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EEG correlates of normal and altered processing strategies to solve the perceptual inference problem

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Summary

The information available through our senses is noisy, incomplete, and to varying degrees ambiguous. The perceptual system has to reconstruct the exogenous world by integrating the limited sensory information with endogenous factors such as memory (von Helmholtz, 1867). This construction process causes the perceptual inference problem, i.e. one single sensory information can be interpreted in multiple ways. In a probabilistic manner, the brain decides for one of those interpretations in order to provide a stable and reliable percept. The present dissertation investigates different aspects of this probabilistic decision in neurotypical participants but also in patients with Schizophrenia Spectrum Disorder (SSD) by comparing visual processing of ambiguous/low-visibility with disambiguated/high-visibility stimuli.

Ambiguous figures are paradigmatic when studying the perceptual inference problem, because in those figures one sensory information allows for two possible interpretations. Using electroencephalography (EEG), previous studies already found large event-related potential (ERP) differences 200 ms and 400 ms after stimulus onset between ambiguous stimuli and disambiguated variants thereof (Kornmeier and Bach, 2009; Kornmeier et al., 2016), i.e. the *ERP Ambiguity Effects*. In the first part of this dissertation (see also my publication Joos et al., 2020b), I replicated one experiment using ambiguous stimuli (by Kornmeier and Bach, 2009; Kornmeier et al., 2016) and studied whether these ERP Ambiguity Effects also occur with low-/high-visibility stimuli. I found that not only different levels of stimulus ambiguity, but also different degrees of stimulus visibility evoke those ERP effects. The stimuli used were smiley faces with two different emotional expressions that were either clearly or less visible. Ambiguous figures impose different demands on the perceptual system compared to low-visibility stimuli. Common to both types of stimuli is, however, that they evoke uncertainty. The ERP effects identified by Kornmeier et al. (2009, 2016), and replicated in the current work might thus reflect a certainty rating of perceptual constructs at a higher cognitive level, beyond sensory details. The effects are accordingly re-labelled to *ERP Uncertainty Effects*.

Patients with SSD show fundamental differences in the process of perception (Silverstein et al., 2015), in the integration of sensory with endogenous information (van Assche and Giersch, 2011), and reveal difficulties in processing of ambiguous emotional expressions (Kohler et al., 2000) compared to controls. Thus, the experimental paradigm and stimuli from the first part of this thesis were investigated in patients with SSD in the second part of this thesis. Due to the Corona pandemic, I was not able to finish data acquisition during the time of my PhD. Therefore, the following results are preliminary. The ERP Uncertainty Effects were replicated in both groups. An observable tendency for smaller ERP effects in patients compared to controls did not reach statistical significance. Additional exploratory analyses indicated significant differences in the processing of perceptual (un)certainty in patients with SSD compared to controls. These results are interpreted within the predictive coding theory (Friston, 2012), which postulates that the brain continuously forms models about the external world and continuously updates these models with new sensory information. Patients with SSD show alterations in those updating mechanisms (e.g. Notredame et al., 2014). The current results might reflect these altered updating mechanisms by means of altered reliability attribution to the sensory information, which ultimately might result in altered (un)certainty ratings as found in this study.

Helmholtz' inferential approach on perception postulates that the brain uses information from previous experiences in order to appropriately reconstruct the exogenous world despite the limited sensory information. Currently discussed predictive coding theories are based on this idea and further assume that the brain (1) always forms a prediction about the to-be-created perceptual interpretation, (2) integrates these predictions with the current sensory information, and (3) concurrently creates new predictions for an upcoming moment. The ERP Uncertainty Effects show unusually large effect sizes and individual statistical significance, which makes the understanding of their functional roles even more interesting. Previous experimental evidence suggested the involvement of the ERP effects in the above mentioned processes, but their exact role could not be systematically investigated due to the experimental paradigm. In the third part of this dissertation (see also my publication Joos et al., 2020a), I modified the experimental paradigm in order to investigate the functional role of the ERP Uncertainty Effects with a particular focus on predictive coding theories. The results of this third study confirm the involvement of the ERP Uncertainty Effects in predictive mechanisms. They further confirm the strong influence of temporal aspects on perceptual processing. Particularly, the perceptual system seems to automatically and unavoidably exploit regularities from past perceptual experiences in order to generate predictions about the immediate perceptual future. This seems to be the case even in situations where the perceptual past and the perceptual future are irrelevant for a current task related to a currently seen stimulus. The present results further indicate that our expectations about the immediate perceptual future influence how we perceive the present.

The findings of this dissertation should be considered when investigating physiological correlates of psychiatric diseases. Particularly, altered predictive processes in patients with SSD could be investigated by means of the experimental paradigm from the third part of the dissertation. Further, emotional expressions in smiley faces with different degrees of their visibility (as in the first and second part of this thesis) could be used as stimulus material. In future studies these modifications would allow to measure predictive processes in patients with psychiatric diseases and in neurotypical participants in a state of perceptual uncertainty, which closely resembles difficult situations within the patients and controls everyday life, i.e. dealing with uncertainty in social interactions.

Thesis Structure

The current cumulative dissertation introduces the background, motivation, and research questions of this PhD project in chapter 1.

In the three following chapters, the two published manuscripts (chapter 2, chapter 4) and an unpublished manuscript (chapter 3) are presented. The contribution of the three manuscripts to the general research question and its scientific relevance are discussed in chapter 5.

There are two numbering systems within this dissertation, one is related to the dissertation structure and the other is inherent to the specific publication/manuscript.

Included Articles

E. Joos, A. Giersch, L. Hecker, J. Schipp, S. P. Heinrich, L. Tebartz van Elst, and J. Kornmeier. Large EEG amplitude effects are highly similar across Necker cube, smiley, and abstract stimuli. *PLOS ONE*, 15(5):1–26, 05 2020. doi = 10.1371/journal.pone.0232928.
URL `https://doi.org/10.1371/journal.pone.0232928`.

E. Joos, E. Koning, L. Tebartz van Elst, J. Kornmeier, A. Giersch.
Preliminary manuscript: Perceptual uncertainty effects in Schizophrenia Spectrum Disorder – an EEG study.

E. Joos, A. Giersch, K. Bhatia, S. P. Heinrich, L. Tebartz van Elst, and J. Kornmeier.
Using the perceptual past to predict the perceptual future influences the perceived present – a novel ERP paradigm. *PLOS ONE*, 15(9):1–35, 09 2020. doi = 10.1371/journal.pone.0237663.
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1. Introduction

The exogenous world provides a huge amount of information at a given time point. The human access to this information, however, is limited by the sensory organs. The three dimensional world that we live in, for example, is projected onto a two-dimensional retina and with this, the direct access to the third dimension is lost (e.g. Todd, 2004). If visual perception would be based only on exogenous information entering through the limiting sensory organs, a poor quality image would be the consequence (von Helmholtz, 1867).

The rich and detailed experience made during human visual perception can be explained by a reconstruction process of the information given the limited sensory evidence. Endogenous information like memories of previous experiences and learnt regularities about the world are integrated into perception. The third dimension, for example, can be inferred by including secondary depth cues, like occlusion, central perspective, etc. and the knowledge of light originating above us (Rock, 1995).

Due to this limited sensory access, multiple interpretations of a given sensory input are possible. This perceptual inference problem is solved by the brain in a probabilistic manner by using the temporal and spatial context (von Helmholtz, 1867). For example, if the representation of another person on one's retina decreases in size, it is much more probable that this person is moving away from oneself, rather than the interpretation that the person is shrinking (for other examples read von Helmholtz, 1867). Our everyday experience shows that this is an efficient strategy, because the reconstruction of the exogenous world is usually reliable and effective. It is, however, important to notice that our perception does not reflect the exogenous world as it is.

1.1 Ambiguity vs. Visibility

1.1.1 Ambiguity

The perceptual inference problem becomes obvious in situations in which the probabilistic mechanisms during perception do not reveal a unique and highly probable interpretation. The term ambiguity refers to this situation and to the Latin word *ambi*, meaning both. Ambiguity is defined as the 'Capability of being understood in two or more ways [...]' (Dictionary, 2019). Studying ambiguity allows to explicitly investigate the neural processes underlying the constructive, probabilistic mechanisms that are present in every perceptual decision.

In classical ambiguous figures, one single sensory information allows for two or more possible interpretations. Examples for binary perceptual decisions can be found in binocular rivalry, when the two eyes receive mutually exclusive information and perception alternates between the perceptual interpretations of the two eye's input (Pitts et al., 2010; Blake, 2001; O'Shea et al., 2013). Another category of binary perceptual decisions are classical ambiguous figures like the famous Necker cube (Necker, 1832), Rubin's face-vase illusion (Rubin, 1921), and Boring's Old/Young Woman (Boring, 1930) all result in two mutually exclusive perceptual interpretations, which alternate spontaneously.

