there are differences in scalp distribution, inferring also a bigger role of exogenous physical attributes of stimuli to P3 generation.

To sum it up, in case of no differences in scalp topography (H_0) the most straightforward conclusion would be that the neural underpinnings are identical. A further conclusion would be that the P3 is a purely endogenous potential and independent of the physical attributes of the incoming stimuli. In case of differences, partially different neural underpinnings and at least partially exogenous role of stimuli for the P3 potential could be concluded.

Chapter 3 gives a definition of attention and presents a concise background on relevant and important research in that area to the reader.

3 Background

3.1. Overview over Research on Attention

Attention has been one of the first questions of interest in Psychology and is still one of the most studied topics in the field of Cognitive Science.
Since the establishment of Psychology as a scientific discipline, a lot of research has been done investigating it with top-down as well as bottom-up approaches.

3.1.1. Attention: Introduction and Definition

In Principles of Psychology, William James, defines attention as

> the taking possession by the mind, in clear and vivid form, of one out of what seem several simultaneously possible objects of trains of thought. […] It implies withdrawal from some things in order to deal effectively with others. (James, 1890)

To properly focus on one out of several possible objects of perception, the other objects that are of less interest to us must remain in the background while the objects of interest are put in focus. This is not only related to objects in the external world but is also valid for thoughts, imaginations, and other internal processes that require our attention. Attention can also be described as the cognitive process of selectively concentrating on one aspect of the environment while ignoring others, also described as the allocation of resources. (Anderson, 2005)

For the purposes of my thesis however, it suffices to define attention as the process that enables focused processing of the relevant data out of the enormous amount of incoming information available through our senses, and cognitive processes (De Weerd, 2003; Rao, 2003). It includes conscious and unconscious processes and allows us to use our limited mental resources according to the stimuli that are of interest or importance to us. (Bahrami, Carmel, Walsh, Rees, & Lavie, 2008; Shear, 1999).

3.1.2. Brief Overview

The study of attention in experimental psychology started with Wilhelm Wundt, who is considered as the father of experimental psychology[1] and founded the first laboratory specialized for psychological research in 1879. (Schacter, Gilbert, Wegner, 2010; Sternberg, 2012).

Donders (1869)[2] studied the speed of mental processes in laboratory. To measure this, subjects had to identify the stimulus and initiate a motor response afterwards. The time between stimulus discrimination and motor response initiation was then measured.

William James made a distinction between sensorial attention (directed to a physical stimulus) and intellectual attention (directed to ideal objects or mental representations).
He also distinguished between immediate attention (directly and physically perceived at a given moment) and derived attention (not directly perceived at a given moment, and not physically present). According to James attention makes us perceive, conceive, distinguish, remember, and shorten reaction time. (James, 1890)

Between 1910 and 1949 research in behaviorism became the mainstream epistemology and researchers lost interest on the topic of attention. However, important research on attention still has been done. Jersild (1927) found out that the context plays an important role for the processing of stimulus. He could show, that pure lists (e.g. a list consisting only of names of animals) were easier and faster to process than mixed lists (e.g. a list consisting of names of animals interspersed with names of fruits).
Another important finding was the psychological refractory period, discovered by Telford (1931). He discovered that neurons have a refractory period after stimulation, making them less sensitive to ongoing stimulation during this time frame.
J.R. Stroop developed the eponymous task, which elicited the Stroop Effect (1935). The Stroop task consisted of a list of names of colors. The word itself was about a different

[1] See http://plato.stanford.edu/entries/wilhelm-wundt/
[2] See also Kosinski, 2008

color than the actual letters showed, e.g. Green Blue Red Purple Green. This incongruence of word and color lead to substantially prolonged reaction times.

As information technology began to increase, a change in the mainstream epistemology shifted in the 1950s from behaviorism towards realism (also known as the "cognitive revolution" (Harré, 2002)) and research on attention flourished. This was also due to the contribution of David Broadbent and the notion of capacity limitations (from technologies such as telephone exchange) influencing discussions of perception and attention.[3] He remarked that

> […] the point of permanent value which will remain in psychology if the fashion for communication theory wanes, will be the emphasis on problems of capacity. […] The fact that any given channel has a limit is a matter of central importance to communication engineers, and it is correspondingly forced on the attention of psychologists who use their terms. (Broadbent, 1958, 5)

With the cognitive revolution, processes as attention, that have been neglected in the paradigm of behaviorism, began to be addressed again as objects of scientific study.

[3] See also http://plato.stanford.edu/entries/attention/

4 Event - Related Potentials (ERPs)[4]

In this chapter, the most important and basic information on the event-related potentials (ERP) technique is presented. A brief overview over its history, the advantages and disadvantages of EEG/ERP measurements, basic underlying electrical concepts, neural origins of ERPs and an introduction to the major and relevant ERP components will be elaborated as well.

4.1 Electroencephalography (EEG)[5]

In 1929, Hans Berger revealed that one could measure the electrical activity of the human brain by placing electrodes on the scalp, amplifying the signal and plotting the changes in voltage over a period of time and termed this electrical activity the electroencephalogram (EEG). These voltage deflections reflect the sum of several underlying latent components that can be relatively independent from another (Luck 2005).

The electrical potential generated by a single neuron is too small to be detected by EEG. The recorded activity therefore always reflects the summation of synchronous activity of thousands or millions of neurons that have a similar spatial orientation. As voltage fields fall off with the square of distance, activity from deeper brain sources is more difficult to detect on the scalp than currents flowing near the skull.
EEG proved to be very useful in both clinical and scientific applications. In its raw form however, it is very difficult to measure highly specific neural processes with EEG, which is the actual interest in the Cognitive Sciences. EEG itself represents hundreds of different neural sources activity, measuring the conglomeration of the whole activity on the scalp surface at the same time. Therefore, it is very difficult to isolate neurocognitive

[4] For this chapter, Luck (2005) is mainly used as reference.
[5] See also (Luck, 2005, p.3-4)

processes. In order to do so, sensory, cognitive and motor processes need to be extracted by averaging, which leads us to the Event-related Potentials (ERPs).

4.2 Introduction to Event-Related Potentials (ERPs)[6]

An ERP is the measured brain response via EEG, which is associated with the presence or absence of a specific sensory, cognitive, or motor event. It can be defined as “scalp-recorded neural activity that is generated in a given neuroanatomical module when a specific computational operation is performed” (Luck, 2005, 59), where the same module represents the same cognitive function.

As the brain response to a single stimulus or event of interest is not visible in the EEG recording of a single trial, many of them must be carried out, so that random brain activity (so-called “noise”) can get averaged out, with the relevant waveform of interest remaining.

Originally, ERPs were termed evoked potentials (EPs), as their generation is evoked by a stimulus, in contrast to spontaneous EEG measurements. Nowadays the most common used term is event-related potential, to “display stable time relationships to a definable reference event” (Vaughan, 1969, 46) and to warden the fact, that absence of an important stimulus and merely psychological events may also generate an electrical potential response.

In 1964, the modern era of ERP research began with the discovery of the first cognitive ERP component, named contingent negative variation (CNV) (Walter, Cooper, Aldridge, McCallum, & Winter, 1964). In this study, subjects were presented with a warning signal followed by a target stimulus, which appeared 500ms or 1000ms later. Only when subjects were required to press a button upon detecting the target they expected, a large negative voltage, the CNV, at frontal electrode sites were observed during the

[6] See ebd., p.3-7

warning signal and the target. The CNV depends on the expectancy, attention and arousal level of the subject for the upcoming target (Walter et al., 1964; Tecce, 1972).

The next big step in ERP research was made with the discovery of the P3 component (Chapman & Bragdon, 1964). In 1965, the P3 component was already introduced as a function of the subject's degree of uncertainty with respect to the sensory modality of the stimulus (Sutton, Braren, Zubin, & John, 1965). When subjects failed to predict whether the next stimulus would be auditory or visual, the stimulus elicited a large positive P3 component that peaked around 300ms after stimulus onset. In cases where they were able to predict the next stimulus modality, a much smaller P3 component was generated.
Over the next years, research focused on identifying cognitive ERP components and the development and improvement of recording methods and analysis. In 1980's ERP research flourished due to the availability of inexpensive computers and the general increase of research in cognitive neuroscience.

Currently, ERP is one of the most widely used methods in Cognitive Neuroscience, as it offers some advantages, which other neuroscientific methods of measurement (e.g. fMRI) lack.

4.2.1 Advantages and Disadvantages[7]

4.2.1.1 Comparison with Behavioral Measures

In comparison with behavioral measures, the first big advantage is, that ERPs

> provide a continuous measure of processing between a stimulus and a response, making it possible to determine which stage or stages of processing are affected by a specific experimental manipulation. (Luck 2005, 21)

[7] See ebd., p.21-26

If we look at e.g. a behavioral and an ERP measurement of the Stroop task, it can be seen that on the behavioral level it, would be hard to determine whether the result of slower reaction times in the Stroop task would be due to a longer processing of perceptual information or due to post-perceptual response processing. While studies of the P3 potential show longer latency when perceptual processing needs more effort, no such latency has been observed in the case of the Stroop task. This finding indicates, that the delay lies in the response time on a post-perceptual stage rather than on the perceptual level itself. Another advantage is the possibility of online measurement of processed stimuli without behavioral response.

One of the main disadvantages however, is the large number of trials needed to detect ERPs in recordings, as their signal is very small.
Also, the fact "that the functional significance of an ERP component is virtually never as clear as the functional significance of a behavioral response" (Luck 2005, 22), is a disadvantage compared to many behavioral measures.

Another huge disadvantage is, that it is very hard to determine which biophysical events underlie the production of specific ERP responses or its consequences for information processing. To give an example:

> When the reaction time (RT) [for button pressing in a behavioral task, D.A.] in condition A is 30ms longer than the RT in condition B, we know that the amount of time required to encode, process and act on the stimuli was 30ms longer in condition A than in condition B. In contrast, when the peak latency of an ERP component is 30ms later in condition A than in condition B, we can draw no conclusions without relying on a long chain of assumptions and inferences […]. (Luck 2005, 22)

4.2.1.2 Temporal and Spatial Resolution

ERPs have a temporal resolution of 1ms or better under good conditions, whereas e.g. hemodynamic measures have a resolution of several seconds. Therefore, it is very easy to detect immediate changes and differences in time.

However, while modern high-resolution EEG provides a great temporal and scalp-based spatial resolution, it can never provide assumption-free and unambiguous answers to questions regarding the anatomical location of the underlying neuronal sources of measured EEG potentials. This is not a technological limitation that can be solved by increasing the number of recording channels, but a fundamental limit imposed by the laws of electrostatics. In spite of this huge limitation, some questions regarding the anatomy of neuronal sources still can be precisely addressed. While different neuronal sources can produce identical scalp EEG topographies, different topographies should be generated by different neuronal circuits.

4.2.1.3 Other Advantages

Other advantages are the non-invasiveness of this technique and the costs.
ERP research is much less expensive than many other techniques (such as PET, fMRI, Single-unit recordings). Therefore much more research labs can afford to conduct brain research by this method.

4.2.2 Basic Electrical Concepts[8]

In this chapter the basic principles of electricity that are relevant for EEG measures are briefly explained.

4.2.2.1 Voltage (E), Current (I), Resistance (R), and Impedance (Z)

Luck (2005, 332) describes electricity as "the flow of charges through a conductive medium. […] In the nervous system much of the electricity is due to the movement of small ions across cell membranes." The most fundamental terms in electricity are voltage, current and resistance.

[8] See ebd., p.333-337

- Voltage is also called electrical potential to signify the potential for electrical current to flow from one pole to another (Luck 2005, 333).
- “Current is the number of charged particles that flow past a given point in a specific amount of time.” (Luck 2005, 333)
- “Resistance is the ability of a substance to keep charged particles from passing (resistance is the inverse of conductance). Three main factors contribute to resistance: (1) the composition of the substance, (2) its length, and (3) its diameter.” It is measured in Ohms (Ω).” (Luck 2005, 334)

The relationship of voltage, current and resistance is summarized by Ohm’s law, which is E = IR, meaning that voltage is equal to the product of the current and resistance.

4.2.2.2 Impedance (Z)

If the current varies over time (called alternating current or AC) the term Impedance is more appropriate than resistance, which applies only for current that is constant over time (also called direct current or DC). As ERPs vary over time, impedance is generally the most relevant concept. For most practical purposes, impedance is analogous to resistance. However, there are few factors that contribute to impedance, but not to DC, such as inductance and capacitance. Most impedance meters measure the using a small sine-wave voltage oscillating at around 10Hz.

4.2.2.3 Electricity and Magnetism

There is no electricity without magnetism:

> Electricity and Magnetism are fundamentally related to each other. […] Current flowing through a conductor generates a magnetic field that flows around the conductor. Moreover, if a magnetic field passes through a conductor, it induces electrical current. […] This is how electrical noise in the environment can induce electrical activity in an ERP subject, in the electrodes, or in the wires leading from electrodes to amplifier. (Luck, 2005, p.336ff)

For this reason, the electrical shielding of the EEG environment is an important factor for noise reduction.

4.2.3 Basics of ERP Experiments[9]

To conduct ERP experiments, electrodes need to be attached on the scalp to pick up the EEG data. The data must then be filtered and amplified and are stored on a computer. Several artifacts like eye blinks should be inspected and removed. Afterwards, the data normally gets averaged to extract the desired ERPs from the overall EEG data. Various filters are then applied to the EEG data to remove noise. Noise can be defined as "any source of variation in the data that is unrelated [to the signal, D.A.], you are trying to record.[…] One researcher's noise may be another researcher's signal." (Luck 2005, 339) The size and timing of the ERP potentials of interest are then measured and analyzed statistically (e.g. ANOVA).

4.2.4 Neural Origins of ERPs[10]

4.2.4.1 Electrical Activity in Neurons

Action potentials and postsynaptic potentials are the two main types of electrical activity of neurons. Action potentials are discrete voltage spikes that travel from the axon hillock of a cell body down to the axon terminals where usually neurotransmitters are released. When these neurotransmitters bind to the receptors of the postsynaptic cell, ion channels open or close as a result. This leads to a graded change in the potential across the cell membrane.

In the majority of cases, surface electrodes that are used in EEG cannot detect action potentials due to reasons of timing and the physical arrangement of axons. When an action potential is generated, current flows first into the axon and then out of it along the axon and down to the axon terminal. The main problem hereby is, that neurons rarely fire at the same time. In this case the current at a given spatial location will be flowing into one axon at the same time that it is flowing out of the other axon, leading to a

[9] See ebd., p.12
[10] See ebd., p.27-34

cancellation of the signal. Therefore only a very small signal will be generated, too small to be properly detected by the surface electrodes.

4.2.4.2 Summation of Postsynaptic Potentials

While action potentials last only about 1 millisecond, postsynaptic potentials usually last tens or hundreds of milliseconds. They are largely confined to the dendrites and cell body and occur instantaneously. These factors allow the postsynaptic potentials to summate rather than to cancel each other out, yielding much stronger signal detection at the scalp. In order to be recordable, these summated voltages must occur at approximately the same time across thousands or millions of neurons and the dipoles of responsible neurons must be spatially aligned.
This occurs most likely in pyramidal cells, which are aligned perpendicular to the surface of the cortex. A dipole is a pair of positive and negative electrical charges that are separated by a small distance.
Whenever the dipoles are more than 90 degrees from each other, they will cancel each other out, yielding a weaker signal with a total cancellation at 180 degrees.