ERP Ambiguity Effects: Interesting in this context are findings by Kornmeier et al. who investigated event-related potential (ERP) correlates of ambiguity in classical ambiguous figures (Kornmeier and Bach, 2009; Kornmeier et al., 2016). In one experimental condition, they presented the Necker lattice (Kornmeier et al., 2001), a variant of the Necker cube, and in another condition disambiguated variants thereof (see Figure 1.1, left column). Two prominent ERP components differed between conditions, an anterior P200 (positive ERP component 200 ms after stimulus onset) and a posterior P400 (positive ERP component 400 ms after stimulus onset), which constitute the so-called *ERP Ambiguity Effects*. Amplitudes of both ERP components increase as stimulus ambiguity decreases (Kornmeier et al., 2016). Importantly, the ERP Ambiguity Effects were found for three different stimulus categories, with very different manifestations of ambiguity, i.e. geometry (Necker lattice), motion (SAM/'motion quartet': Schiller, 1933), and Gestalt perception (Boring's Old/Young Woman: Boring, 1930, see Figure 1.1). This generality along with the late occurrences (200 ms and 400 ms after stimulus onset) indicate that the ERP Ambiguity Effects are likely to reflect higher cognitive functions after the initial processing of sensory information. The current interpretation (Kornmeier et al., 2016) suggests that the perceptual system constructs perceptual interpretations as fast as possible and in a highly automatic manner (for further discussion see Kornmeier and Bach, 2012). It is proposed that only after this initial formation of a certain percept, the reliability of this perceptual construct is rated. Importantly, it is proposed that the ERP Ambiguity Effects reflect this reliability estimation of the perceptual construct with large amplitudes in the case of high reliability (disambiguated stimuli) and small amplitudes in the case of low reliability (ambiguous stimuli).

1.1.2 Visibility

In the case of classical ambiguous figures, the perceptual decision becomes difficult because one and the same sensory information allows for two mutually exclusive interpretations. Making a perceptual decision, however, can also be difficult because the information available to our senses is of low quality, e.g. during rain and fog or during low luminance. In this case, the difficulty of the perceptual decision is based on poor visibility.

A relevant situation in which poor visibility might lead to impaired social interaction is when emotional expressions are interpreted. Everyone knows situations where it is difficult to infer another person's emotional state from her/his facial expressions. Particularly, the differences in facial expressions between different emotional states can be tiny. A slight smile for example might express that a person is a little bit happy, but it might also express that the person is insecure. Not only the six basic emotions as defined by Ekman (Ekman, 1992), but many

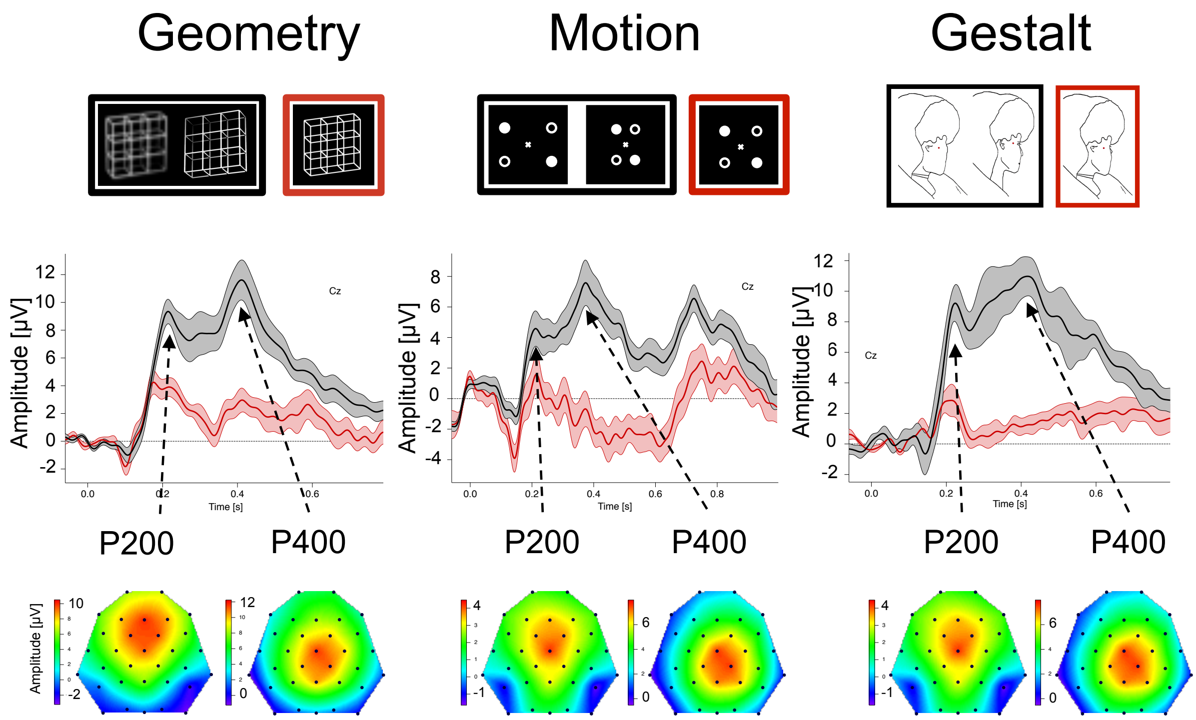

Figure 1.1: ERP Ambiguity Effects described by Kornmeier et al. (2009, 2016). The ERP Effects were found for geometry (left), motion (middle), and Gestalt perception (right). In the upper row the respective stimuli are depicted with black frames around the disambiguated stimuli and red frames around the ambiguous stimuli. The middle row depicts the grand mean ERPs along with the SEM at electrode Cz. Consistently larger ERP traces are found in response to disambiguated (black trace) compared to ambiguous (red trace) stimulus variants (effect sizes between 0.8 and 2.1). The ERP Ambiguity Effects comprise a positivity 200 ms (P200) and a positivity 400 ms (P400) after stimulus onset. The spatial distribution of those two ERP components can be inspected in the bottom row. The P200 is located at fronto-central electrodes, while the P400 shows a centro-parietal distribution.

nuances in-between them can be perceived. Emotions and the related facial expressions can thus be represented in a multidimensional space. One particular dimension, like the axis from happy to sad, has a continuous scale rather than a binary one, which is the case in classical ambiguous figures. In order to quantify the aspects of visibility easily, I reduced the complexity of the stimuli to a minimum by presenting smiley faces. Further, I reduced complexity of the emotional expression by only presenting either happy (mouth curvature upwards) or sad (mouth curvature downwards) smileys. In addition to this, the emotional expressions could either be highly visible (strong mouth bending) or less visible (slight mouth bending).

1.1.3 First research question

The first research question is: Can the ERP amplitude effects, labeled as ERP Ambiguity Effects by Kornmeier et al. (Kornmeier and Bach, 2009; Kornmeier et al., 2016), also be evoked by high- and low-visibility stimuli? In chapter 2, I compared the ERP Ambiguity Effects in response to disambiguated and ambiguous Necker lattices with possible ERP Ambiguity Effects in response to more or less visible emotional expressions of smiley faces.

If similar neural responses for those very different stimulus types were found, then the EEG effects are not related to a certain stimulus category but rather reflect very high-level cognitive processes. It is proposed that both ambiguity and poor visibility can lead to unreliable perceptual interpretations. In turn, unreliable perceptual interpretations might result in a state of perceptual uncertainty, whereas reliable perceptual interpretations might result in a state of perceptual certainty. This perceptual (un)certainty might be reflected in the ERP effects.

1.2 Perception in Schizophrenia Spectrum Disorder (SSD)

Schizophrenia Spectrum Disorder (SSD) is a complex set of neurodevelopmental disorders with a prevalence in the population of around 1% (Jardri and Deneve, 2013). The DSM-V defines Schizophrenia Spectrum Disorder "by abnormalities in one or more of the following five domains: delusions, hallucinations, disorganized thinking (speech), grossly disorganized or abnormal motor behavior (including catatonia), and negative symptoms" (American Psychiatric Association, 2013, page 87). Decreased emotional expression and avolition (drive disorder) are the two main occurring negative symptoms in schizophrenia, while alogia (speech impairment), asocialtiy, and anhedonia (reduced experience of positive emotions) occur less frequent. So far, diagnoses are based on behavioural parameters, while reliable physiological markers do not exist.

1.2.1 Altered perceptual processing in SSD

As mentioned above, our perceptual experience is stable and reliable, even though the sensory information is limited. One fundamental mechanism of the brain to solve the perceptual inference problem is based on the integration of exogenous with endogenous contextual information, like perceptual memory on different time scales. It has been proposed that patients with SSD show fundamental deficits in the process of perception (Silverstein et al., 2015). Further, patients with SSD reveal impairments in the integration of sensory information with memorised concepts (Notredame et al., 2014) and spatial and temporal contexts (van Assche and Giersch, 2011).

Ambiguous figures are paradigmatic in this context, because even though the sensory information is the same, different perceptual interpretations are possible. The different interpretations can thus be traced back to the endogenous information used for constructing the percept. Studying ambiguity resolution in patients with SSD has been proposed in order to provide a promising tool to investigate the underpinnings of the disorder (Jardri and Deneve, 2013; Notredame et al., 2014; Bortolon et al., 2016; Fujino et al., 2016). It has already been found that patients with SSD show different processing of ambiguous figures compared to controls (Notredame et al., 2014; King et al., 2017; McBain et al., 2011). Particularly, patients with SSD show impairments in disambiguating stimuli with emotionally ambiguous content (Dlabac-de Lange et al., 2018) and in estimating emotional states from facial expressions (Turetsky et al., 2007; Kohler et al., 2003, 2000).

1.2.2 Second research question

The previously introduced ERP Uncertainty Effects (Kornmeier and Bach, 2009; Kornmeier et al., 2016; Joos et al., 2020b) show physiological differences in response to different degrees of ambiguity, with large ERP amplitudes in the case of unambiguous and small ERP amplitudes in the case of ambiguous stimuli. The ERP Ambiguity Effects might represent a successful solution of the perceptual inference problem, because one highly probable perceptual interpretation that results in perceptual certainty (unambiguous stimuli) evokes larger ERP amplitudes than two equally likely perceptual interpretations that result in perceptual uncertainty (ambiguous stimuli). In the current line of research it is hypothesised that the ability to solve the perceptual inference problem is altered in patients with SSD compared to neurotypicals. As a consequence, SSD patients should show an altered pattern of the ERP Uncertainty Effects compared to controls. Further, patients with SSD have been shown to reveal impaired emotion processing (Dlabac-de Lange et al., 2018; Turetsky et al., 2007; Kohler et al., 2003) and might therefore show stronger alterations during the study of perceptual processing if the stimuli contain emotional expressions. I thus adopted the paradigm from chapter 2 and introduced perceptual (un)certainty by low- and high-visibility of emotional expressions in smiley faces. I measured the related neural responses in patients with SSD and in matched control participants.

The second research question of this PhD project is: Do patients with SSD process perceptual (un)certainty differently than controls? If yes, then the pattern of ERP Uncertainty Effects should be altered.

The ERP Uncertainty Effects (Kornmeier and Bach, 2009; Kornmeier et al., 2016; Joos et al., 2020b) reveal large effect sizes (Cohen's d between 0.6 and 1.2) and are typically visible in individual participants. The latter is the exception rather than the rule in ERP studies. If this project were to provide altered ERP effects in patients compared to controls, they may be promising physiological markers for clinical diagnostics.

1.3 Influences of the temporal context

The previously presented experimental paradigms were focused on the investigation of a currently shown stimulus. The influence of previously seen and predicted stimuli on a currently seen stimulus has so far been neglected. However, it was already highlighted by von Helmholtz (1867) that the integration of previous experiences is crucial for solving the perceptual inference problem, i.e. reducing the infinite number of possible interpretations of one sensory input to one most probable interpretation. Our environment typically only changes slightly from one moment to the other, therefore it is efficient to use information from the past to expect future events. This strategy avoids unnecessary re-categorisation of information that is constant over time.

1.3.1 Empirical findings

Several lines of research investigate influences of previously shown stimulus-specific features (e.g. orientation of a Gabor patch) on the perception of the same feature of a currently presented stimulus. Positive aftereffects, e.g. positive priming (Long et al., 1992; Dehaene et al., 1998), positive hysteresis (Liaci et al., 2018; van Rooij et al., 2016), and serial dependence (Fischer and Whitney, 2014; Cicchini et al., 2017; Chambers et al., 2017), show that current perception is shifted towards the previous percept. There are also negative aftereffects, e.g. adaptation (Bach and Ullrich, 1994; Heinrich and Bach, 2002) in which current perception is shifted away from the previous percept. The empirical findings reveal influences of the past on different time scales, mostly studied in the milliseconds range but they were found to last for up to 10 seconds in serial dependence (Fischer and Whitney, 2014). Further, different processing steps are involved in the integration of previous experiences, ranging from specific retinotopic locations in adaptation and priming to attention-modulated influences in serial dependence.

1.3.2 Theoretical frameworks

The empirical findings can be explained by theoretical frameworks such as Bayesian probability (Kersten and Yuille, 2003) and predictive coding (Friston, 2012; Kok and de Lange, 2015). According to these theories, the brain creates a model about the external world. With every new sensory input, the *prediction error* between the model and the input is calculated and the model is updated accordingly (e.g. Friston, 2012).

In typical studies, frequently presented stimuli are infrequently disrupted by deviant stimuli. The assumption is that the frequently presented stimuli optimise the model such that upcoming sensory information is reliably predicted. The deviant stimuli, on the other hand, should evoke large prediction errors, which the authors then measure both behaviourally and electrophysiologically (Näätänen et al., 2007; Stefanics et al., 2014).

1.3.3 Third research question

The stimuli used in the temporal context studies introduced above were typically unambiguous, highly visible, and mainly differed in their occurrence frequency. However, in our natural environment, exploiting the perceptual past and relying on a predicted future may be very important in perceptual situations with low quality of the sensory input, e.g. when the stimulus is ambiguous. Stimuli from the immediate past that are ambiguous, may make predictions about the immediate perceptual future less reliable compared to unambiguous previous stimuli. The experimental paradigm introduced in chapter 2 and chapter 3, however, does not allow for the investigation of the influence of low quality stimuli on predictive processes. In the third part of this dissertation the paradigm is modified such that those influences can be systematically investigated.

The third research question is thus: Is a currently seen stimulus perceived and processed differently if the previous and the predicted stimulus are ambiguous compared to unambiguous? In chapter 4 the previously introduced ERP Uncertainty Paradigm was modified to a paired stimulus paradigm, where a first stimulus (*S1*) was followed by a second stimulus (*S2*). In a first experiment, a paired design (2x2) was applied by presenting all possible combinations of ambiguity levels (ambiguous vs. unambiguous) of S1 and S2. Ambiguity levels thus varied between but stayed constant within experimental conditions. This experimental design allowed for the investigation of neural responses elicited by the same S1 stimuli with different levels of ambiguity in its temporal context, i.e. preceding S2 of the previous pair and predicted S2

of the current pair. In a second experiment, preceding S2 stimuli were replaced with abstract symbolic information about the future stimulus and it was studied whether this replacement evokes similar ERP and reaction time results as found in the first experiment.
If differences of ambiguity levels in the temporal context stimuli evoke different ERP Uncertainty Effects, then the particular modulations would reveal fundamental steps in the process of perception and related predictive processes and should help to unravel the functional role of the exceptionally large ERP Uncertainty Effects.

In the current dissertation, different processing strategies for solving the perceptual inference problem will be investigated. First, it will be investigated whether the same neural correlates of solving the perceptual inference problem can be found in case of stimulus ambiguity and low visibility of a stimulus. Second, normal and altered perceptual processing will be investigated in patients with SSD and neurotypicals in case of low visibility. Third, temporal aspects of solving the perceptual inference problem, i.e. integrating information from the immediate perceptual past and predicted information about the immediate perceptual future into processing of the perceptual present, will be investigated.

2. PhD article No. 1: Large EEG amplitude effects are highly similar across Necker cube, smiley, and abstract stimuli

2.1 Summary

The previously reported ERP Ambiguity Effects (P200, P400; Kornmeier and Bach, 2009; Kornmeier et al., 2016) revealed large EEG differences in response to classical ambiguous figures compared to disambiguated variants thereof. Specifically, the differences were found in two ERP components, 200 ms (P200) and 400 ms (P400) after stimulus onset, with large amplitudes in response to disambiguated and small amplitudes in response to ambiguous stimuli. The ERP effects were found for ambiguity in geometry, motion, and Gestalt perception. Due to the late occurrences – in perceptual processing time scales – of the ERP components at 200 ms and 400 ms after stimulus onset and their generality across stimulus types, the effects are interpreted as a reflection of high-level cognitive processes, which are not directly related to the actual stimulus information. It was already proposed by Kornmeier et al. that the ERP Ambiguity Effects might reflect high-level evaluations of the perceptual outcome with large amplitudes when the perceptual outcome is reliable (unambiguous stimuli) and with small amplitudes when the perceptual outcome is unreliable (ambiguous stimuli). If the effects really reflect the brains reliability estimation of the perceptual outcome, then the source for the (un)reliability should not matter.

Testing this hypothesis was one of the goals of the current study. To this end, another source of (un)reliability, namely poor visibility, was tested within the ERP Ambiguity Paradigm. Highly visible stimuli were contrasted with less visible stimuli and it was investigated whether the same ERP effects were present in this case compared to (un)reliability evoked by unambiguous and ambiguous Necker lattices.

Manipulating visibility was achieved by presenting smiley face stimuli with different emotional expressions, which were evoked by varying only one parameter, i.e. the mouth curvature. The mouth curvature could have been (1) highly visible with a clearly happy (mouth strongly bended upwards) or a clearly sad (mouth strongly bended downwards) expression in order to induce reliable perceptual contstructs. The mouth curvature could also have been (2) less visible

with unclear happy (mouth slightly bended upwards) or unclear sad (mouth slightly bended downwards) expressions in order to induce unreliable perceptual constructs.
In addition to the smiley stimuli, ambiguous and disambiguated Necker lattices were presented to replicate previous findings (Kornmeier and Bach, 2009; Kornmeier et al., 2016). Furthermore, abstract stimuli were presented, which had the same low-level features as the smiley stimuli, but differently arranged such that hardly any face could be recognised. These low-visibility and high-visibility abstract stimuli were presented for two reasons: (1) to investigate a face-specific ERP component (N170), which was hypothesised to be present in smiley but not in abstract figure stimuli. Larger N170 amplitudes for smileys compared to abstract figures would indicate face-specific processing of the smileys. (2) To investigate whether the same ERP Effects were evoked only through a difference in curvature bending present in the abstract stimuli.
It was found that ERP Effects (P200 and P400) were similarly evoked by Necker lattice, smiley, and also by abstract stimuli. Given a prominent face-selective ERP component (N170) in response to smiley, but not to abstract stimuli, it was assumed that the smileys were indeed processed as faces.
The paper "Large EEG amplitude effects are highly similar across Necker cube, smiley, and abstract stimuli" (Joos et al., 2020b) indicates that the ERP effects are the same between very different stimulus categories such as classical ambiguous figures and visibility of emotional facial expressions. This generality of the ERP effects indicates a high-level evaluation of the perceptual outcome, which is independent of sensory details. The similar modulation of two ERP components that are 200 ms apart from each other suggests that not only one event of reliability estimation in time but rather a longer-lasting brain state of (un)certainty arises through sensory information of low quality (ambiguity and low-visibility). Therefore, the term *ERP Uncertainty Effects* might be more appropriate than *ERP Ambiguity Effects* and will be used in the following.