4.2.4.3 Volume Conduction

Electricity does not simply run directly between the two poles of a conductive medium but rather spreads out through the conductor, i.e. the brain. Therefore ERPs spread out and as electricity naturally tends to follow the path of least resistance they spread laterally when they encounter high resistance of the skull. These factors greatly blur and affect the surface distribution of voltage.

4.2.4.4 ERP Localization[11]

In the case of ERP localization we are confronted with the inverse problem: An observed voltage distribution can be explained by an infinite number of different dipole configurations (Helmholtz, 1853). Thus it is impossible to certainly prove the exact anatomical sources/generators responsible for a given voltage distribution alone with EEG. ERP localization techniques generate models of underlying distributions of electrical activity and are evaluated under several constraints. It is not a direct measurement of the internal distribution, but rather a model of the internal configuration of electrical activity.

4.2.5 Major ERP Components[12]

4.2.5.1 General Remarks

An ERP waveform consists of several components comprised of positive or negative voltage fluctuations observed at a distinct point in time. Although different ERP components can be named equally they can be totally unrelated in a functional manner and are not necessarily linked to the same underlying brain activity. If we take components such as P1 and N1, we can easily determine the polarity of the amplitude and the position within the waveform after stimulus onset: P1 indicates the first positive peak and N1 the first negative peak of the overall signal of the ERP component. Sometimes the number after the polarity indicates the latency in milliseconds instead of the position: N100 indicates a negative component with a maximum peak 100ms after stimulus onset, but these indicated latencies can vary significantly in each experiment. The P1 potential could designate e.g. the first positive deflection in a visual modality as well as in an auditory modality. Still one has to be aware of the fact, that they don't designate the same function nor the same evoked potential. Some late components,

[11] For a more detailed discussion on ERP Localization see also ebd., p.267-301
[12] See ebd., 34-45

such as P3 seem modality-independent, but can have modality-specific subcomponents. Even for a single modality, a certain ERP component may be different or unrelated from one experiment to another (Luck 2005, 10ff.)
Besides that it shall be remarked, that different labs have different traditions of plotting the voltages: While some laboratories plot negative voltages upwards, others plot them downwards.

4.2.5.2 Visual Sensory Responses

The first major visual component is the C1 wave and its polarity can vary (i.e. be positive or negative). The C1 wave seems to be generated in the primary visual cortex (area V1), which is folded into the calcarine fissure. The lower visual field is coded on the upper part of the fissure and the upper visual field is coded on the lower part of it. The result is that the recorded voltage on the scalp above the fissure can be either positive or negative, depending on the visual field being processed (Clark, Fan, & Hillyard, 1995; Jeffreys & Axford, 1972). It typically has an onset of 40-60ms poststimulus and peaks 80-100ms poststimulus. It is very sensitive to stimulus parameters like contrast and spatial frequency. Usually the C1 wave is summated with the P1 wave into a single wave.

P1

The P1 potential typically has an onset of 60-90ms poststimulus with a peak between 100-130ms. It is supposed that the early portion of this potential arises from the dorsal extrastriate cortex, showing some later activation at the fusiform gyrus (Di Russo, Martinez, Sereno, Pitzalis, Hillyard, 2002). Similar to the C1 wave, the P1 potential is sensitive to stimulus parameters, including the direction of spatial attention (Hillyard, Vogel, & Luck, 1998) and the subject's state of arousal (Vogel & Luck, 2000).

N1

After the P1 wave, N1, a negative-going voltage deflection can be observed, consisting of several subcomponents. The first subcomponent peaks 100-150ms poststimulus at anterior electrode sites and around 150-200ms two other subcomponents arise from the parietal cortex and from lateral occipital cortex. Spatial attention influences these components (Hillyard et al. 1998, Mangun, 1995). When subjects are performing in discrimination tasks rather than in detecting tasks the occipital N1 subcomponent is larger, reflecting eventually discriminative processing (Hopf, Vogel, Woodman, Heinze, Luck, 2002; Ritter, Simson, Vaughnan, Friedman, 1979; Vogel & Luck, 2000).

P2

The N1 wave is followed by the P2 wave at anterior and central scalp sites. Stimuli containing target features elicit a larger component and enhance it when the targets appear infrequently (Luck & Hillyard, 1994). In this manner, the P2 and P3 potential share common properties. However, the P2 generation is restricted to fairly simple stimulus features, whereas the P3 wave is also generated for complex categories.

4.2.5.3 Auditory Sensory Responses

Very Early Components

Within the first 10ms after the onset of an auditory stimulus peaks arise from various stages along the brainstem auditory pathways called brainstem evoked responses (BERs) or auditory brainstem responses (ABRs). The BERs are then followed by the midlatency components between 10-50ms poststimulus and probably arise partially from the medial geniculate nucleus and the primary auditory cortex. The first reliable effects of attention can be observed for the midlatency components, which are then followed by the auditory P1 wave around 50ms poststimulus. It is largest at frontocentral electrode sites.

N1

Similar to the visual N1 potential, the auditory N1 consists of subcomponents: a frontocentral component that peaks around 75ms and seems to be generated at the auditory cortex; a vertex-maximum potential that peaks around 100ms, and a laterally distributed component that peaks around 150ms, generated in the superior temporal gyrus (Näätänen & Picton, 1987) and that is sensitive to attention.

Mismatch Negativity

The mismatch negativity (MMN) is observed when subjects are exposed to a repetitive train of identical stimuli with occasional mismatching stimuli, such as an occasional difference in the frequency of a tone (Näätänen, Gaillard, & Mäntysalo, 1978). It is a negative-going voltage deflection that is largest at central midline scalp sites and peaks around 160-220ms. It is thought to reflect an automatic process that compares incoming stimuli to a sensory memory trace of already presented stimuli.

The N2 Family

A repetitive, non-target stimulus elicits an N2 deflection (Näätänen & Picton, 1986). If other stimuli occasionally appear in the repetitive train a larger N2 deflection can be observed. If these deviant stimuli are task-relevant, a later N2 effect can be observed, named N2b. It is larger for less frequent targets and is thought to be a sign of the stimulus categorization process. For auditory stimuli it is largest over central sites, whereas for visual stimuli it is for posterior sites.

The P3 Family

The P3 potential consists of several distinguishable components. The first major distinction is a frontally maximal P3a component and a parietally maximal P3b component (Squires et al., 1975). Both are elicited by unpredictable infrequent shifts in e.g. tone shifts. However, the P3b is only present for task-relevant stimuli. Other studies

revealed that an unexpected, unusual, task-irrelevant stimulus within an attended stimulus train elicits a frontal P3-like response (Courchesne, Hillyard, & Galambos, 1975; Polich & Comerchero, 2003; Soltani & Knight, 2000).

Although the P3 is one of the best-studied ERPs there is still no clear consensus regarding what neural or cognitive process the P3 wave reflects. For one reason, the P3 wave is present in almost every ERP experiment, making it hard to designate a specific function to it. Another reason is that it is very likely that a lot of overlapping components appear within the time range of the P3 component. These overlapping components reflect various cognitive processes and make it hard to solely isolate the P3 component.

Donchin (1981) proposed the context updating theory (see Figure 1). The key factor for the elicitation of a P3 wave is target probability. As target probability gets smaller, the P3 amplitude gets larger. P3 amplitude also gets larger when subjects put more effort to a task, leading to the idea that this component can be used as a measure of resource allocation (Isreal, Chesney, Wickens, Donchin, 1980). If the subject is uncertain of whether a given stimulus was the target or non-target, the amplitude gets smaller. Therefore, one has to consider these two increasing and decreasing factors, which can coincide in an experimental setting.

The P3 is generated after stimulus categorization processing. Therefore, any manipulation that occurs before stimulus categorization must increase P3 latency. On the contrary, P3 latency is not sensitive to the time required to select and execute a motor response after stimulus categorization (Kutas, McCarthy, & Donchin, 1977; Magliero, Bashore, Coles, Donchin, 1984). There is also converging evidence that there are other positive waveforms that arise during the time range of the P3 wave and the negative-going phase that follows. In some cases these late positive components appear as secondary peaks and are labeled as positive slow waves (PSW) (Squires et al., 1975; Johnson & Donchin, 1985; McCallum, 1987; Ruchkin, Johnson, Canoune, Ritter, & Hammer, 1990). PSW components are very similar in morphology and

topography and in the functional correlates that have been attributed to P3 (García-Larrea & Cézanne-Bert, 1998).[13]

Figure 2 summarizes the major ERP components elicited after auditory stimulus presentation.

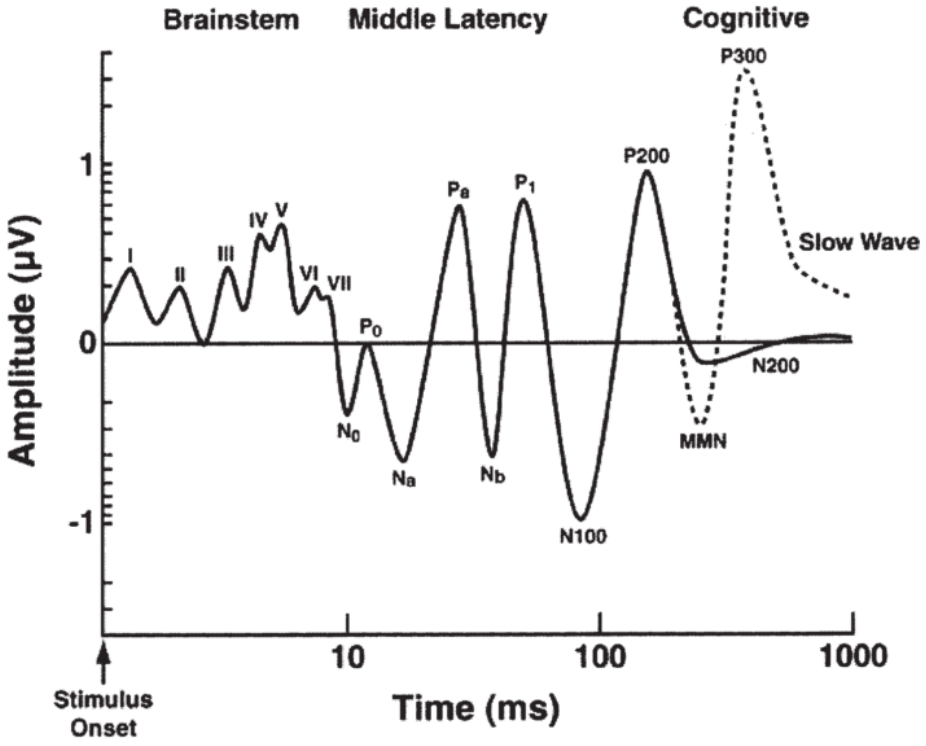

Figure 2: A depiction of evoked potentials (EPs) as well as event-related potentials (ERPs) after auditory stimulus presentation. Potentials are divided in brainstem, middle latency and cognitive components and are characterized by amplitude and latency. Logarithmic scales for amplitude and latency are used. Copyright Cahn & Polich, 2006.

[13] It has been attributed to response related processes (Ruchkin, Munson, & Sutton, 1982; Johnson & Donchin, 1985; Roth, Ford, & Kopell, 1978; Kok & Looren de Jong, 1980; Naylor, Halliday, Callaway, Yano, & Walton, 1987; Falkenstein, Hohnsbein, & Hoormann, 1994) and to sustained attention to task performance (Gevins et al., 1996) while other authors have suggested that PSW might index very late processes arising after the response has been already completed (Ruchkin et al., 1990; Stuss & Picton, 1978; Falkenstein et al., 1994). Johnson and Donchin (1985) proposed that positive parietal SWs could be interpreted as additional P3s occurring whenever a subject takes serial decisions after target evaluation. Within the context updating theory, such additional P3s were thought to reflect the updating of working memory prompted by each of the decisions. Although this model explains many aspects related to PSW generation, it appears too restrictive to account for all of them (García-Larrea & Cézanne-Bert, 1998).

5 A Closer Look on P3

Chapter 5 will focus on the P3 component in greater detail, discussing the endogenicity of P3, its subcomponents as well as its neural origins. Before focusing on specific arguments for the endogenicity, some general remarks on endogenous and exogenous attention are presented in the following subchapter.

5.1 Endogenous and Exogenous Attention

Top-down processing, also called executive attention, goal-driven, or endogenous attention, is largely under volitional control of the attending subject and is mediated primarily by the frontal cortex and the basal ganglia (Posner & Peterson, 1990; Posner & Rothbart,1998). The focus of attention can be influenced purposefully (e.g. by staying voluntarily anticipatory for a specific stimulus that is about to occur).

Bottom-up processing, also called stimulus-driven or exogenous attention, describes attentional processing, which is driven by the physical properties of an object. It is mediated primarily by the parietal and temporal cortices, as well as by the brainstem (Posner & Peterson, 1990). A sudden noise or quick motion usually attracts our attention in a non-volitional, automatic manner (Theeuwes, 1991).

In ERP research the early sensory responses are called exogenous components as their generation relies rather on external than internal factors in contrast to endogenous components, which indicate the greater importance of internal than external factors (Luck, 2005).

5.2 Endogenicity of P3

In 1978, Donchin et al. defined several exogenous and endogenous ERP components. Since then, the P3 potential has been considered as endogenous, information

processing, component. It has been shown that the generation of the P3 component is independent from physical parameters of the eliciting stimulus and can be evoked even in the absence of a stimulus, when trains of regular stimuli are interrupted by stimulus omissions (Naumann et al., 1992; Linden 2005). Its generation seems modality independent if the stimulus task role is equivalent (Donchin et al., 1978). Additionally, its dependency on the attention and arousal of the subject is important as well (Polich & Kok, 1995). It is an active decision process and leads to a strong similarity among different P3 distributions (Snyder, Hillyard & Galambos, 1980).

5.3 P3a and P3b

It has been shown that presented stimuli, when ignored by the subject, lead to smaller amplitude or even to a lack of the P3 response. Researchers found out, that subjects who were instructed to ignore the target tone, still exhibited a P3 signal. This led to the assumption that the P3 consists of subcomponents. Squires et al. (1975) compared P3 signals between subjects who paid active attention to the stimuli with conditions where the subjects paid no attention at all. The results showed that the two P3 potentials differed in latency and scalp topography. In the conditions, where subjects ignored the rare tones, a positive-going potential, which occurred with a latency of 220ms - 280ms was generated. This component was termed P3a and has its maximum amplitude over frontal-central electrode sites (Comerchero & Polich, 1999). In contrast to the P3a they also observed a positive-going potential that occurred when subjects paid attention to the infrequent tones 310ms - 380ms poststimulus, termed P3b. It is associated with attention-related processing as well as the processing of novelty and can be observed during orienting and involuntary shifts to changes in the environment (Polich, 2003). The P3b has its maximum over temporo-parietal electrode sites, is associated with attention and seems to be related to memory processing. In contrast to the P3b, the P3a habituates with repeated presentations (Polich, 2007).

5.4 Neural Origins of P3[14]

Even though the P3 potential has been extensively studied, the neural generators are still imprecisely delineated. Nevertheless there are some important findings, which will be presented in greater detail in the following subchapters.