Contribution to the paper I was part of the funding acquisition, as well as the conceptualisation and administration of the project. I was responsible for data curation, formal analysis, investigation, methodology, software, validation, visualisation, writing the original draft and reviewing and editing the manuscript.

2.2 Main Manuscript

PLOS ONE

RESEARCH ARTICLE

Large EEG amplitude effects are highly similar across Necker cube, smiley, and abstract stimuli

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Abstract

The information available through our senses is noisy, incomplete, and ambiguous. Our perceptual systems have to resolve this ambiguity to construct stable and reliable percepts. Previous EEG studies found large amplitude differences in two event-related potential (ERP) components 200 and 400 ms after stimulus onset when comparing ambiguous with disambiguated visual information ("*ERP Ambiguity Effects*"). These effects so far generalized across classical ambiguous figures from different visual categories at lower (geometry, motion) and intermediate (Gestalt perception) levels. The present study aimed to examine whether these ERP Effects are restricted to ambiguous figures or whether they also occur for different degrees of visibility. Smiley faces with low and high visibility of emotional expressions, as well as abstract figures with low and high visibility of a target curvature were presented. We thus compared ambiguity effects in geometric cube stimuli with visibility in emotional faces, and with visibility in abstract figures. ERP Effects were replicated for the geometric stimuli and very similar ERP Effects were found for stimuli with emotional face expressions but also for abstract figures. Conclusively, the ERP amplitude effects generalize across fundamentally different stimulus categories and show highly similar effects for different degrees of stimulus ambiguity and stimulus visibility. We postulate the existence of a high-level/meta-perceptual evaluation instance, beyond sensory details, that estimates the certainty of a perceptual decision. The ERP Effects may reflect differences in evaluation results.

Introduction

The information available through our senses is incomplete, noisy and sometimes ambiguous. For example, we see objects only from one perspective, they are often partially occluded, or

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seen in suboptimal conditions e.g. during rain or fog. Further, the available sensory information at a given moment can be ambiguous and thus allow for several about equally probable but mutually exclusive interpretations. The perceptual system has to overcome such sensory limitations and resolve ambiguities in order to create stable and reliable representations of the external world [1].

Ambiguity can arise in different modalities [2], in different forms [3,4], and at different levels of stimulus complexity. Most prominent scientific examples of ambiguity are classical ambiguous figures like the Necker cube [5] (see the Necker lattice [6,7], a variant of the Necker cube in Fig 1A left graph) or Rubin's face-vase illusion [8]. Here one and the same sensory information allows for two or more possible and about equally probable interpretations. During prolonged observation, our perception becomes unstable and alternates repeatedly between different interpretations [see 3 for a review of the phenomenon].

Interestingly, there are many different uses of the term "ambiguity". One prominent area beyond perception science is art, where–at first sight–this term seems to have a different meaning. One most prominent example is Da Vinci's famous "Mona Lisa" painting. The English essayist and writer Walter Pater affirmed in a prominent essay, that Mona Lisa's smile holds an "emotional ambiguity", revealing first a "promise of an unbounded tenderness", but soon after also a "sinister menace" [9]. A large number of articles about Mona Lisa focus on this ambiguity in her emotional facial expression [10–12], which seems to be very different from the ambiguity examples in perceptual science. Mona Lisa's emotional expression is not perceived as either clearly happy or clearly sad but rather more or less happy or sad. Several nuances of emotional expressions and therefore several slightly different interpretations are theoretically possible when observing Mona Lisa.

There is an obvious qualitative difference in the perception between such types of ambiguity and ambiguity as used with the classical ambiguous figures, like the Necker cube. In the case of the Necker cube, perception oscillates between two clear-cut perceptual alternatives, i.e. a perspective from above and a perspective from below. Therefore the perceptual decision here seems to be binary. The interpretation of emotional facial expressions, on the other hand, has different preconditions and is probably more complicated compared to the Necker cube. The relations between the relevant face muscles [13] need to be analysed and related to emotional states experienced by ourselves. The necessary reference system for emotional states is thus endogenous and theory of mind concepts are needed [see 14 for related concepts of embodiment]. Based on internal perceptual statistics generated from memorized perceptual experiences over lifetime, specific patterns of face-muscle-relations receive specific probability values for representing certain emotional states. The ambiguity of an emotional face is thus rather based on a continuous scale of theoretically possible perceptual outcomes.

A closer look at the Necker cube relativizes its binary nature. The source of ambiguity of the Necker cube is the projection of a 3D world on 2D retinae during the first step of vision, and the fact that two different 3D grid objects produce identical projections on the retinae. However, one could imagine in principle infinitively many other 3D grid objects and even some 2D objects projecting identically on the retinae as the Necker cube, as Fig 2C in Kersten and Yuille [15] demonstrates nicely. This implies that the theoretically possible interpretations of the Necker cube are manifold rather than twofold. The reason for the preference of two 90˚ object interpretations is simply that 90˚ angles are much more frequent in our environment than any other angles and thus more probable. To reduce the infinitely many possible interpretations of the Necker cube to the two most probable interpretations, one "only" has to match the sensory evidence to an internal statistics about perceptual experiences, learned over lifetime.

Thus, ambiguity of emotional faces and of geometric cube stimuli may share one basic principle. The fact that the identical sensory information is compatible with several

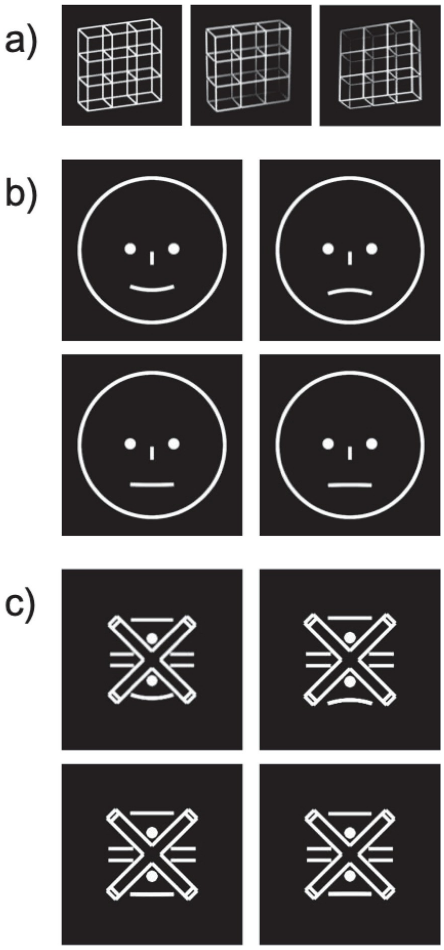

Fig 1. Stimuli. (a) depicts the ambiguous Necker lattice (left) and the disambiguated variants thereof (middle and right). Smiley (b) and abstract figure (c) stimuli are enlarged for better visibility of the "mouth" curvature. (b) depicts the high-visibility (upper row) and low-visibility (bottom row) smileys. Happy smileys are depicted in the left column, sad smileys in the right column. The emotional expression of the smileys was only created through the mouth curvature. In a control condition we embedded the same mouth curvatures into abstract figures (c). Strongly bended "mouth" curvatures are depicted in the upper row and slightly bended "mouth" curvatures in the bottom row (upwards on the left, downwards on the right).

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theoretically possible perceptual interpretations holds for both, the Necker cube and Mona Lisa, and reflects the ambiguity of both stimulus types. However, the reduction of the number of possible interpretations to a lower number of highly probable interpretations, the underlying probability distributions, and the subjective experience seem to differ. The commonality between Necker cube perception and perception of "ambiguous" emotional face expressions may thus be the resulting perceptual uncertainty during their observation, given insufficient sensory evidence.