5.4.1 Lesion studies

Patients with frontal lobe lesions had a diminution of P3a amplitude, whereas the same patients demonstrated a parietal maximum for the P3b, indicating that frontal lobe integrity is crucial for P3a generation (Knight, 1984; Knight, Grabowecky, & Scabini, 1995; Daffner et al., 2000a). Patients with hippocampal lesions showed a reduction in P3a amplitudes from novel distractors across modalities, but normal P3b amplitudes from targets (Knight, 1996). However, other studies such as from individuals after temporal lobectomy (Johnson, 1988; Smith & Halgren, 1989) and from patients with medial temporal lobe damage (Onofrj et al., 1992; Rugg, Pickles, Potter, & Roberts, 1991) did not show a direct contribution of the hippocampal formation to P3 generation (Molnar, 1994). Patients with bilateral hippocampal lesions demonstrated no reliable P3 differences relative to controls (Polich & Squire, 1993), strengthening the assumption of no direct hippocampal contribution. Severe reductions in P3 amplitude were consistently observed with unilateral lesions to the temporo-parietal junction, in particular for the auditory (Knight & Nakada, 1998; Verleger, Heide, Butt, & Kömpf, 1994) and somatosensory targets (Yamaguchi & Knight, 1992; Yamaguchi & Knight, 1991), and less effect on the visual modality (Verleger et al. 1994; Knight, 1997). These findings on the temporo-parietal junction suggest a circuit pathway between frontal and temporo-parietal areas for the P3a and P3b (Soltani & Knight, 2000; Polich, 2003).

Altogether, P3b seems to be mainly affected by temporo-parietal junction lesions, whereas P3a responses are compromised in patients with a wide range of lesions, including the medial temporal, frontal, and parietal lobes (Linden, 2005).

[14] For reviews on neural generators see Polich 2007; Linden 2005; Soltani & Knight 2000.

5.4.2 Intracranial Recordings

Studies of the hippocampal formation via intracranial recordings in humans suggested that at least some portion of the P3 is generated in the medial temporal lobe (Halgren et al., 1980; McCarthy, Wood, Williamson, & Spencer, 1989). Many other possible generators have been reported such as in the prefrontal cortex and the parietal lobes (Smith et al., 1990; Halgren et al., 1995), the temporal lobe (Halgren et al., 1995) and the anterior cingulate (Smith et al., 1990; Wang, Ulbert, Schomer, Marinkovic, & Halgren, 2005). All these areas responded across stimulation modalities. However, the primary and secondary auditory cortices showed a modality-specific target response for auditory stimuli (Halgren et al., 1995).

5.4.3 Other Findings

fMRI[15] and ERP studies have demonstrated frontal lobe activity for the detection of rare and alerting stimuli (McCarthy, Luby, Gore, & Goldman-Rakic, 1997; (Potts, Liotti, Tucker, & Posner, 1996; Verbaten, Huyben, & Kemner, 1997). Initial neural activation during auditory oddball discrimination may originate from right frontal cortex (Polich et al., 1997), as P3 amplitude is larger over the right compared to left frontal and central areas (Alexander et al., 1995, 1996). Studies indicate that P3a and P3b generation stems from frontal and temporo-parietal activations (Ebmeier et al., 1995; Kirino, Belger, Goldman-Rakic, & McCarthy, 2000; Wronka, Kaiser, & Coenen, 2012). Neural responsivity to novelty seems to be governed by a frontal attention mechanism (Daffner

[15] For a general critique on fMRI-ERP comparisons on P3 sources see Wronka, Kaiser, & Coenen, 2012: "Functional magnetic resonance imaging (fMRI) can provide maps of brain activation with millimeter spatial resolution however it is limited in its temporal precision to the order of seconds. This technique [...] does not allow to define which of these differences [i.e. brain activations elicited by distinct stimuli, D.A.] are specifically related to the generation of the P3a or the P3b. [...] Moreover, it can not be completely excluded that the brain activation pattern observed in neuroimaging studies also reflects the generation of the ERP components other than the P3 (e.g. N2). Therefore, it is difficult to say whether results obtained with fMRI and the scalp-recorded positive ERP components dubbed as the P3a and P3b actually correspond to the same physiological processes. Hence, so far it is not clear to what extent frontal and parieto-temporal brain regions are involved in generation of P3a and P3b." (Wronka, Kaiser, & Coenen, 2012, 2ff.)

et al., 2000a, 2000b, 2000c; Suwazono, Machado, & Knight, 2000; Wronka et al., 2012), implying a top-down control (Bledowski, Prvulovic, Goebel, Zanella, & Linden, 2004; (Dien, Spencer, & Donchin, 2004; Kiehl et al., 2005; Opitz, Mecklinger, Cramon, & Kruggel, 1999; Opitz, 2003). Attentional resources to maintain memory items in parietal regions may result from response organization via bottom-up processing (Conroy & Polich, 2007; Nieuwenhuis, Aston-Jones, & Cohen, 2005; Verleger, Jaśkowski, & Wascher, 2005; Wronka et al., 2012).

Visual and auditory target detection activated a network around the Sylvian fissure, including the supramarginal gyrus, inferior and middle frontal gyrus, the insula, and midline areas, including the anterior and posterior cingulate as well as the supplementary motor area (McCarthy et al., 1997; Menon, Ford, Lim, Glover, & Pfefferbaum, 1997; Linden et al., 1999; Yoshiura et al., 1999).

Modality-specific sources were identified in the contralateral insula (Tarkka, Micheloyannis, & Stokić, 1996) and prefrontal cortex (Valeriani, Fraioli, Ranghi, & Giaquinto, 2001) for somatosensory stimulation and in higher auditory areas for auditory stimulation (Rogers et al., 1991; Tarkka, Stokić, Basile, & Papanicolaou, 1995; Hegerl & Frodl-Bauch, 1997). However, most of the presumed sources of the P3b seemed to be independent of sensory modality. fMRI studies showed sensory-specific activation in the auditory cortex for auditory stimulation, and in the occipital cortex for visual stimulation as well as along the intraparietal and postcentral sulci (Linden et al., 1999; Yoshiura et al., 1999).

5.4.4 Conclusions

There is strong evidence to implicate the inferior parietal lobe and the temporo-parietal junction, in particular the supramarginal gyrus, in the generation of the P3a and P3b potential. Lateral prefrontal areas seem to contribute only to the P3a generation. Parietal areas showed higher involvement in P3b responses. The cingulate gyrus was found consistently active in fMRI studies and intracranial recordings of target detection (Smith et al., 1990; Wang et al., 2005). Converging evidence of at least two measurement techniques that provide information on localizations of P3 generators are presented in

table 1.

These findings are

> in line with the hypothesis that P3a is related to alerting activity during the initial allocation of attention, while P3b is related to activation of a posterior network when the neuronal model of perceived stimulation is compared with the attentional trace (Wronka et al., 2012, p.51).

Authors	Technique & Strategy for Analysis	Stimulus Modality	Paradigm	Distractor/ Novelty Responses	Target Responses
Bledowski, Prvulovic, Hoechstetter, and others (2004)	fMRI/EEG (separate sessions), fMRI-based seeding of regional sources	Visual	Three-stimulus oddball	FEF, PPC, IPL, IT, INS	PPC, IPL, IT, INS
Brazdil and others (2005)	fMRI/intracranial ERP	Auditory	Two-stimulus oddball		fMRI: IPL, SMG, IFG, MFG, ACC, PUT; ERP only: PAH, HIP, STG
Menon and others (1997)	fMRI/EEG (separate sessions), fMRI-based dipole seeding	Auditory	Two-stimulus oddball		IPL
Mulert and others (2004)	fMRI/EEG (simultaneous), LORETA	Auditory	Two-stimulus oddball		TPJ, INS/IFG, right MFG (left MFG in EEG only), PCU, left STG, left IPL, SMA/ACC
Opitz, Mecklinger, Friederici, and von Cramon (1999)	fMRI block design/EEG (separate sessions), fMRI-based dipole seeding	Auditory	Novelty oddball	Middle STG	
Opitz, Mecklinger, von Cramon, and Kruggel (1999)	fMRI block design/EEG (separate sessions), fMRI-based dipole seeding	Auditory	Two-stimulus oddball		Posterior STG right > left

EEG = electroencephalography; FEF = frontal eye field; PPC = posterior parietal cortex; IPL = inferior parietal lobule; IT = inferior temporal; INS = insula; SMG = supramarginal gyrus; IFG = inferior frontal gyrus; MFG = middle frontal gyrus; ACC = anterior cingulate cortex; PUT = putamen; ERP = event-related potential; PAH = parahippocampal gyrus; HIP = hippocampus; STG = superior temporal gyrus; LORETA = low-resolution electromagnetic tomography; TPJ = temporoparietal junction; PCU = precuneus; SMA = supplementary motor area.

Table 1: Results of Combined Functional Imaging and Source Localization Studies. Copyright Linden, 2005.

The following chapter concerns the actual study. Aim of the study, methods, results as well as the discussion is presented here.

6 Present Study

The following study was conducted at the Laboratory for Cognitive Neuroscience, Department of Neurology (Jurij Dreo, Zvezdan Pirtošek) in cooperation with the Department of Neurophysiology at the University Medical Centre Ljubljana as well as the Department of Psychology (Grega Repovš).

Even though four decades have passed since the P3 was first described, the interest in the scientific community has not waned (Figure 3). A roughly representative summary of studies on Pubmed revealed that the number of papers referencing the P3 in conjunction with EEG/ERPs is at an all-time high in absolute and relative terms, reaching about 6% of total studies referencing EEG/ERPs. It is obvious from these results that research into the neuronal underpinnings of the P3 is crucial not only for advancing basic scientific understanding, but also for the interpretation of clinical research using the P3 as an electrophysiological marker of cognition.

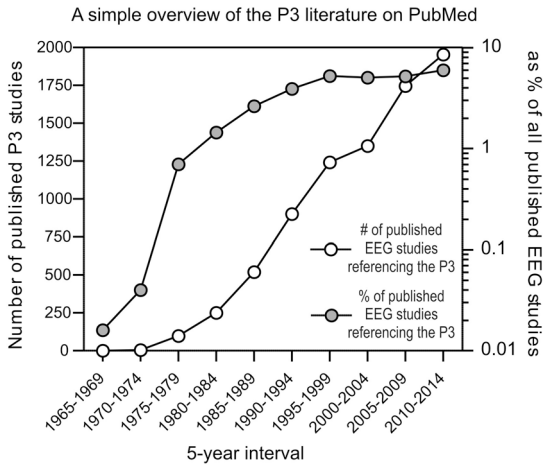

Figure 3: Number of studies found using two search terms within indicated time intervals. For the number of studies referencing the P3 in conjunction with EEG/ERPs the search term: "((P300) OR (P3) OR (P3b) OR (P3a) OR (late positive component) OR (late positive complex)) AND ((EEG) OR (electroencephalography) OR (evoked potentials) or (event related potentials))" was applied to "All fields". The total number of studies referencing

EEG was estimated by excluding the first "P3 part"; this was then used to calculate the % of studies referencing both EEG and the P3. Left axis (number) is linear, right axis (%) is logarithmic. Last time-interval only includes data up to April 2014.

6.1 Aim of the Present Study

Even though the P3 potential is a very well-studied ERP, the exact mechanisms of its generation and the distribution of its neural generators within the brain still remain unclear (Polich & Criado, 2006). In addition, some limited epidemiological data has shown that the auditory and visual P3 exhibit different tendencies for change in families who were at high risk for alcoholism (Polich & Bloom, 1999). This observation re-opens the question of P3 generators since it can be viewed as circumstantial evidence against the notion that P3 sources are identical across sensory modalities. If the P3 is indeed strictly endogenous and its neural generators are in fact identical for different sensory modalities, this should be reflected in a stable P3 topography across different types of sensory stimulation (Katayama & Polich, 1999; Ji, Porjesz, Begleiter, & Chorlian, 1999).

Several studies have addressed the question of P3 topography in different sensory modalities. Early work (Simson, Vaughan & Ritter, 1977; Squires, Donchin & Squires 1997; Picton, Stuss, Champagne & Nelson, 1984) focused merely on raw (non-normalized) P3 amplitudes and concluded that there were no topographical P3 differences between sensory modalities. Later studies addressed some of the inherent methodological and statistical limitations of this early work and employed various amplitude-normalization approaches (Synder et al. 1980; Barrett, Neshige, & Shibasaki, 1987; Johnson, 1989; Naumann et al., 1992; Sangal & Sangal, 1996; Katayama & Polich, 1999; Comerchero & Polich, 1999; Ji et al., 1999). The idea behind the amplitude normalization procedure is to determine whether an interaction between an experimental condition and electrode site reflects a difference in the internal generator sources. To account for that, data gets normalized to remove differences in the overall amplitudes of

the conditions.[16]

A comprehensive summary of these studies is presented in Table 2.

N	Study	# Subjects	# Channels	EEG ref	P3a			P3b		
					A	L	T	A	L	T
1	Snyder, Hillyard & Galambos, 1980	12	5/9	RMR	-	-	-	x	x	=
2	Barrett, Neshige, & Shibasaki, 1987	27	7	LER	-	-	-	x	x	=/x
3	Johnson, 1989	40	9	LER	-	-	-	x	x	x
4	Naumann et al., 1992	61	11	LER	-	-	-	x	x	=
5	Sangal & Sangal, 1996	40	31	?/CSD	-	-	-	x	x	=
6	Comerchero & Polich, 1998	16	3	LER	x	x	=	x	x	=
7	Katayama & Polich, 1999	12	15	LER	x	x	=	x	x	=
8	Ji et al., 1999	41	61	nose/CSD	-	-	-	=	x	=/x

Table 2: A summary of studies that quantitatively assessed P3 topographies in different sensory modalities with various amplitude-normalization approaches. RMR = right mastoid reference, LER = linked ear/mastoid reference, CSD = current source density. P3 assessment legend: A = raw (non-normalized) amplitude assessment, L = latency assessment, T = topographical (normalized amplitude) assessment. Study conclusions legend: equal sign = is identical across sensory modalities, x = is different across sensory modalities, minus sign = not evaluated/reported. Squares indicating no difference in P3

[16] Once the normalized values have been computed, the difference in amplitude between the conditions, and the condition x electrode site interaction is no longer distorted by the relationship between the magnitude of the internal generator and the distribution of voltage across electrodes. Thus, any significant interaction obtained with the normalized values should be due to a change in the relative distribution of internal brain activity. (Luck, 2005) Unfortunately, this approach leaves out some possible distortions, leading to possibly false results and conclusions. For a substantial critique on that matter, see Urbach & Kutas, 2002 who conclude: “Consideration of the consequences [...] the practice should be discontinued. [...] [I]t is not clear that much is lost by abandoning the procedure. Indeed, much is gained if experimental results that do not constitute good evidence for differences in the spatial configuration of neural generators are not treated as if they did.“ (Urbach & Kutas, 2002)

topography across sensory modalities are colored gray. Studies 3-8 compared visual and auditory stimulation, study 1 also used somatosensory and study 2 used auditory and somatosensory stimuli.

Only 1 of 8 studies conducted on this question unambiguously concluded that P3 topographies differ between sensory modalities (Johnson, 1989); two studies reported some possible difference in P3 topographical distribution. Barrett et al. (1987) however noted the confounding factor of task difficulty, which prevented a straightforward interpretation of their results. Ji et al. (1999) reported some effects of modality on P3 topography when employing a high-resolution EEG method (CSD, current source density) calculated on a medium-density EEG cap (61 channels). But the effect was restricted only to the right hemisphere. The authors found no medial or left-sided differences. In accordance with the studies reviewed in Table 2, most authors today conclude that P3 generation and processing is independent of sensory modality (Polich & Criado, 2006; Katayama & Polich, 1999; Polich & Bloom, 1999). It is however worth noting that the reviewed past studies either used very low numbers of recording channels or did not avail themselves of more modern high-resolution EEG approaches such as the spline Laplacian (sometimes also called current source density, CSD), which greatly increase the spatial-resolution of scalp recorded EEGs (Nunez & Pilgreen, 1991; Srinivasan et al., 1996). For this reason, the lack of previously reported differences in P3 topography might be due to past inabilities to detect small differences in spatial distribution of the observed potential.

To address this possibility, we observed a whole-scalp topographical distribution of the P3 evoked with auditory and visual stimulation, using a high-density 128-channel EEG and compared its brain-surface distribution calculated via the spherical spline Laplacian (SSL) method (also called current source density, CSD). Topographic maps are derived from the amplitude data and can take two forms: raw voltage or current source density (CSD). The raw voltage topographies present the summation of cortical and subcortical neural activity that occurs in a set time window, whereas, the CSD topographies represent only the cortical surface activity (Soltani & Knight, 2000). Neuroelectric signals

recorded at the scalp are principally distorted by the effects of the skull and conductive tissues. This distortion acts as a spatial low-pass filter, which causes the potentials at the scalp to appear blurred. The SSL method can be applied to the blurred scalp data to improve the spatial frequency resolution (Le, Menon, & Gevins, 1994). This method tries to most optimally explain the scalp potential field by intracranial sources by estimating the location and strengths of the current sources that generate the measured data.[17]

In addition, we controlled for task difficulty to exclude it as a possible explanation for any observed differences (Comerchero & Polich, 1999; Polich & Bloom, 1999). While different neuronal generators can produce identical surface potential distributions, the inverse is not true: differences in surface potential distributions necessarily imply that there are differences in the underlying neuronal generators. Therefore, while detecting no differences in P3 topographies across sensory modalities might still leave the question of its neuronal underpinnings open, any detected topographical differences must necessarily confirm differences in its generators.

6.2 Methods

6.2.1 Subjects, Experimental Procedure and Tasks

17 right-handed volunteers, mostly university-level students, aged 25.5±2.8 (22-31) years, 6 females took part in the study. All subjects were free of known neurological or psychiatric diseases or disorders and were not taking any medication known to affect the central nervous system. Each subject gave written informed consent before being included in the study, which was approved by the local medical ethics committee. Subjects were well rested before the experiment, which was conducted between the hours of 9-22 o' clock. Each subject performed four different three-stimuli Oddball tasks (using frequent, target and distractor type stimuli) (Figure 4) to elicit the desired ERP responses, requiring active responses to targets in the form of button presses. Task

[17] See http://www.scholarpedia.org/article/Source_localization

variants were: easy and hard visual oddball task , and easy and hard auditory oddball task.

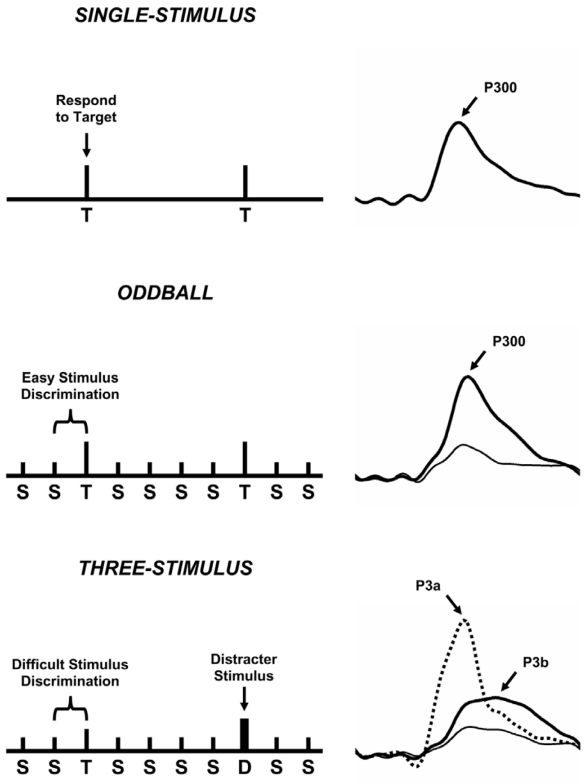

Figure 4: Illustration of elicited ERPs (on the right) from a single-stimulus (top), an oddball (middle) and a three-stimulus oddball (bottom) paradigm. During the single-stimulus task only one infrequent target (T) is presented to the subject in the absence of any other stimuli. In the oddball task frequent standard stimuli (S) and infrequent target (T) stimuli are randomly presented. In the three-stimulus oddball task, an infrequent distractor, such as white noise (D) is added to the sequence of standard and target tones. The distractor elicits a P3a and the target a P3b. In all three tasks, the subject was instructed to respond exclusively to the target stimulus. Copyright Polich, 2007.

The visual oddball tasks consisted of 400ms displays of Gabor patches sinusoidal line gratings inside a Gaussian envelope (Figure 5) with targets differing from frequents in terms of rotation angle and distractors differing in rotation angle and color. Targets and frequents were yellow and distractors blue. All stimuli were presented on a uniform black

background. Each stimulus display was followed by a 2500±100ms fixation interval during which a small white cross was displayed, followed by another stimulus. Frequents always had an angle of +55° with respect to the vertical and distractors -35° (positive angles turn counterclockwise and negative clockwise). The task difficulty was determined by the difference in the angle between the targets and frequents. For easy targets, the angle was kept constant at -35°. To determine the hard target angle, each subject performed an initial calibration task in which patches with increasingly large angle differences from frequents (starting at +58° and increasing in steps of +3°) were presented. The first Gabor patch that was correctly recognized as differing from frequents four times with no more than one miss in five successive presentations was designated as the hard target. Calibrated hard target angles were +63.6±3.3° (+58° to +70°).

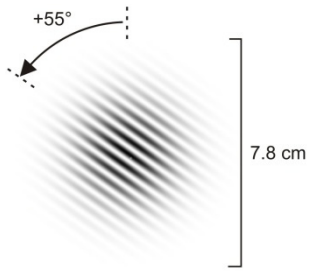

Figure 5: A schematic representation of a Gabor patch used to evoke the visual P3. Positive angles turn counterclockwise and negative clockwise. Frequents always had an angle of +55°, easy targets and distractors -35°, hard targets were calibrated to +63.6±3.3°. Stimuli were presented on a uniform black background. Frequents and targets were yellow, distractors blue.

The auditory oddball tasks consisted of 100ms sounds (5ms up and down slope) with frequents and targets being monotones of different frequencies. Distractors consisted of white noise. Frequents always had a frequency of 1000Hz and easy targets of 500Hz. Similar to the visual oddball a calibration task was performed to determine the hard target frequency. The calibrated hard target frequencies were 516.7±6.3Hz (506-524Hz).

Each of the 4 oddball tasks was divided into 6 shorter blocks of 2.5 minutes each for a total of 24 blocks lasting cca. 70 minutes (with intermittent breaks). The order of task blocks was pseudo-randomized and counterbalanced across subjects. Each task presented a total of 192 frequent, 48 target and 48 distractor stimuli resulting in a 66.7%, 16.7% and a 16.7% global probability of displaying a frequent, target and distractor, respectively.

6.2.2 EEG Recording and Processing

EEG recordings were performed in a sound-attenuated and partially EM-shielded room with subjects sitting comfortably in a chair 100cm in front of a 21" CRT monitor set to a 100Hz refresh rate. Standard computer-grade speakers were used to deliver stereo auditory stimulation at a sound level of 60dB. A 128 channel digital EEG amplifier (BrainAmp MRplus, Brain Products, GmbH, Germany) combined with a 130-electrode cap with active electrodes arranged according to the 10-5 system (Oostenveld & Praamstra, 2001; ActiCap, Brain Products, GmbH, Germany) was used to record EEGs. The raw data was analogue filtered between 0.016-250 Hz, sampled at 5000 Hz and later down-sampled to 500 Hz for offline analysis (BrainVision Analyzer 2.04, Brain Products, GmbH, Germany). FCz was used as a recording reference and AFz as the ground. Each recording was first visually inspected for bad channels (electrode disconnected/poorly connected to scalp or technical malfunction) and for clear non-brain or non-eye-movement related electrical activity (muscle noise, sweating, movement, etc.). Bad channels (2.1±1.0 per subject) and artifactual data portions were removed from further analysis. Ocular artifacts were corrected using a custom-devised Independent Component Analysis (ICA) procedure, which removes components based on temporal and spatial correlations with known blinking and eye-movement activity. The number of excluded components was 2.4±0.8 per subject. After ICA, the previously removed channels were interpolated with spherical splines (spline order=4, max. degree of Legendre polynomials=10, $\lambda=10^{-5}$). EEG data was segmented based on each type of task (visual easy & hard, auditory easy & hard) and stimulus (frequents, targets,

distractors) into individual sets ranging [-500, +2500]ms with respect to each stimulus onset. The first 500ms were used for baseline correction and the first and last 200ms for DC correction. Using a custom-written artifact rejection procedure, channels within individual sets containing amplitudes further than ±3.5 standard deviations from the subject and channel-specific means, across a subset of sets in which no channel exceeded ±120 μV, were rejected from the average. Only sets with correct responses were averaged (button presses for targets, no presses for frequents and distractors). The final average (across all subjects, tasks, stimuli-types, sets and channels) contained 89.2±4.2% of the total recorded data.

6.2.3 EEG Evaluation

To maximize the spatial resolution of the final ERP data, the spherical spline Laplacian (SSL, also called current source density) transform was applied to averaged individual ERPs (Nunez & Pilgreen, 1991; Srinivasan et al., 1996). All comparisons were performed on these transformed potentials that highly correlate (>95%) to brain-surface potentials caused by radial current sources when calculated on high-density scalp EEG data (Nunez et al. 1994; Nunez, Wingeier & Silberstein, 2001; Nunez & Srinivasan, 2006). EEG data was evaluated in three distinct ways. Firstly as stimulus-locked ERP time curves for a characteristic set of 6 midline electrodes (Fz, Cz, CPz, Pz, POz, Oz; see Figure 6). These compare the tasks across relevant time intervals in a raw (non-normalized) manner with their inherent amplitude, topographical and time-course (phase) differences left intact.

Since the primary aim of the study is to compare differences in ERP distribution (topography) across the brain/scalp and not to focus on previously described (and well known) absolute amplitude/timing differences, each tasks' P3 was normalized inside a 100ms long window which was chosen based on maximum task-specific global field power (GFP) values (Skrandies, 1990; Hamburger & vd Burgt, 1991; Michel et al., 1993) averaged across all subjects (Figure 8). During these intervals average P3 amplitudes

were first computed for each EEG channel and were then divided by the maximum average amplitude found among all 128 channels. The EEG channel with the highest average amplitude is therefore assigned the value of 1. The EEG topographies thus obtained represent normalized P3 amplitudes, which are not time-locked to the same instant after stimulus presentation (as with ERP time-curve comparisons on Figure 7), but are time-locked to the interval of maximum P3 activity for each specific task. This comparison was designed to compensate for differences in timing and absolute amplitude of task-specific P3 activity and to focus the comparison merely on differences in P3 potential distribution/topography.

A third type of EEG evaluation was performed by calculating temporal and topographical (spatial) correlations between different sensory modalities. Averaging together the averaged waveforms of the individual subjects creates grand averaged waveforms. These mask the variability across subjects, which makes it easier to see similarities, but may not accurately reflect the pattern of individual results on the other hand (Luck, 2005). Here, each subject's ERP data belonging to a particular task variant was correlated to the grand average ERP data (excluding the subject itself) belonging to the visual or auditory modality (and separately for the easy, hard, and pooled variant).
The temporal correlations correlated data belonging to each channel across a time interval relevant to each task (intervals are depicted in Figure 8). The obtained temporal correlation coefficients were averaged across all channels to obtain the average temporal correlation coefficient. The topographical (spatial) correlations correlated data belonging to a particular point in time across all EEG channels. The obtained topographical correlation coefficients were averaged across all points in time relevant to the tasks (again, on intervals depicted in Figure 8). Each of the correlation graphs on Figure 10A thus presents 34 data points (17 in white and 17 in gray). Each point depicts one subject's average temporal or spatial correlation (depending on the graph) with the grand average ERP (excluding the particular subject) for one sensory modality (X axis = auditory, Y axis = visual). White circles are correlations with subjects' ERP data obtained with auditory stimulation and gray dots on data obtained with visual stimulation. If there are no temporal or topographical differences in P3 generation (centered around peak P3

activity) between visual and auditory stimulation, then the white and gray circles on each graph should cluster mixed together along the dashed diagonal (resulting in small d_{SUM} values around 0). If there are actual topographical and/or temporal differences in P3 potentials belonging to each sensory modality, then the white circles should cluster more in the lower-right and the gray in the upper-left quadrant (resulting in large positive d_{SUM} values). This final analysis took a completely different approach to the evaluation of ERP-distribution; not by averaging and normalizing the data inside a time-window and then comparing it in a channel-by-channel basis but by taking into account all channels and points in time simultaneously via correlations (which inherently ignore differences in absolute amplitude). Since these correlations were performed during times of task-specific maximum P3 activity, they also accounted for differences in ERP timing.

Unless otherwise noted all reported numerical values are group-wide averages followed by ± 1 standard error of the mean and ranges in parentheses, where considered appropriate. Two-tailed, paired t-tests were used to perform statistical comparisons, differences were deemed significant at the $p<0.01$ level.

6.3 Results

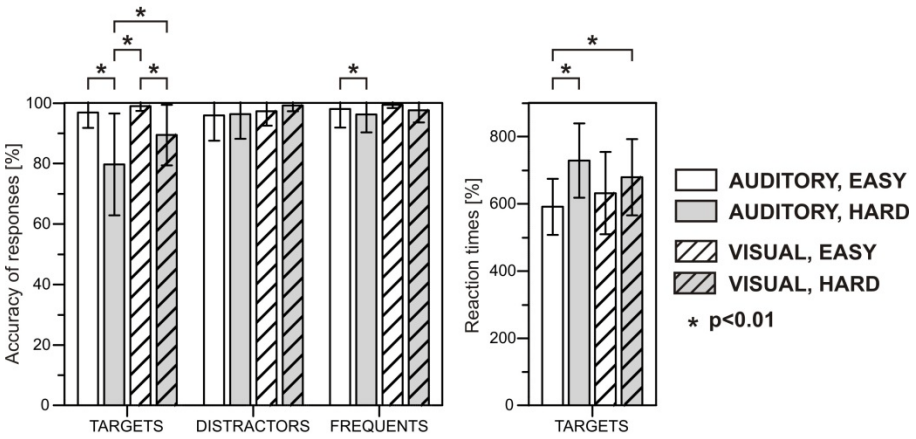

Figure 6: Behavioral results for all tasks. The correct response to targets was a button press, the correct response to distractors and frequents was the absence of a button press, thus only targets have associated reaction times. Statistically significant differences are marked.