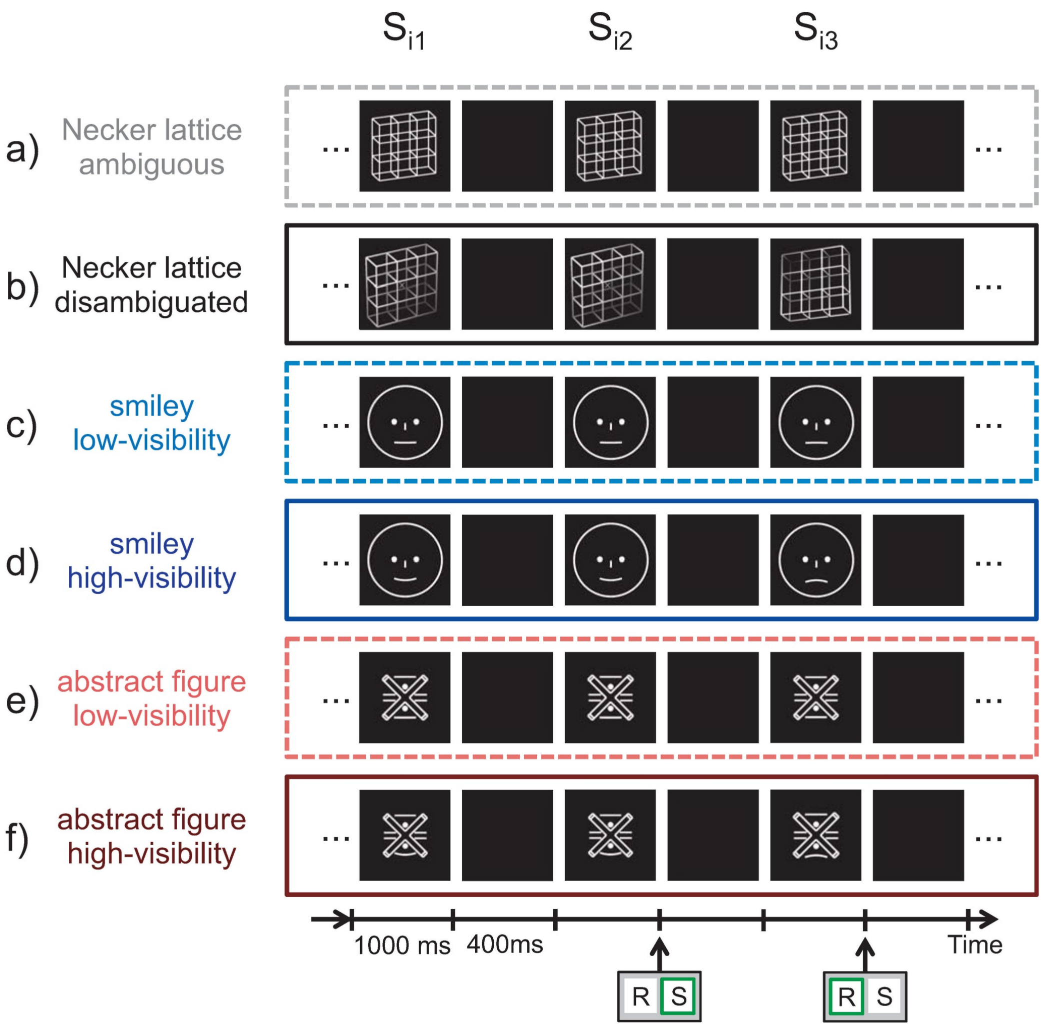

Fig 2. Experimental paradigm. Stimuli were presented discontinuously for 1000 ms with an inter-stimulus interval of 400 ms. Participants compared the current stimulus with the immediately preceding one. In case of identical percepts across two consecutive stimuli, participants pressed 'S' (stability) on a keyboard (represented as squares with the letters 'R' and 'S' below the time axis). If perception changed from one stimulus to the next, participants pressed 'R' (reversal). Stimulus type and ambiguity/visibility level stayed unchanged within experimental conditions (within rows), but differed between experimental conditions (different rows). The order of conditions (rows) was pseudo-randomized. The specific sequences of stimuli (Si1, Si2, Si3) in b—f are for demonstration purposes.

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Interesting in this context are two EEG studies by Kornmeier et al. [16,17]. They compared event-related potentials (ERPs) evoked by ambiguous and disambiguated versions of the Necker cube and found unusually large amplitude differences in two components, an anteriorly distributed P200, followed by a posteriorly distributed P400. Both components show small amplitudes for ambiguous stimuli and large amplitudes for the respective disambiguated stimulus variants. The same pattern of results was found for ambiguity in motion (von Schiller's stroboscopic alternative motion stimulus—also known as the SAM/'motion quartet' [18]) and also in Gestalt perception (Borings ambiguous Old/Young Woman [19]). This is remarkable, because of the dramatic differences in the low-level features and in the sources of ambiguity. One obvious commonality between these different stimulus types is ambiguity at a more abstract level, i.e. that one and the same sensory information is about equally compatible with different interpretations. Based on this consideration Kornmeier et al. labelled these effects the "ERP Ambiguity Effects" [16,17] with ambiguity representation at a higher-level, beyond sensory details. In the current study we were interested in whether the "ERP Ambiguity Effects" further generalize across stimuli with emotional facial expressions and thus whether they may be rather "ERP Uncertainty Effects". Until this issue is resolved, we decided to adopt a neutral nomenclature, "ERP Effects", for the methods, results and part of the discussion section.

The above-mentioned example for "ambiguity" in emotion, the Mona Lisa, is a highly complex painting, which has multiple sources for uncertainty. We aimed at having maximal control over the source of uncertainty and thus created simpler line drawings of a face (smileys). It has been found, that the mouth region is of high importance for emotion perception in faces [e.g. 20], therefore we only varied the mouth curvature of the smileys to introduce happy and sad emotional facial expressions. We created two smiley variants with highly visible happy and sad expressions (mouth curvatures with strong bending), corresponding to the disambiguated versions in the Necker lattice. Both stimulus types (smiley, Necker lattice) should result in perceptual outcomes with low uncertainty. We further created two smiley versions with less visible emotional expressions (mouth curvatures with weak bending) that could be perceived either as slightly happy or as slightly sad, corresponding to the ambiguous Necker lattices and evoking high perceptual uncertainty. The choice of specific smiley stimulus variants was based on a pilot psychophysical experiment (for details see Supporting Information S1 File). There, participants were instructed to make binary decisions concerning the perceived emotional expression (happy/sad) of the smiley faces. With these responses we could identify those stimulus variants that were perceived in half of the trials as happy and in the other half as sad (low-visibility), which were chosen as the "less visible" emotion expressing stimulus variants. We here define the term "visibility" as the ability to spatially resolve the difference between the mouth curvatures bending.

The smiley stimuli evoke perceptual (un)certainty due to the visibility of their mouth curvatures. These, in turn, evoke the perception of emotional expressions (see e.g. Fig 1B). Emotional expressions are inevitably linked to their low-level features (e.g. mouth curvature) and cannot be studied in isolation. This makes assumptions about the origin (line bending or emotional expression) of perceptual (un)certainty in the case of smileys difficult in the current study.

Face processing, however, is known to be holistic in the sense that the individual stimulus features are processed and integrated simultaneously rather than in a hierarchical manner [21,22]. Thus, if the smileys are perceived as faces they should also be processed holistically. Then the mouth curvature should be integrated into the face, automatically resulting in the percept of an emotional face. To test whether smileys were at all perceived as faces, we introduced a control condition with "abstract figures" containing the same low-level stimulus features as in the smileys. However, these low-level visual details were differently arranged to prevent the recognition of a face, with one exception: the curvatures representing the mouth in the smiley stimuli were presented in the same size and at the same position within those abstract figures as in the smileys. This abstract figure condition had two purposes: (1) to investigate if face-specific ERP signatures are present with smileys and absent with abstract figures. (2) Both the occurrence of the ERP Effects in very different stimulus types (Necker cube, SAM, Boring's Old/Young Woman) and their relatively late occurrences (on a visual processing time scale) indicate that the ERP Effects reflect higher-level processes beyond stimulus specific features. Therefore, the second purpose of presenting the abstract figures was to investigate whether the ERP Effects also generalize across the curvature ambiguity in abstract figures.

Methods

Participants

Twenty healthy participants (11 females) between 19 and 34 years (mean: 25.1 years) with normal or corrected-to-normal visual acuity participated in this study. All gave their informed written consent. The study was approved by the ethics committee of the University of Freiburg and performed in accordance with the ethical standards laid down in the Declaration of Helsinki [23].

Stimuli

Three stimulus types were used: Necker lattice stimuli, smileys, and abstract figures (see Fig 1). In separate experimental conditions, either ambiguous or disambiguated variants of the Necker lattice were presented. Smileys could have either low or high visibility of the mouth curvature. The respective separate experimental conditions are labelled as "low-visibility smileys" and "high-visibility smileys". Abstract figures could have either low or high visibility of a line curvature located beneath the fixation cross. The respective separate experimental conditions are labelled as "low-visibility abstract figures" and "high-visibility abstract figures".

The ambiguous Necker lattices–a combination of nine Necker cubes (Fig 1A left graph, [5,7])–and disambiguated Necker lattices were presented in white on a dark background. The stimuli had a size of 7.5°×7.5° degrees of visual angle ("VA"). We created two disambiguated Necker lattice variants corresponding to the two perceptual interpretations of the ambiguous Necker lattice by adding depth cues like shading, central projection, and aerial perspective [see 24 for the OpenGL lighting model]. Both ambiguous and disambiguated Necker lattice variants had an overall luminance of 40 cd/m^2. For the disambiguated Necker lattice variants this luminance value represents an average across corners. A cross in the centre of the Necker lattices served as fixation target.