A summary of task-specific behavioral results is depicted in Figure 6. More difficult task variants had lower accuracies in target detection in both the visual and auditory modality. There were no significant differences in response accuracy to distractor stimuli and only a slight (but significant) difference in response accuracy to frequent ones between the easy and hard variant of the auditory task. Easy tasks also produced consistently shorter average reaction times but the difference was only significant in the auditory modality (and between the easy auditory and hard visual modality).

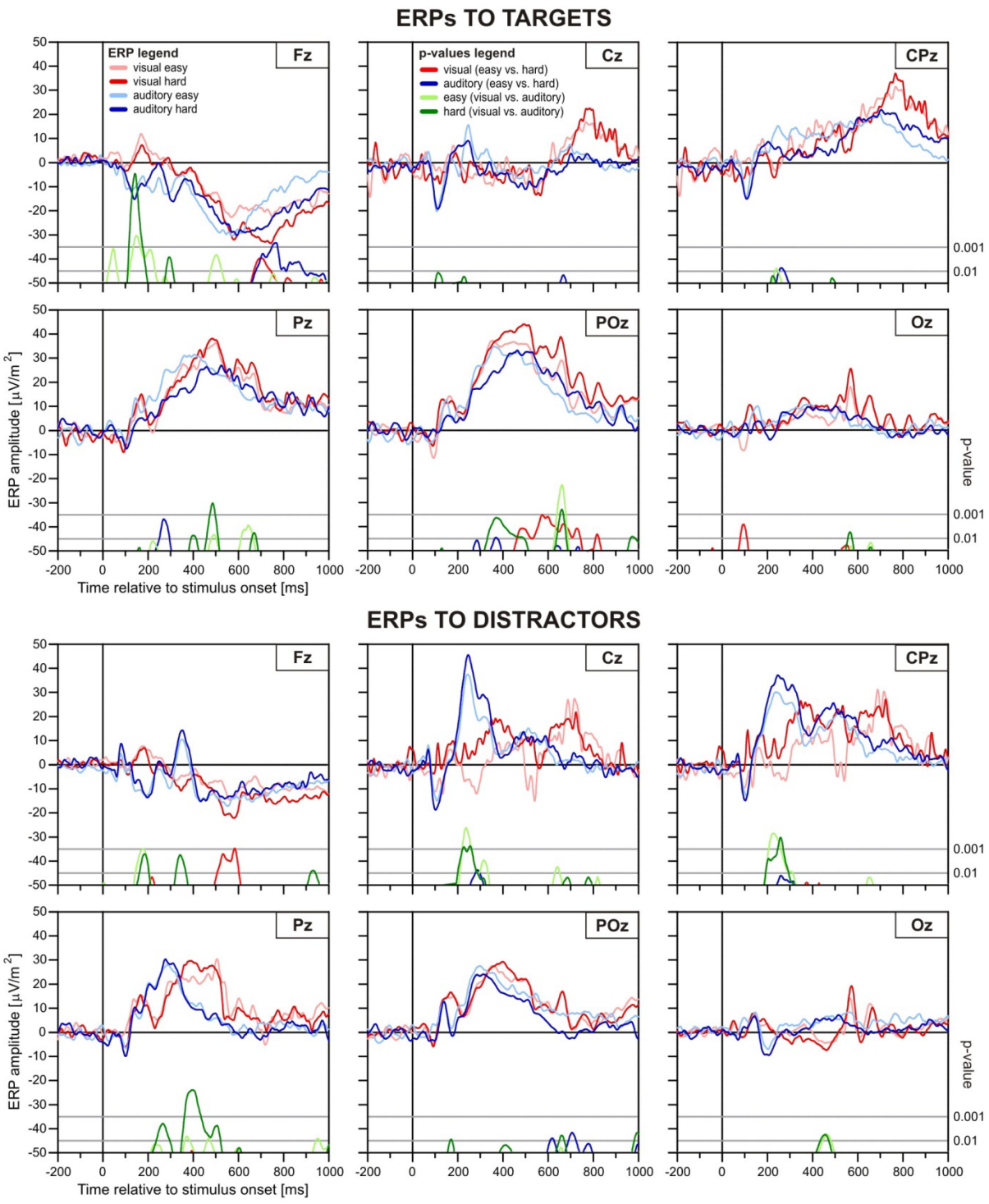

Figure 7: Stimulus-locked ERP time-curves for all 4 task variants (auditory easy, hard and visual easy, hard) on 6 representative midline EEG channels. ERP SSL-values are on the left linear axis and p-values for curve comparisons on the right logarithmic axis. Depicted color legend applies to all graphs.

Raw (non-normalized) SSL-values corresponding to radial-source associated brain-surface potentials (Nunez et al., 1994; Nunez & Srinivasan, 2006) showed characteristic differences in P3b (targets) and P3a (distractors) amplitude and timing when compared time-locked to stimulus onset. Analysis of task difficulty effects revealed a significantly larger P3b in the hard compared to the easy visual variant of the task observed at the site (POz) and time interval (500 to 700ms) of maximum amplitude. In the auditory modality a slight, earlier difference was observed at the same site at roughly 275 and 375ms, probably reflecting a difference in P3b timing: the easy variant produced an earlier rise in P3b potential. The hard visual variant also produced a larger occipital P1 potential at around 100ms (Oz) than the easy variant. A comparison of stimulus modalities (green p-curves on Figure 7) reveals differences in amplitude between the visual and auditory modality in the hard task variants: Pz [400, 500]ms and POz [350, 500]ms and again around 650ms, with visual stimuli generating larger P3b amplitudes. Similar but less pronounced differences can be observed for the easy task variants. P3a potentials were not significantly different between the easy and hard task variants for either stimulus modality among the six chosen midline channels. However, when comparing different stimulus modalities, the auditory P3a was much more centrally distributed with larger amplitudes at Cz, CPz and Pz during the interval [200, 300]ms and smaller amplitudes at Pz during [350, 500]ms compared to the visual P3a with more parietal-frontal distribution. This difference was present on both easy and hard variant of the task.

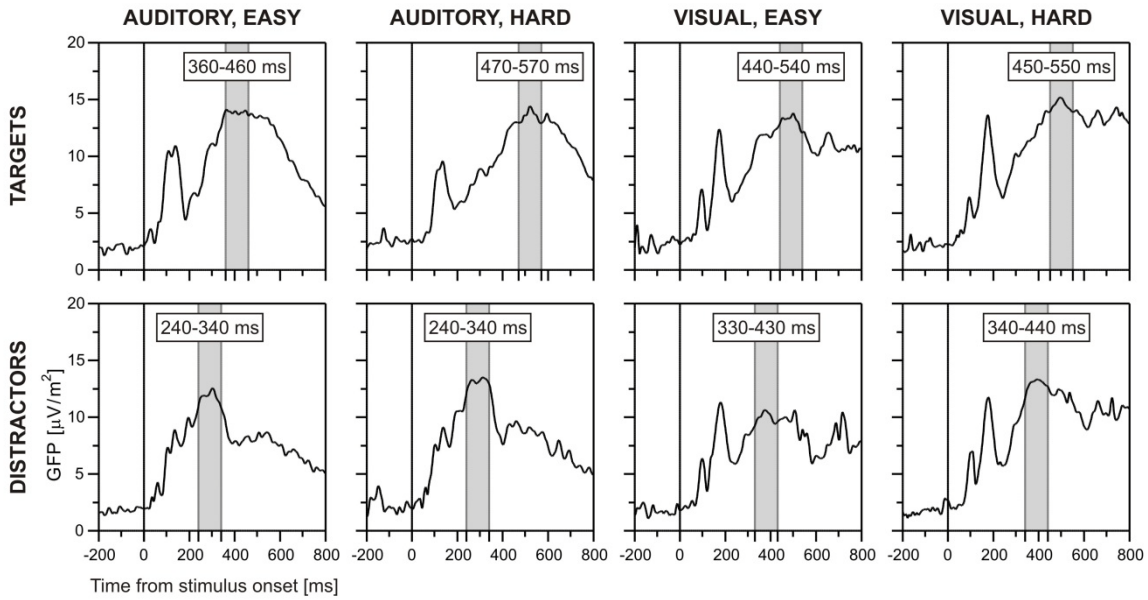

Figure 8: Task-specific 100ms long normalization intervals used for P3 topography comparison in Figure 9 and correlation calculations in Figures 10A and 10B. Each graph represents global field power (GFP) values averaged across all subjects. The chosen intervals correspond to peak P3 (and GFP) activity for each task.

Auditory stimuli generally produced shorter P3b latencies than visual ones. Additionally easy task variants generally produced shorter latencies than hard ones. Based on intervals of maximum P3 activity as judged by the peaks of GFP values in Figure 8, normalized P3 topographies corresponding to all task variants were calculated and are depicted in Figure 9.

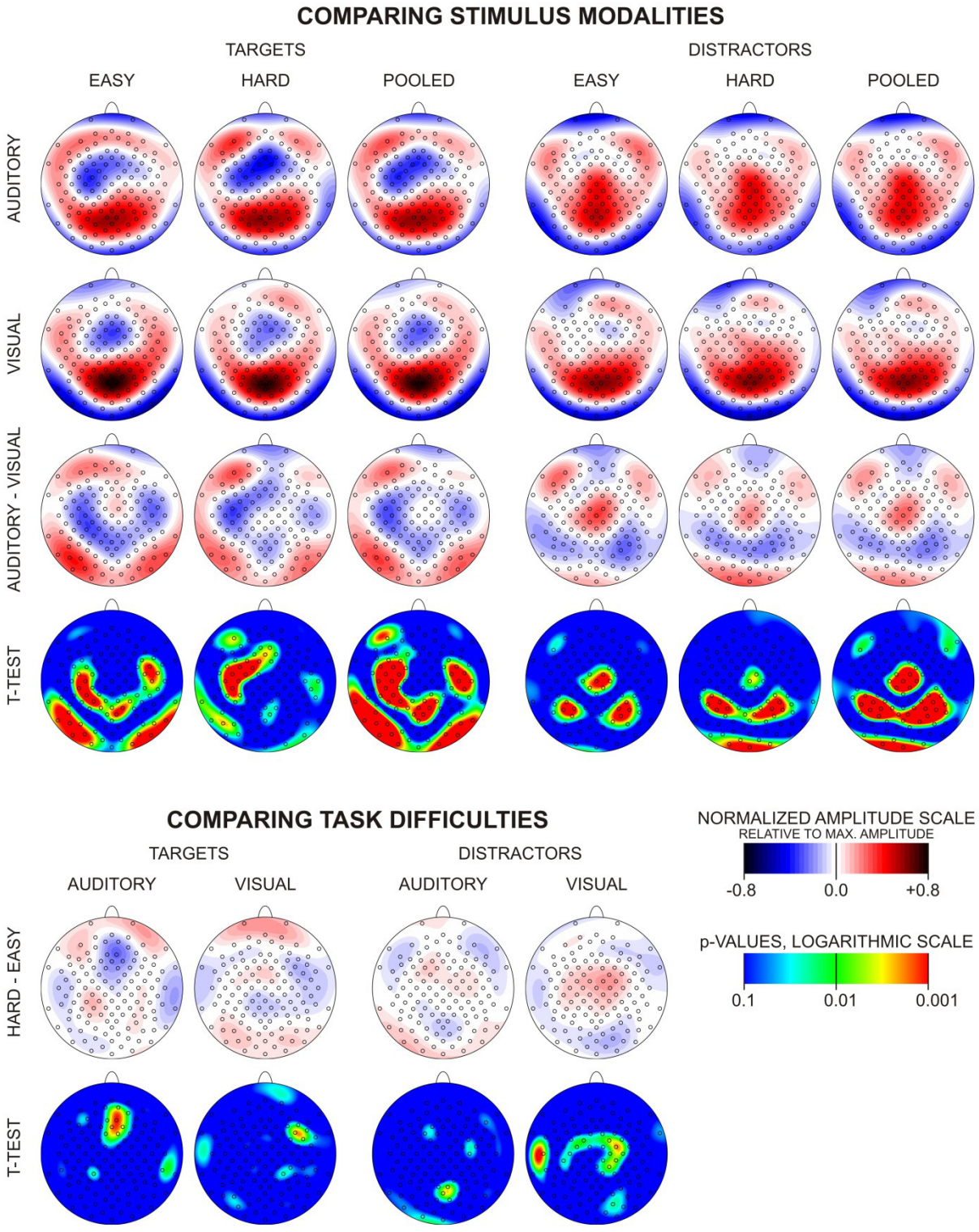

Figure 9: A comparison of amplitude-normalized P3 topographies during 100ms intervals of task specific maximum P3 activity (Figure 8). Averages across task difficulty are marked as "POOLED". Each topography shows data from the vertex (at its center = 0°) to ear level (at its outer rim = 120°).

A comparison of amplitude-normalized P3b topographies time-locked to 100ms intervals of task specific maximum P3 activity obtained from target averages (Figure 9, left panel) revealed highly significant differences between stimulus modalities. There are three distinct topographical differences that can be described. Firstly, the visual P3b distribution was larger (more focused) in the medial parieto-occipital region, specifically around sites: Pz, POz, PPO1h, and PPO2h. Secondly, it was generally more frontally-displaced and less extended bilaterally in the parietal direction. It thus exhibited more negative bilateral parieto-occipital SSL values around sites (just for the left hemisphere): P7, P9, PPO9h, PO7, PO9, POO9, and I1. Thirdly, the visual P3b distribution exhibited more positive values over bilateral central regions (just for the left hemisphere): FCC3h, FCC5h, C3, C5, CCP3h, and CCP5h. These changes were generally more pronounced for the easy task variant, but were also highly significant for the pooled data (easy and hard averaged together). Similarly, we can describe three distinct topographical differences between visual and auditory stimulation for the P3a potential obtained from distractor averages (Figure 9, right panel). While the visual modality again produced on average more focal and stronger parietal peaks of P3a activity in the same region as described for the P3b, this finding was not statistically significant. The first (and most frontal) significant difference between the auditory and visual P3a was however observed around sites FCC1h, FCC2h, Cz, CCP1h and CCP2h and was due to a more frontally-extended (and thus more frontally positive) auditory P3a. Secondly, while the auditory P3a was more frontally-extended, the visual P3a extended more bilaterally in both parietal regions and produced significantly more positive values around sites (just for the left hemisphere): CP5, CPP5h, TPP7h, P1, P3, P5, P7 and PPO5h. Thirdly, the visual P3a did not extend as far occipitally compared to the auditory one and produced significantly less positive values at I1, Iz and I2, but this was only apparent for the hard (and pooled) task's data. In contrast to the differences observed when comparing different sensory modalities, the distribution of P3a and P3b is fairly uniform across task difficulties. Slight differences are observed in the frontal region for auditory stimulation and fronto-central region for visual stimulation. These differences are much less pronounced (mostly border on statistical significance at $p<0.01$) and also do not overlap with the previously described differences observed between stimulus modalities.