The present smileys were emotional face stimuli (see Fig 1B) with a minimal parameter space that allows maximal stimulus control and thus makes it easy to quantify levels of low and high visibility of the emotional expression. The face border was described by a white circle with a diameter of d = 4° VA on a black background. The eyes were two filled circles with a diameter of 0.214° VA and a distance to the face symmetry axis of 0.611° VA to the left and right respectively. The nose was indicated by a simple vertical line with 0.377° VA length and 0.102° VA width, located on the face symmetry axis at 2.076° VA distance from the upper central face border. Two smiley variants with happy and sad expressions at two visibility levels with less and highly visible happy and sad expressions were produced. Happiness/Sadness was only controlled via the mouth curvature. The upper (sad expression) and lower (happy expressions) arcs of a circle with two different radii r (r = 100.662/4.601° VA for slightly/strongly happy and sad smileys) indicated the mouth.

In a pilot study those mouth curvatures were determined that could still be discriminated, but were as similar as possible. Therefore we used the method of constant stimuli [25] (see Supporting Information S1 File). The common anchor point of the four mouth variants/circle arcs was the central point of the circle arcs that was kept constant at a distance of 0.916° VA to the lower central face border across stimulus variants. Imaginary vertical lines at 0.611° VA left and right from the (vertical) face symmetry axis defined left and right end points of the four mouth variants/circle arcs.

In this study we created new smiley stimuli and thus had to verify that they were perceived as faces. Therefore, we introduced a control condition with the following stimuli: we used the same less and highly visible mouth elements/circle arcs as in the smileys and embedded them into an abstract figure. These abstract figures had the same total line length and luminance (40 cd/m^2) as the smileys, but the line elements were arranged in a way that hardly any face could be recognized (see Fig 1C). Larger amplitudes of the face-specific N170 ERP component [26–28] for smileys compared to abstract figures would be evidence for face-specific processing of the smileys.

Procedure

In total we presented six separate experimental conditions, with two ambiguity/visibility levels for each stimulus type (Necker lattice, smiley, abstract figure). In two experimental conditions, either ambiguous or disambiguated variants of the Necker lattice were presented. In two conditions either low-visibility or high-visibility smileys and in two other conditions either low-visibility or high-visibility abstract figures were presented.

Necker lattice blocks lasted for 7 minutes, smiley and abstract figures blocks lasted for 6 minutes. The order of experimental conditions within one day was pseudo-randomized. The measurements were performed within two sessions on two different days (median time between two sessions: 2 days, range: 1–6 days). The abstract figures and Necker lattices were always presented in the first session, the smileys in the second.

Within the disambiguated/high-visibility stimulus conditions, the two respective stimulus variants were alternated randomly to simulate the spontaneous perceptual reversals of the ambiguous variants. The disambiguated Necker lattice variants were alternated with a reversal probability of 30% according to the average reversal probability of the ambiguous lattices as known from the literature [29,30]. Low-visibility and high-visibility smileys and abstract figures were also presented with a 30% reversal probability.

Stimuli were presented discontinuously for 1000 ms with a blank inter-stimulus interval of 400 ms (see Fig 2 and [16,17]). Participants were instructed to compare their current percept to the immediately preceding percept and to indicate perceptual reversals (change from one percept to the other) or perceptual stability (identical percepts across two consecutive presentations) for each stimulus (Fig 2) by pressing different keys ('S' for stability and 'R' for reversals) on a keyboard with four keys (two keys were not used). Keys were pressed using the thumb and 'S' and 'R' assignment to the left or the right thumb was counterbalanced between participants. Further, participants were instructed to respond as quickly and as precisely as possible. For Necker lattices, the two possible percepts were front-side pointing upwards or downwards (Fig 1A middle and right graph). Smileys could be perceived as either happy or sad. For the abstract figures the ends of the bended line could be perceived as pointing either upwards or downwards.

EEG recording and pre-processing

EEG was recorded with 32 active silver/silver chloride electrodes at scalp locations according to the extended 10–10 system [31]. Impedance was kept below 10 kΩ across electrodes. EEG data were digitized with 1000 Hz sampling rate, and online band-pass filtered with 0.01–120 Hz. Data analysis was executed in Igor Pro 6.3 (Wavemetrics, Inc.). The data was band-pass filtered offline at 0.01–25 Hz. It was re-referenced to the averaged mastoid channels for the analyses of P200 and P400 ERP Effects [16,17] and re-referenced to common average for the analyses of the face-specific N170 ERP component [26].

Trials exceeding an artefact threshold of ±100 μV were excluded from analysis. The baseline was defined as the average from 60 ms before to 40 ms after stimulus onset. For each stimulus type and ambiguity/visibility level, the EEG data was averaged separately for each participant and electrode. The trials started 60 ms before stimulus onset and were analysed until 1000 ms after onset.

Behavioural analysis

For each stimulus type and ambiguity/visibility level, we analysed the median reaction times and interquartile ranges with Wilcoxon signed rank tests. Reaction times are defined as the time between stimulus onset and the key press. Responses were regarded as physiologically plausible when their earliest occurrence was 150 ms after stimulus onset and responses were regarded as valid until the end of the inter-stimulus interval (1200 ms after stimulus onset).

ERP analysis

The analysis focused on the known ERP Effects consisting of two positive ERP components, a P200 with a latency of about 200 ms after stimulus onset and a fronto-central scalp distribution and a P400 with a centro-parietal scalp distribution [16,17] occurring 400 ms after stimulus onset. Following Kornmeier et al. [16,17], we focused on electrode Cz as spatial region of interest (ROI) for both ERP components and on temporal ROIs from 100 to 300 ms for the P200 and from 300 to 600 ms for the P400. We re-referenced the data to the mastoid electrodes P7 and P8.

We further analysed the N170, a negative ERP component 170 ms after stimulus onset most prominent at the temporal electrode positions, which is known from the face processing literature [26,32]. Spatial ROI for the N170 were electrodes P7 and P8, the temporal ROI was from 150 to 220 ms after stimulus onset [26]. For this analysis the data was re-referenced to common-average due to the spatial distribution of the N170 ERP component.

We identified the individual peak amplitudes in the respective spatial and temporal ROIs and measured the average voltage in a ±30 ms time window around the peak [33].

19 participants with at least 30 valid trials per condition were included in the statistical analysis (1 participant had less trials in one condition and therefore was excluded from the analysis). Due to low numbers of perceptual reversals, the statistical analyses were based only on stability trials (see further elaboration in the results and discussion sections).

We conducted separate repeated-measures ANOVAs (rmANOVA) in SPSS (Version 24.0) with the variable *amplitude* for the P200 and the P400 ERP components, both with the factors *stimulus* (Necker lattice, smiley, abstract figure) and *sensory evidence* (ambiguous/low-visibility, disambiguated/high-visibility). A separate rmANOVA was conducted for the N170 component for the variable *amplitude* with the factors *stimulus* (smiley, abstract figure), *sensory evidence* (ambiguous/low-visibility, disambiguated/high-visibility) and *channel* (P7, P8). In case sphericity was violated the respective degrees of freedom and p-values were Greenhouse-Geisser corrected [34].

P-values resulting from the rmANOVAs, post-hoc *t*-tests and reaction time analyses were corrected for multiple testing using the Bonferroni-Holm correction with an alpha of 0.05 [35].

All data (behavioural and EEG) of disambiguated/high-visibility stimulus variants represent only correctly identified stability trials. Because there are no correct answers in the case of ambiguous Necker lattices, all valid indications of perceptual stability trials were included. We adopted the same strategy for low-visibility smiley and abstract figure conditions.

Results

Behavioural results

Trial numbers. Participants responded to reversal and stability trials by using two different keys. In the case of disambiguated Necker lattices, high-visibility smileys, and high-visibility abstract figures participants responded correctly to stability trials in more than 97% (valid trials) of all stimulus presentations on average (disambiguated Necker lattices: Median 97.44%–IQR: 95.6–98.7%, high-visibility smileys: Mdn 100%–IQR: 98.68–100%, high-visibility abstract figures: Mdn 98.46%–IQR: 97.02–99.48%). Ergo less than 3% of all stability trials contained incorrect responses, non-responses or multiple responses to one stimulus presentation. They further responded correctly to reversal trials in more than 85% of all trials on average (disambiguated lattices: Mdn 90.77%–IQR: 89.37–93.51%, high-visibility smileys: Mdn 92.05%–IQR: 87.34–95.69%, high-visibility abstract figures: Mdn 85.37%–IQR: 77.42–93.5%). Ergo less than 15% of all reversal trials contained incorrect responses, non-responses or multiple responses to one stimulus presentation. These incorrect responses, non-responses and multiple responses to one stimulus presentation in disambiguated/high-visibility conditions were excluded from further analysis from both, stability and reversal trials.

In the case of ambiguous Necker lattices there were no "correct" responses, because one and the same stimulus variants was presented and only the perceptual responses were available. We analysed low-visibility smileys and low-visibility abstract figures according to the ambiguous Necker lattices and thus we did not separately analyse correct and incorrect responses to the physical stability and reversal trials, but only classified trials as valid or invalid perceptual responses.

Valid perceptual response trials in the case of ambiguous/low-visibility stimuli are trials where participants gave one response per stimulus in a predefined time-window (not before 150 ms and not after 1200 ms after stimulus onset), for which they had to press one of two predefined keys (indicating a stability or a reversal trial). Participants gave valid perceptual responses in more than 95% of all stimulus presentations on average (ambiguous Necker lattices: Mdn 96.16%–IQR: 95.4–98.33%, low-visibility smileys: Mdn 98.74%–IQR: 95.65–100%, low-visibility abstract figures: Mdn 95.86%–IQR: 91.11–100%). Ergo less than 5% of all trials contained invalid perceptual responses. The invalid perceptual responses in ambiguous/low-visibility conditions were excluded from further analysis.

Table 1 shows the remaining stability and reversal trials with and without EEG artefact removal due to body and eye movements, eye blinks, low-conductance electrodes, etc. One has to differ between perceptual reversal trials (endogenously determined) and physical reversal trials (exogenously determined by the stimulus program). For disambiguated/high-visibility conditions we included only correct responses to physical reversal trials. For ambiguous/low-visibility conditions we included all perceptual reversal trials, irrespective of the correctness regarding physical reversal trials (available for smileys and abstract figures, but not for Necker lattices). The resulting reversal rates can be seen in Table 1 column six, along with the physical reversal rate in column seven (30% for disambiguated Necker lattices, low- and high-visibility smileys, and low- and high-visibility abstract figures).

For low-visibility stimuli the perceptual reversal rate (smileys: 6.18%, abstract figures: 5.5%) is obviously different from the physically determined reversal rate (both 30%). Therefore, we did analyse the correct responses in the low-visibility conditions and found correct responses to low-visibility smileys in 9.86% (Median, IQR: 3.43–16.73%) and to low-visibility abstract figures in 4.88% (Median, IQR: 0.88–14.57%). This explains the large difference between

Table 1. Trial numbers.

	Number of reversal responses (incl. artefact trials)	Number of reversal responses (excl. artefact trials	Number of stability responses (incl. artefact trials)	Number of stability responses (excl. artefact trials)	Reversal rate (incl. artefact trials)	Physical reversal rate (percentage)
Necker lattice – disambiguated	102.58 ±36.09	149.74 ±16.35	254.63 ±78.94	391.53 ±18.58	27.27% (25.84–29.58%)	30%
Necker lattice – ambiguous	64.53 ±47.2	100.11 ±69.54	293.74 ±103.73	467.53 ±71.12	18.56% (8.62–25.41%)	N/A
Smileys – high-visibility	94.16 ±32.01	131 ±25.25	231.89 ±66.32	340.74 ±12.68	28.03% (24.64–31.2%)	30%
Smileys – low-visibility	29.79 (±32.69)	36.74 (±36.92)	317.16 (±109.08)	452.79 (±38.88)	6.18% (2.24–9.21%)	30%
Abstract figures – high-visibility	77.21 (±30.48)	118.11 (±21.78)	199.58 (±82.45)	323.74 (±25.06)	25.74% (23.13–28.68%)	30%
Abstract figures – low-visibility	20.42 (±22.76)	28.74 (±27.76)	280.89 (±114.24)	455.68 (±33.24)	5.5% (0.6–9.52%)	30%

Table 1 displays the mean number of reversal trials (±Standard deviation) excluding artefact trials across participants in the second column and the mean number of all valid reversal response trials including artefact trials (±SD) in the third column, separately for the experimental conditions (rows). Similarly for stability trials, trials excluding artificial trials are presented in column four and trials including artificial trials are presented in column five. Column six shows the median reversal rate in percentage (IQR) including artificial trials. Column seven shows the physical reversal rate implemented in the stimulus presentation program.

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physically determined and perceptual reversal rates and is most probably related to the low visibility of the relevant stimulus information (curvature).

The number of reversal trials for disambiguated/high-visibility conditions after artefact removal (Table 1 column 2) would be sufficient for an analysis of reversal trials. The number of reversal trials for ambiguous/low-visibility conditions after artefact removal (Table 1 column 2), however, is very low and even the mean value of low-visibility smileys and abstract figures is below the criterion of at least 30 valid trials per participant and condition.

Recent studies about the currently investigated ERP amplitude effects had fewer conditions and therewith more trials per condition. Separate analyses for stability and reversal trials were possible and thus realized in these studies [16,17]. The main difference between stability and reversal trials was an additional P3b component superimposed on the P400 in the reversal conditions. In the present study we were not interested in a surprise P3b component and thus restricted our focus on what had been labelled as the "ERP Ambiguity Effect", which was also found for the stability trials. We thus decided to add another experimental condition instead of attempting to collect enough reversal trials.

Reaction times. The Wilcoxon signed rank tests on median reaction times indicated no significant effects, neither for *sensory evidence* nor for *stimulus type* (see Fig 3 top row for graphical illustration and Supporting Information S1 Table).

For all stimulus types, the intra-individual interquartile ranges of the reaction times significantly differed between ambiguous/low-visibility and disambiguated/high-visibility stimulus variants (Necker lattices: $Z = 3.78$, $r = 0.61$, $p = 0.0002$; smileys: $Z = 3.7$, $r = 0.6$, $p = 0.0005$; abstract figures: $Z = 3.54$, $r = 0.57$, $p = 0.002$, see Fig 3 bottom row).

We further compared for each ambiguity/visibility level the intra-individual interquartile ranges of the reaction times between stimulus types. The Wilcoxon tests indicated a significant difference only between disambiguated Necker lattices and high-visibility smileys ($Z = 3.3$, $r = 0.54$, $p = 0.007$, see Fig 3 bottom row and Supporting Information S1 Table). In summary, we found equal median reaction times across stimulus types, but more reaction time variability for ambiguous/low-visibility compared to disambiguated/high-visibility stimulus variants.

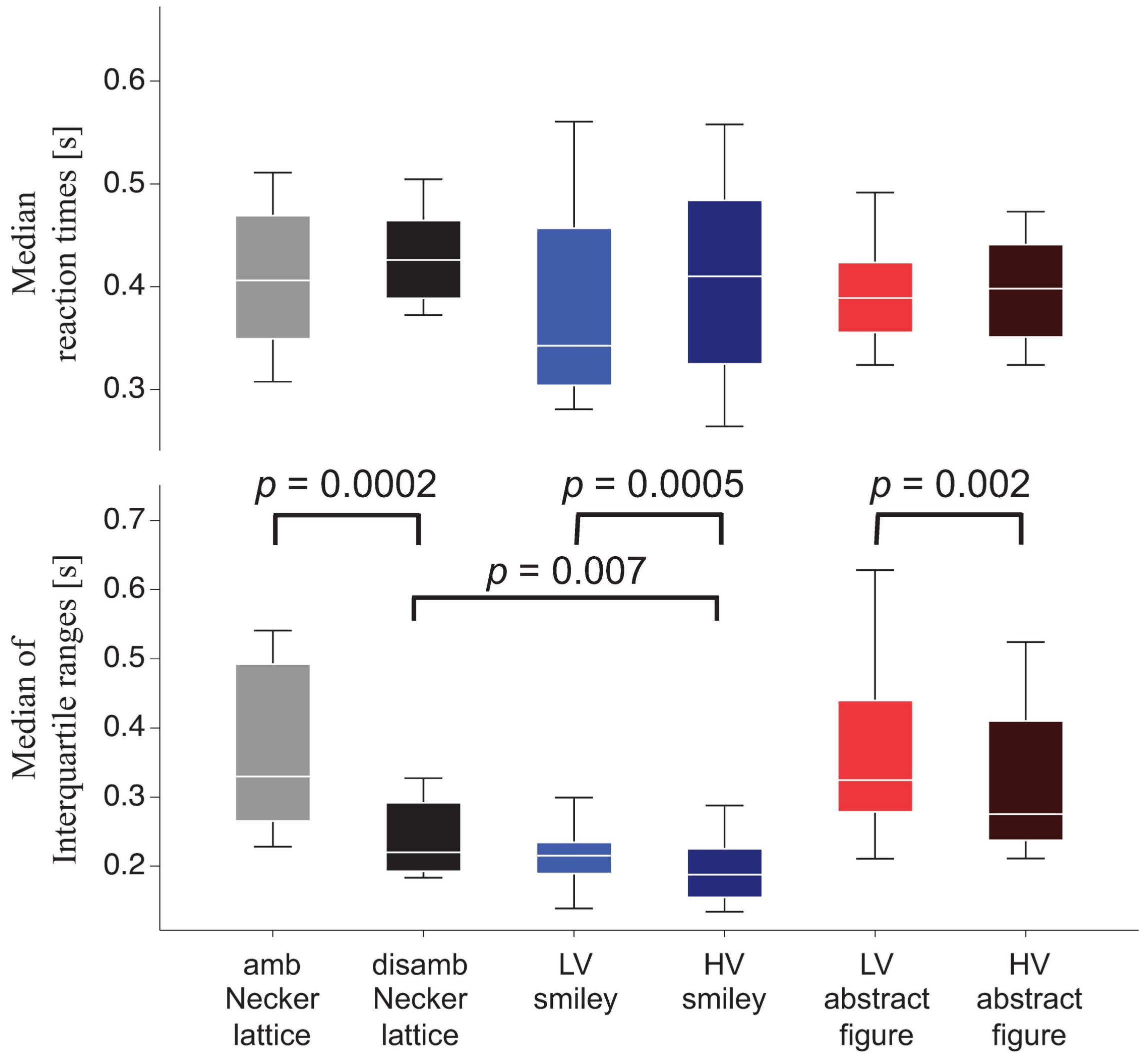

Fig 3. Reaction times. The upper row depicts the median (white line) of the individual median RTs (whiskers depict the interquartile range of reaction times). The bottom row depicts the intra-individual interquartile ranges of reaction times above (white line—median interquartile range; whiskers interquartile range of individual interquartile ranges; amb = ambiguous, disamb = disambiguated, LV = low-visibility, HV = high-visibility).