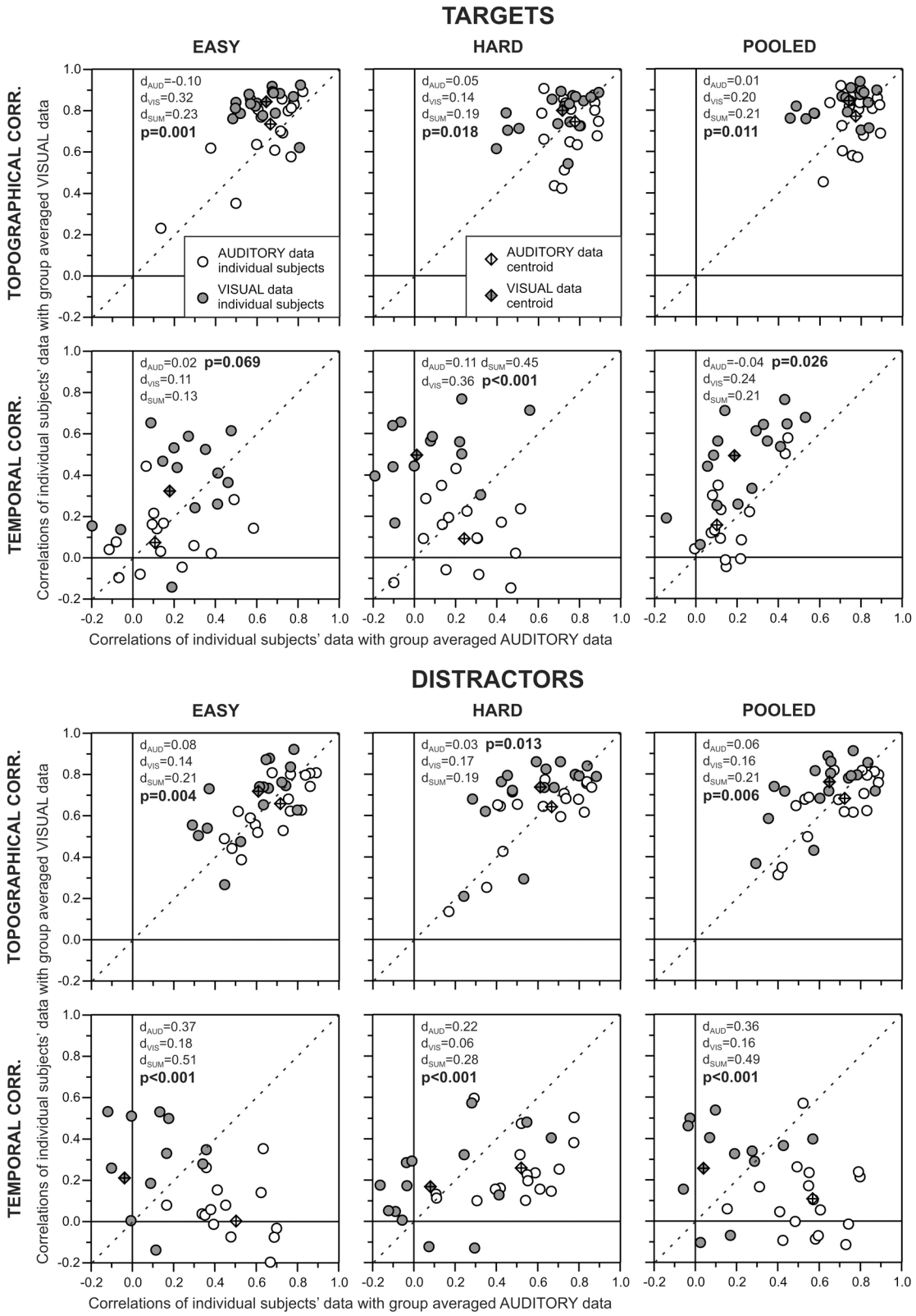
TARGETS
EASY
HARD
POOLED
TOPOGRAPHICAL CORR.
TEMPORAL CORR.
Correlations of individual subjects' data with group averaged VISUAL data
Correlations of individual subjects' data with group averaged AUDITORY data
d_AUD=-0.10
d_VIS=0.32
d_SUM=0.23
p=0.001
d_AUD=0.05
d_VIS=0.14
d_SUM=0.19
p=0.018
d_AUD=0.01
d_VIS=0.20
d_SUM=0.21
p=0.011
AUDITORY data individual subjects
VISUAL data individual subjects
AUDITORY data centroid
VISUAL data centroid
d_AUD=0.02 p=0.069
d_VIS=0.11
d_SUM=0.13
d_AUD=0.11 d_SUM=0.45
d_VIS=0.36 p<0.001
d_AUD=-0.04 p=0.026
d_VIS=0.24
d_SUM=0.21
DISTRACTORS
EASY
HARD
POOLED
d_AUD=0.08
d_VIS=0.14
d_SUM=0.21
p=0.004
d_AUD=0.03 p=0.013
d_VIS=0.17
d_SUM=0.19
d_AUD=0.06
d_VIS=0.16
d_SUM=0.21
p=0.006
d_AUD=0.37
d_VIS=0.18
d_SUM=0.51
p<0.001
d_AUD=0.22
d_VIS=0.06
d_SUM=0.28
p<0.001
d_AUD=0.36
d_VIS=0.16
d_SUM=0.49
p<0.001

Figure 10A: Comparing stimulus modalities. Topographical (across all scalp channels and averaged over time) and temporal (across all time-points and averaged over scalp channels) correlations during 100ms intervals depicted on Figure 8. Pooled data is evaluated on intervals that are averages between the easy and hard tasks' intervals. Legend applies to all graphs. Each graph indicates average distances between data point clusters belonging to each stimulus modality (d_{AUD} and d_{VIS}) and the dashed diagonal line; the sum of both distances (d_{SUM}) is also shown. Positive d_{AUD} values indicate that white dots are below the diagonal, negative values above the diagonal and vice versa for d_{VIS}. If the topographical distribution and temporal course of SSL-calculated brain-surface potentials belonging to each sensory modality is indeed different, then the white circles should tend to cluster below the diagonal and the gray circles above the diagonal, resulting in large positive d_{SUM} values. The p-value was obtained by a bootstrap method, which calculated the percentage of times the d_{SUM} parameter was as large or larger as observed, on random combinations of data that intermixed the auditory and visual groups. 10.000 simulations were run for each graph. If the number of times the d_{SUM} parameter reached values as extreme or more did not exceed 10, the p-value is marked as <0.001.

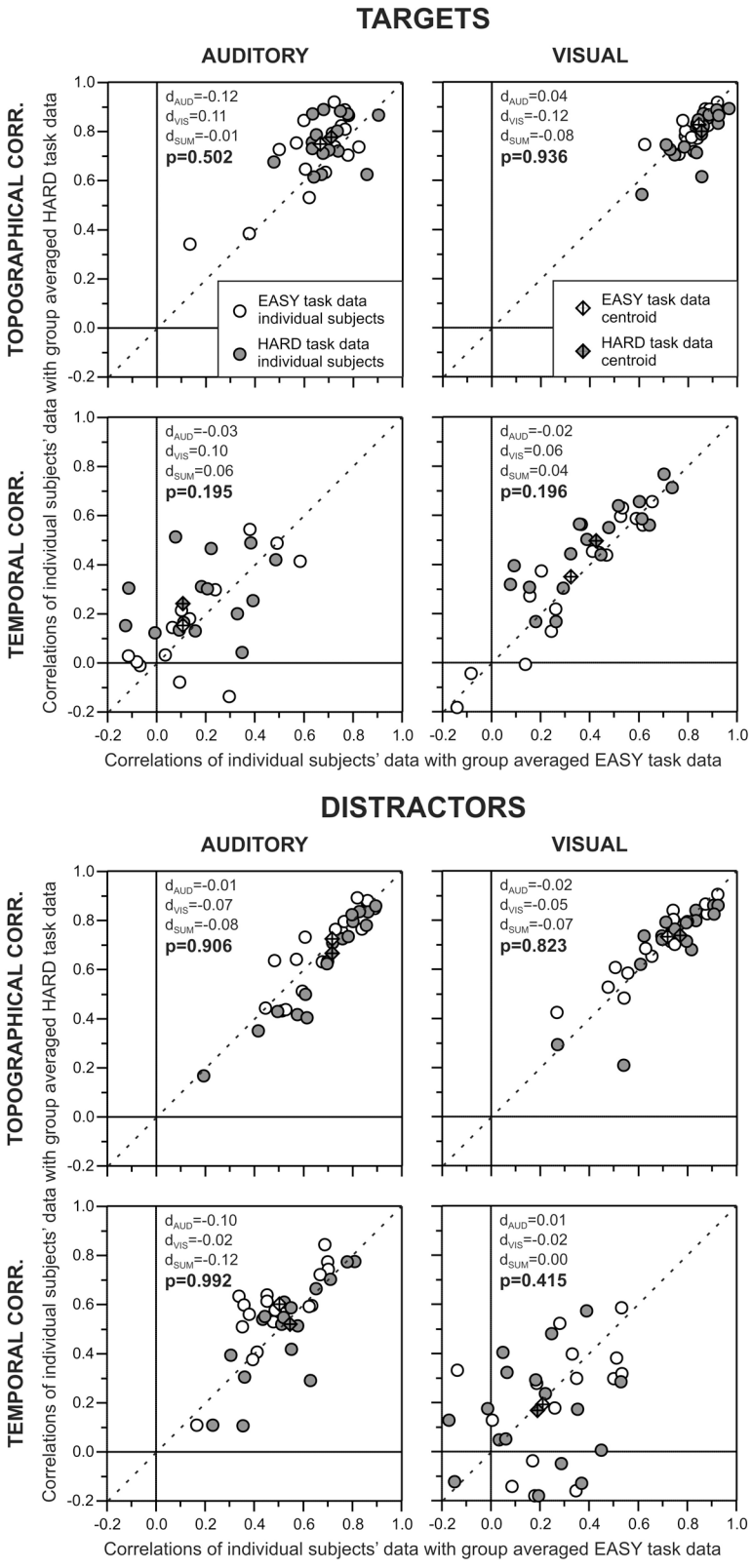
TARGETS
AUDITORY
VISUAL
TOPOGRAPHICAL CORR.
TEMPORAL CORR.
Correlations of individual subjects' data with group averaged HARD task data
Correlations of individual subjects' data with group averaged EASY task data
d_AUD=-0.12
d_VIS=0.11
d_SUM=-0.01
p=0.502
d_AUD=0.04
d_VIS=-0.12
d_SUM=-0.08
p=0.936
d_AUD=-0.03
d_VIS=0.10
d_SUM=0.06
p=0.195
d_AUD=-0.02
d_VIS=0.06
d_SUM=0.04
p=0.196
EASY task data individual subjects
HARD task data individual subjects
EASY task data centroid
HARD task data centroid
DISTRACTORS
AUDITORY
VISUAL
TOPOGRAPHICAL CORR.
TEMPORAL CORR.
Correlations of individual subjects' data with group averaged HARD task data
Correlations of individual subjects' data with group averaged EASY task data
d_AUD=-0.01
d_VIS=-0.07
d_SUM=-0.08
p=0.906
d_AUD=-0.02
d_VIS=-0.05
d_SUM=-0.07
p=0.823
d_AUD=-0.10
d_VIS=-0.02
d_SUM=-0.12
p=0.992
d_AUD=0.01
d_VIS=-0.02
d_SUM=0.00
p=0.415

Figure 10B: Comparing task difficulties. Topographical and temporal correlations obtained by comparing different task difficulties within one sensory modality are shown. General graph properties are identical to Figure 10A, while the meaning of the X and Y axes is switched here into task difficulties.

The topographical (across all scalp channels and averaged over time) and temporal (across all time-points and averaged over scalp channels) correlations during 100ms long intervals of peak P3 activity revealed significant differences in both the spatial distribution and the temporal course of the P3b (targets) and P3a (distractors) potentials (Figure 10A). For the P3b, the difference between visual and auditory stimulation was most pronounced for topographic correlations, whereas the temporal correlations reached statistical significance only for the hard task. For the P3a statistically significant differences were observed on both topographical and temporal correlations for all task difficulties. An analogous control calculation comparing topographical and temporal correlations between different task difficulties (Figure 10B) did not reveal any significant differences in either stimulus modality for either the P3b or P3a.

6.4 Discussion

Most of the early work on the P3 (Simson, Vaughan & Ritter, 1977; Squires, Donchin & Squires 1997; Picton, Stuss, Champagne & Nelson, 1984) indicated that there are no modality-specific differences in P3 distribution over the scalp. This finding was integrated into the classical division of ERPs into endogenous and exogenous components (Donchin, Ritter & McCallum, 1978). While these early studies had some limitations, mostly due to not comparing normalized amplitudes, which might lead to false-positives, this issue was addressed by later studies reviewed in Table 2. Of 8 studies presented therein only 1 unambiguously concluded that there were significant modality-specific differences in P3 topography (Johnson, 1989). Even though this latter work was performed on a fairly large sample (40 subjects, 9 channels) the reported results could not be replicated in a methodologically and statistically rigorous study on a larger sample (61 subjects, 11 channels) (Naumann et al., 1992). Three later studies also confirmed

Naumann's findings (Sangal & Sangal, 1996; Comerchero & Polich, 1998; Katayama & Polich, 1999). Contrary to this trend that was building up since the 1980s, the last reviewed study (Ji et al., 1999) found limited, but statistically significant, differences in P3 topography between a visual and auditory oddball on CSD data (but not on scalp-measured ERP data). The described differences were however limited to the right hemisphere. This last study was also the only one that had a sufficiently high electrode density to be able to semi-accurately estimate brain-surface potentials deriving from radial current sources. Simulations show that correlations between CSD values and brain-surface potentials due to radial sources are around 75% when CDSs are computed on 64-electrode EEG caps (Nunez & Srinivasan 2006), and up to 95% for 128-electrode caps. Since CSD/SSL methods significantly increase the spatial resolution of scalp-recorded EEG and undo some of the "blurring" caused by the high-resistance skull (Nunez et al. 1994; Nunez, Wingeier & Silberstein, 2001; Nunez & Srinivasan, 2006), this somewhat isolated finding of significant topographical P3 differences obtained on medium-density EEG recordings should be viewed as an interesting and intriguing departure from previous work. To help resolve this issue we conducted high-density EEG recordings on 128 channels and compared SSL-derived values between the visual and auditory modality.

Three different methods of P3 analysis were employed: 1) classical stimulus-locked ERP curves on 6 midline channels, 2) a comparison of amplitude-normalized P3 topographies locked to 100ms intervals of peak P3 activity and 3) a novel correlational analysis on temporal and spatial ERP data during the same 100ms of peak P3 activity. The results from the classical analysis of raw (non-normalized) P3 data gathered in the present study are in accordance with previously published results. For the P3b, visual stimulation generally resulted in larger amplitudes and longer latencies compared to auditory stimulation. The auditory P3a was more frontally-displaced and slightly larger in amplitude. Different task difficulties also produced results consistent with the literature (Figure 7 and 8). However, a comparison of normalized P3 amplitudes revealed significant departures from most previous studies. Both the P3b and P3a were found to exhibit highly statistically significant ($p<0.001$) differences in SSL-derived brain surface

potentials in three distinct regions (Figure 9). For the P3b these were: 1) a medial-central region centered on Pz, 2) two bilateral parieto-occipital regions and 3) two bilateral central regions. While we can safely interpret the first two as resulting directly from differences in P3b processing, the third one should be viewed more conservatively. Since both oddball tasks required motor responses to targets, these naturally produced negative motor cortex generated potentials which were superimposed on the P3b. Additionally, the observed differences in modality-specific reaction times (Figure 6), with auditory stimulation producing shorter and more consistent response times, should result in more pronounced negative motor potentials in the auditory task (although in the easy task, a combination of short response time and a lower amplitude motor potential might be possible as well). The third described topographical difference in P3b reflect somewhat more negative values above areas generally covering the left and right motor cortices. While all of our subjects were right-handed and should mostly produce negativity above the left hemisphere, motor potentials are fairly widespread. We therefore conclude, that the previously described bilateral central differences in P3b topography should be viewed more conservatively and should not interpreted as necessarily stemming from differences in P3b generation. In summary, the visual P3b topography was more “focal” (larger amplitudes) in the parietal region over Pz, generally slightly more frontally-displaced and less bilaterally extended in the parietal region. It is worth noting that Ji et al. (1999) described very similar differences in P3b topographies, but there they mostly failed to reach significance.

For the P3a, again, three distinct topographical differences were observed: 1) a central one focused on Cz, 2) two bilateral parietal and 3) one occipital. The latter of these is only present for the hard task and the pooled (easy and hard averaged together) data. The auditory P3a is more frontally-extended resulting in more positive amplitudes frontally (difference 1) and less negative amplitudes occipitally (difference 3). The second difference is, interestingly, less parietally extended P3a for the auditory modality. This is in strong contrast with the P3b, where it was the visual modality that exhibited smaller parietal activations. Any interpretation of modality-specific differences in such an experiment is naturally tempered by the possibility that different sensory modalities

might also differ in inherent task difficulty. Naumann et al. (1992) controlled for possible differences in task difficulty by having their subjects' fill out a subjective-experience questionnaire, which showed that their subjects seemingly did not experience any subjective difference in difficulty between the auditory and visual task. As this runs against the experience in the laboratory, we decided to employ a control comparison using tasks of different difficulties. Any observed changes in P3 topography between tasks differing in difficulty within a single sensory modality could then be excluded from later interpretations of modality-specific differences. As it turned out the control comparisons between tasks of different difficulties within the same sensory modality revealed no topographical differences comparable to the ones observed between sensory modalities. This was true for both the P3b and the P3a. We therefore conclude, that the described differences in modality-specific P3 topographies can hardly be explained by postulating the existence of inherent differences in task difficulty between the visual and auditory oddball.

The novel correlational analysis (Figure 10A) developed for this study takes a different approach to compensate for differences in raw P3 amplitudes and timing. Instead of averaging and normalizing amplitudes inside a 100ms window specific to peak P3 activity, this analysis takes all data points on all channels in two complementary informative ways into account in regard to the P3's spatial and temporal distribution. None of the previously published studies used such an approach, but some focused on slightly different methods of amplitude normalization (Naumann et al., 1992). The obtained results further support the notion of differences in the P3a and P3b between sensory modalities. While this kind of analysis doesn't permit identification of location-specific topographical differences, it does aggregate all available data and is thus a more robust test for the existence of overall differences (irrespective of scalp location). Furthermore, it allows for comparisons of ERP time-courses within P3 peak activity-locked time windows. The P3b only exhibited modality-specific differences in topography, whereas its time course was only significantly different for the hard task. The P3a however exhibited differences in both topography and time course. Control

comparisons (Figure 10B), revealed no significant differences between tasks of different difficulties.

In conclusion, we found that both the P3a and the P3b component exhibit statistically significant modality-specific properties in their topography and time course. The reported differences cannot be merely explained by amplitude, latency and/or task difficulty-related differences between the visual and auditory modality. Based on that we conclude that they are due to differences inherent in the type of sensory stimulation used to evoke the P3. Since any observed difference(s) in the spatial or temporal distribution of surface potentials must necessarily be due to differences in underlying neuronal generators (EEG/ERP sources), we assert that there must be at least some sensory modality-specific neuronal generators of P3. We further conclude that the likely reason why most previous studies failed to find any significant differences is due to insufficient EEG spatial sampling leading to inadequate spatial resolution to detect the differences observed in this study.

7 Conclusion of Thesis

For my master thesis, I investigated whether there are differences in P3 scalp in different stimulus modalities (i.e. auditory and visual) or not.

I started the thesis by giving an introduction to the topic: some general remarks on P3, how it has been found, its function and its relevance. Then I formalized the research question and hypothesis and gave a definition of attention, together with a brief overview of research in this area.
Afterwards the basics of ERP methodology were explained, starting from the underlying electrical concepts to the neural origins of ERPs and an overview of the major ERP components.
Before presenting the actual study, I focused on P3 in greater detail, elaborating arguments for its endogenicity and possible neural sources of the potential.
Finally, I presented the examined study: aim, methodology, results were presented and concluded in a discussion of the findings and possible issues.

8 Acknowledgements

First of all, I would like to thank Zvezdan Pirtošek for supervising me, for providing me with the necessary facilities, and for giving me the ability to conduct the research of my interest. I also want to give many thanks to Jurij Dreo for assisting me with the EEG recordings and his valuable feedback and contributions to the experimental setup and analysis of the data. Many thanks go to Grega Repovš as well, who made the major contributions to the experimental paradigm and provided me with valuable feedback and support.

Furthermore, I thank Anka Slana for her support and assistance, Jure Bon, Blaž Koritnik, and all of the involved employees of the Department of Neurology and the Department of Neurophysiology at the University Medical Centre Ljubljana as well as the Department of Psychology.

Lastly, I would like to express special thanks to my parents for their continuous support in my academic pursuits.

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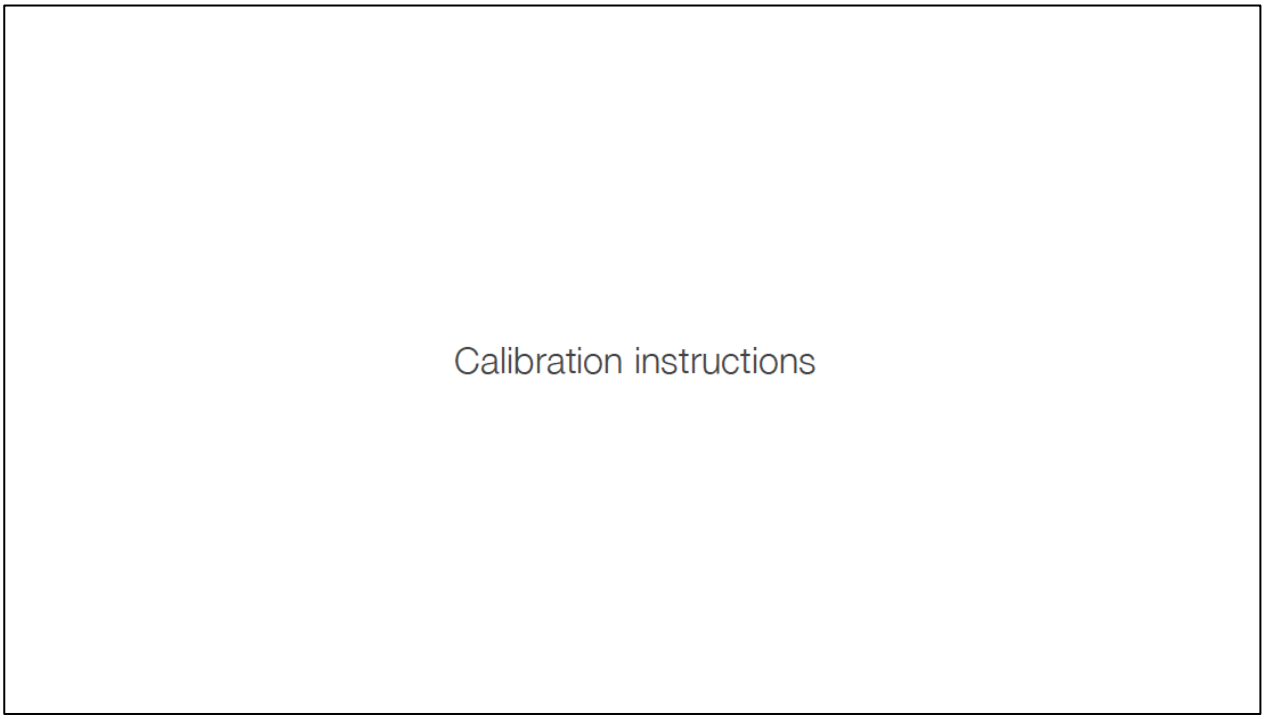
10 Appendix

10.1 Paradigm & Instructions

EEG screen instructions for the Oddball paradigm:

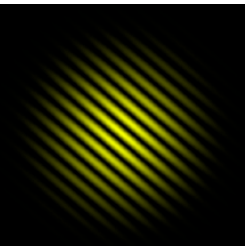


Auditory calibration task

This task is used to check the smallest difference in pitch that you are able to detect. In the task you will be presented with a series of tones. Every now and then a tone with a slightly higer pitch will be played. Your task is to press a button as soon as you detect such a tone.

Press any button to start.

Visual calibration task



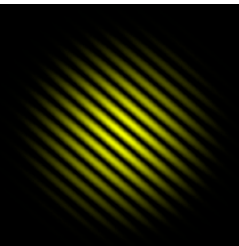
This task is used to check the smallest difference in visual stimulus orientation that you are able to detect. In the task you will be presented with a series of stimuli of a specific orientation. Every now and then a stimulus will be preseted rotated slightly left. Your task is to press a button as soon as you detect such a tone.

Press any button to start.

Auditory calibration task

Congratulations! We have recorded the tone pitch that you consistently recognize as higher than the standard.

Visual calibration task



Congratulations! We have recorded the stimulus orientation that you consistently recognize as different than the standard.

Auditory calibration task

Congratulations! We have recorded the tone pitch that you consistently recognize as higher than the standard.

General instructions

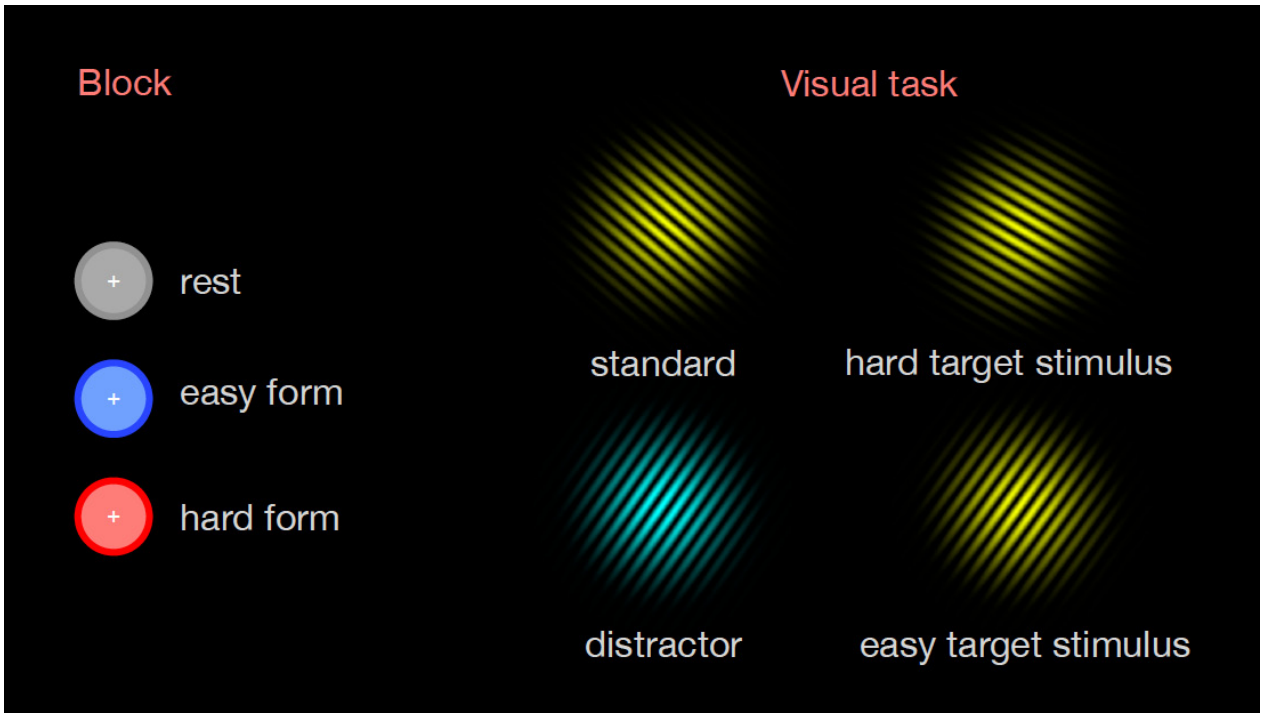
Welcome to the **oddball** task!

In this study your task will be to pay attention to the presented stimuli. Three types of stimuli will be presented:

- frequent stimuli
- rare target stimuli (easy and hard to recognize)
- rare distractors

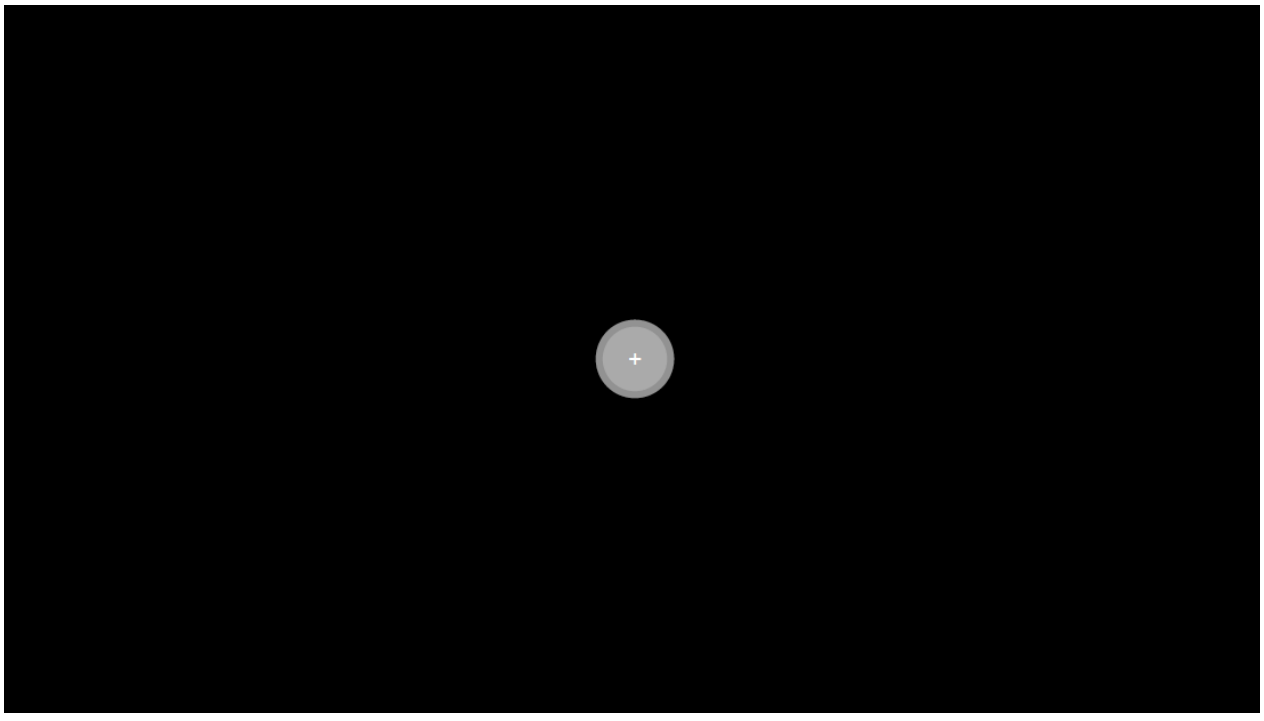
Your task will be to pay attention to the rare target stimuli and press a button as soon as you recognize it. Three modalities will be used, auditory, visual and somatosensory. In each modality there will be two levels of difficulty, easy and hard. Before each run, you will be shown short instructions and examples of stimuli. Within the run three types of blocks will be interleaved, easy task (blue circle), hard task (red circle) and rest period (gray circle).

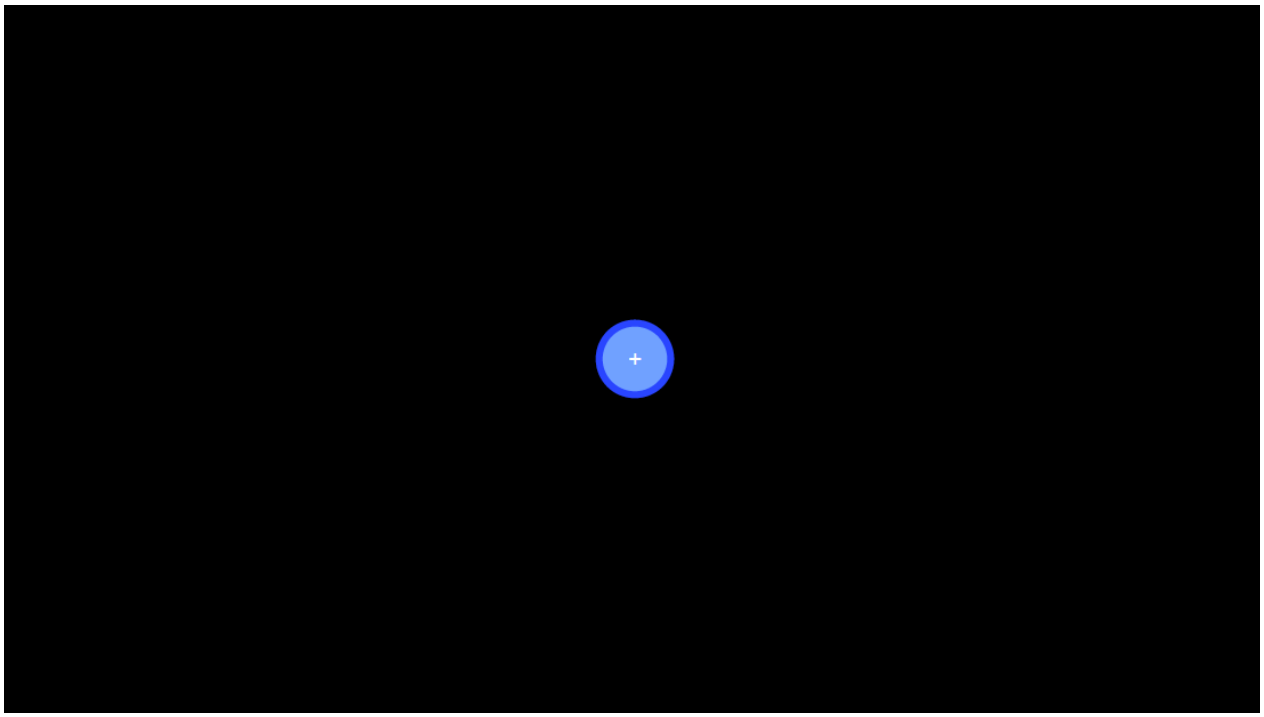
Specific instructions

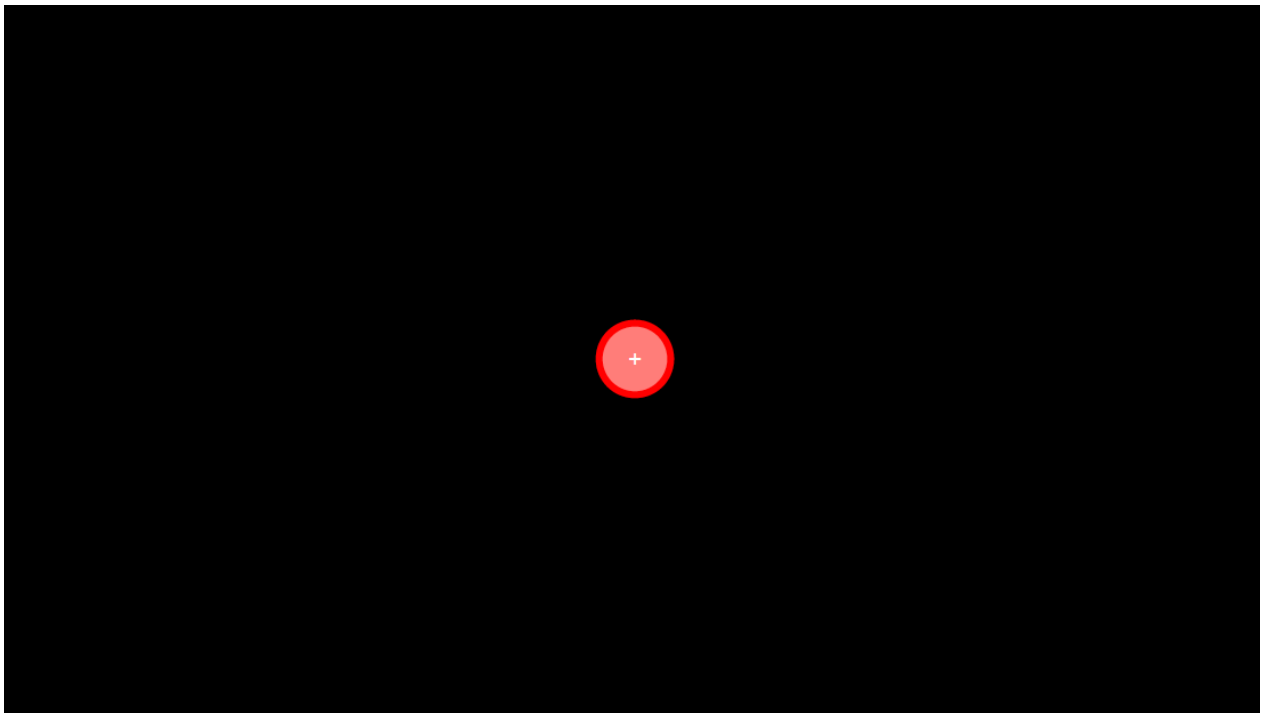

Block
Visual task
rest
easy form
hard form
standard
hard target stimulus
distractor
easy target stimulus


Block
Auditory Task
rest
easy form
hard form
low tone
standard
slightly higher tone
hard target stimulus
markedly higher tone
easy target stimulus
noise
distractor

Fixation points
(rest, easy, hard block)







10.2 Abstract / Zusammenfassung

Abstract

In everyday life, the rapid detection of changes in our environment is crucial for survival. For that reason several attentional mechanisms have evolved. One of the best-studied physiological “windows” on attention is the P3 potential (also called P300 or late positive component), first measured by Chapman and Bragdon (1964). It is an event related potential (ERP), with a maximum amplitude latency of roughly 250 - 600ms that can vary depending on the stimulus modality, task conditions, age, gender (Katayama & Polich, 1998; Brumback, Arbel, Donchin, & Goldman, 2012; Polich & Kok, 1995) and a multitude of environmental factors, such as ethanol, marijuana and nicotine intake (Polich & Criado, 2006; Evans, Maxfield, Van Rensburg, Oliver, Jentink, & Drobes, 2013). The P3 is considered to be an endogenous potential (Donchin, Ritter & McCallum, 1978; Katayama & Polich, 1999), generated irrespectively of the actual sensory modality (visual, auditory, somatosensory).

The subject’s reaction is crucial for the generation of the P3 potential, which has been tied to attentional, evaluative, categorization and memory processes (Polich, 2007; Squires, Squires, & Hillyard, 1975; Comerchero & Polich, 1999). The context updating theory proposes that after initial sensory processing, the new incoming stimulus is compared with the previous neural representation of the stimulus environment, which is stored in the working memory (Polich, 2007). If the stimulus remains the same or similar enough, only sensory evoked potentials (N1, P2, N2) are generated. However, if the incoming stimulus is significantly different, the stored neural representation of the environment gets updated, resulting in the generation of P3 potential (Polich, 2007; Polich, 2003). In spite of more than 40 years of research, fundamental questions regarding the nature of its neural generators remain unresolved. Most studies concluded that the P3 is a genuine classical endogenous potential, and that its surface potential distribution remains constant across sensory modalities. These results are largely based on low-density EEG recordings, without the use of high-resolution methods such as the spherical spline Laplacian (SSL). In this study, 17 healthy participants performed a

three-stimulus oddball task in visual and auditory modality while their EEG was recorded using a 128-channel system. The comparison of amplitude-normalized SSL derived P3 brain-surface potentials and the analysis of spatial and temporal correlations revealed significant differences between visual and auditory evoked P3 topography. Based on these results we conclude that there must be at least some sensory-modality specific neuronal generators of the P3.

Zusammenfassung

Der Mensch ist mit verschiedenen überlebenswichtigen Aufmerksamkeitsmechanismen ausgestattet um im Alltag und in Gefahrensituationen angemessen reagieren zu können. Die schnelle Erfassung von Veränderungen in unserer unmittelbaren Umgebung kann überlebenswichtig sein. Einer der bestuntersuchten physiologischen Marker der Aufmerksamkeit ist das P3-Potential (auch P300 genannt). Es ist ein ereigniskorreliertes Potential (EKP, engl.: ERP), das erstmals von Chapman und Bragdon (1964) gemessen und entdeckt wurde. Die maximale Amplitudenlatenz beträgt ungefähr 250 – 600ms und kann je nach Stimulusmodalität, Aufgabenstellung, Alter, Geschlecht (Katayama & Polich, 1998; Brumback, Arbel, Donchin, & Goldman, 2012; Polich & Kok, 1995) und einer Vielzahl anderer Einflüsse wie Ethanol, Marihuana und Nikotinzufuhr variieren (Polich & Criado, 2006; Evans, Maxfield, Van Rensburg, Oliver, Jentink, & Drobes, 2013). Es wird angenommen, dass das P3-Potential ein von der involvierten Sinnesmodalität (visuell, auditiv, somatosensorisch) unabhängiges, endogenes Potential ist (Donchin, Ritter & McCallum, 1978; Katayama & Polich, 1999). Ausschlaggebend für die Entstehung des P3-Potentials, das in Zusammenhang mit Aufmerksamkeits-, Evaluierungs-, Kategorisierungs- und Gedächtnisprozessen zu stehen scheint (Polich, 2007; Squires, Squires, & Hillyard, 1975; Comerchero & Polich, 1999), ist die Reaktion des Subjekts. Die “Context Updating Theorie“ nimmt an, dass nach anfänglicher sensorischer Verarbeitung der neu-eingehende Stimulus mit der vorherigen neuronalen Repräsentation des Stimulus und Stimuluskontexts, welche im Arbeitsgedächtnis gespeichert ist, verglichen wird (Polich, 2007). Wenn der neu-eingehende Stimulus gleich bleibt – oder dem vorhergehenden ähnlich genug ist – werden lediglich

sensorisch evozierte Potentiale (N1, P2, N2) generiert. Unterscheidet sich der neue Stimulus jedoch signifikant, wird die gespeicherte neuronale Repräsentation aktualisiert und ein P3-Potential generiert (Polich, 2007; Polich, 2003).

Trotz der bereits mehr als 40 Jahre andauernden Forschung, sind grundlegende Fragen bezüglich der neuronalen Erzeuger noch unzureichend geklärt. Die meisten Studien gelangten zu dem Schluss, dass das P3-Potential ein klassisch-endogenes Potential ist, und dass die Oberflächenpotentialverteilung (engl.: „surface potential distribution“) zwischen verschiedenen Sinnesmodalitäten konstant ist. Diese Resultate basieren jedoch größtenteils auf niedrigauflösenden EEG-Aufzeichnungen, ohne die Verwendung hochauflösender Methoden wie die „Sherical-Spline-Laplacian (SSL)“ Methode. 17 gesunde Teilnehmer vollzogen einen sogenannten visuellen und auditiven „drei-stimulus Oddball Task“ („three-stimulus oddball task“), während deren EEG mit einem 128-Kanal-System aufgezeichnet wurde. Ein Vergleich von amplitudennormalisierten SSL Oberflächenpotentialen und die Analyse von räumlichen und zeitlichen Korrelationen, weisen auf signifikante Unterschiede zwischen der visuell und auditiv evozierten Modalität hin. Auf Grundlage dieser Resultate kommen wir zu dem Schluss, dass es zumindest sensorisch-spezifische neuronale Generatoren des P3-Potentials geben muss.

10.3 Curriculum Vitae

PERSONAL DATA

Name:	Daniel Attia
E-Mail:	daniel_attia@outlook.com

EDUCATION

November 2014	**University of Vienna / Ljubljana** Cognitive Science (MSc)
November 2011	**University of Vienna** Philosophy (BA)
February 2010 – July 2010	**Université Nice Sophia-Antipolis** Philosophy (Erasmus Exchange Program)
October 2006 – Juli 2007	**Caritas WG Refugio** Assistance of Minor Refugees Compulsory Community Service
June 2006	**GRG II Zirkusgasse (Grammar School)** University-Entrance Diploma

RESEARCH EXPERIENCE

March 2013 – February 2014	**Department of Neurology, Ljubljana & Mind & Brain Lab, Ljubljana** Assessing P3 topographies of different sensory modalities via EEG & fMRI measurements (supervisor: Zvezdan Pirtošek, Grega Repovš)
October 2012 – February 2013	**Department of Neurology, Ljubljana** Assisting at EEG/ERP studies (supervisor: Zvezdan Pirtošek)
March 2012 – July 2012	**Department of Philosophy, Vienna**

Social Psychology Study on Deterministic Belief & Cooperative Behavior (supervisor: Alexander Batthyany)

PUBLICATIONS AND PRESENTATIONS

Dreo, J., Emeršič, A., **Attia, D.**, Repovš, G., Pirtošek, Z. (2014). The advantage of high-resolution EEG recordings for cognitive evaluation. Published abstract and poster presentation at the *18th biennial Conference of the IPEG-Society*. Leipzig: Germany, September 2014.

Attia, **D.**, Dreo, J., Pirtošek, Z. (2013). Comparing P3 Topography In Different Sensory Modalities. Testing the Common Pathway Hypothesis of P3 Generation. Published abstract and talk at the *International Conference in Cognitive Science*. Ljubljana: Slovenia, October 2013.

Attia, **D.**, Repovš, G., Dreo, J., Pirtošek, Z. (2013). Comparing P3 Topography In Different Sensory Modalities. Testing the Common Pathway Hypothesis of P3 Generation. Poster presentation at the *Sinapsa Neuroscience Conference*. Ljubljana: Slovenia, September 2013.

Attia, D., Lechner, S., Batthyany, A. (2012). How does the (dis-)belief in free will affect satisfaction in life and cooperative behaviour? Published abstract and poster presentation at the *Mei:CogSci Conference*. Bratislava: Slovakia, June 2012.

ADDITIONAL INFORMATION

Native Language	German
Other Languages	English (fluent), French (fluent), Arabic (basic)
Computer Skills	MS Office, SPSS, Brain Analyzer, Matlab, Python