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P200 and P400 ERP effects

One aim of this study was to replicate the P200 and P400 ERP Effects in the Necker lattice stimuli reported in previous studies [16,17]. A second aim was to investigate whether the effects are also present with the smiley stimuli and in the control condition with abstract figures.

Fig 4 (a1, b1, c1) displays the grand mean ERP traces at electrode Cz for disambiguated/high-visibility (solid lines) and ambiguous/low-visibility (dotted lines) stimulus variants. The

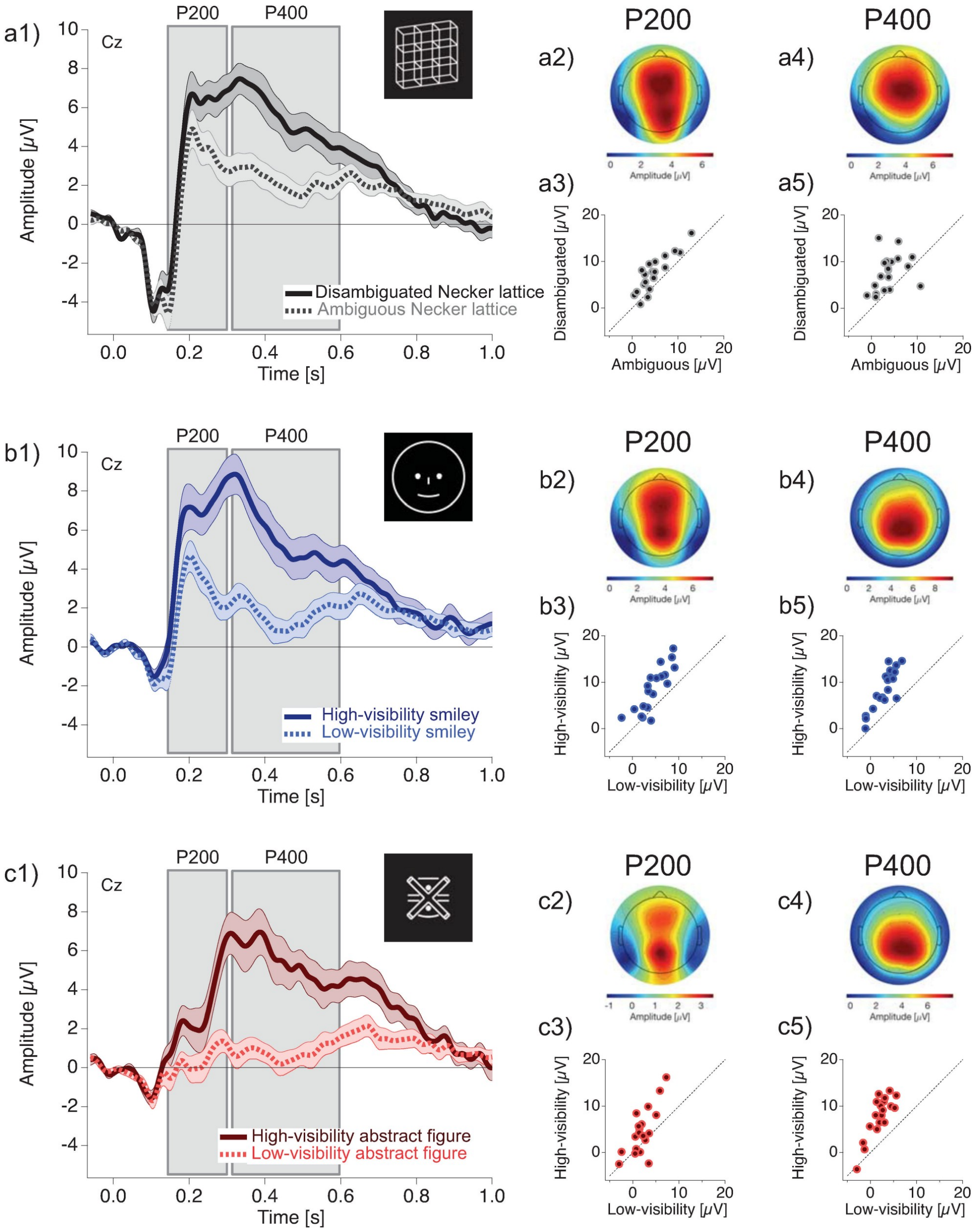

Fig 4. P200 and P400 ERP effects. P200 and P400 ERP Effects (re-referenced to the averaged mastoid electrodes) for Necker lattices (a1-a5), smileys (b1-b5), and abstract figures (c1-c5). Graphs (a1), (b1), and (c1) depict grand mean ERP traces for disambiguated/high-visibility (solid lines, dark colours) and ambiguous/low-visibility (dotted lines, light colours) stimuli. Graphs (a2, a4), (b2, b4), and (c2, c4) show grand mean voltage maps of the P200 (a2, b2, c2) and the P400 (a4, b4, c4) of the respective stimuli. Graphs (a3, a5), (b3, b5), and (c3, c5) show scatter plots for

the P200 (a3, b3, c3) and the P400 (a5, b5, c5) with amplitudes of individual participants for the disambiguated/high-visibility (ordinate) versus ambiguous/low-visibility stimuli (abscissa). In all scatter plots the vast majority of data points are above the bisection line, indicating larger amplitudes for disambiguated/high-visibility compared to ambiguous/low-visibility stimulus variants.

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P200 and the P400 show larger amplitudes with disambiguated/high-visibility compared to ambiguous/low-visibility stimuli.

The rmANOVA for the P200 ERP amplitudes showed a significant main effect of *sensory evidence* ($F(1,18) = 37.6$, $p = 0.0002$, $\eta_p^2 = 0.68$). The P200 has its maximal amplitudes from frontal to parietal electrodes near the midline for Necker lattices (Fig 4 a2), smileys (Fig 4 b2), and abstract figures (Fig 4 c2). Fig 4 a3, b3, and c3 depict scatterplots with P200 amplitudes from individual participants. Amplitudes are larger for disambiguated/high-visibility than for ambiguous/low-visibility stimuli (i.e. above the identity line) for the vast majority of participants (Necker lattices: 17 out of 19; smileys: 18 out of 19; abstract figures: 15 out of 19).

The rmANOVA for the P400 ERP amplitudes also showed a significant main effect of *sensory evidence* ($F(1,18) = 27.15$, $p = 0.0013$, $\eta_p^2 = 0.6$). The P400 has its highest activation at centro-parietal electrodes for all of the three stimulus types (see Fig 4 a4, b4, c4). Scatter plots in Fig 4 a5, b5, and c5 depict the individual P400 amplitudes, which are larger (i.e. above the bisection line) for disambiguated/high-visibility than for ambiguous/low-visibility stimuli for the vast majority of participants (Necker lattices and abstract figures: 18 out of 19 participants respectively; smileys: 19 out of 19 participants).

Comparison of P200 and P400 ERP effects across stimulus types

Fig 4 (a1), (b1), and (c1) depict similar P200 and P400 ERP Effects across stimulus types. Fig 5 upper row allows a direct comparison of the mean amplitudes (±SEM) for the P200 (a) and the P400 (b) ERP components.

Neither the rmANOVA on P200, nor on P400 ERP amplitude show a significant main effect for the fact *stimulus* (P200: $F(2,36) = 3.85$, $p = 0.41$; P400: $F(2,36) = 0.81$, $p = 0.91$). There were significant interactions between the factors *stimulus* and *sensory evidence* for both, the P200 ($F(2,36) = 13.24$, $p = 0.001$, $\eta_p^2 = 0.42$) and the P400 ($F(2,36) = 40.97$, $p = 1e\text{-}08$, $\eta_p^2 = 0.69$). In post-hoc *t*-tests we compared the peak differences between disambiguated/high-visibility and ambiguous/low-visibility stimulus variants between stimulus types (see Fig 5 bottom row). There were no significant effects of the peak differences between stimulus types in neither the P200 (Necker lattice vs. smiley: $t(18) = -2.28$, $p = 0.42$, Cohen's d = 0.52; Necker lattice vs. abstract figure: $t(18) = 0.09$, $p = 0.93$, Cohen's d = 0.02; smiley vs. abstract figure: $t(18) = 1.91$, $p = 0.62$, Cohen's d = 0.44), nor in the P400 (Necker lattice vs. smiley: $t(18) = -1.19$, $p = 0.92$, Cohen's d = 0.27; Necker lattice vs. abstract figure: $t(18) = -2.84$, $p = 0.19$, Cohen's d = 0.65; smiley vs. abstract figure: $t(18) = -2.7$, $p = 0.23$, Cohen's d = 0.62). We additionally calculated the effects size (Cohen's d) of the difference between disambiguated/high-visibility and ambiguous/low-visibility conditions for each stimulus type separately. The results can be found in the following Table 2.

In summary, we replicated the P200 and P400 ERP Effects for the Necker lattice stimuli [16,17] and found highly similar ERP Effects (concerning timing, location and amplitude effect sizes) for the smileys and abstract figures.

N170 ERP results for smileys and abstract figures

The N170 is known to be related to face-specific processing [26] and can thus provide evidence for or against the processing of the smileys as faces. If smileys were perceived as faces, they

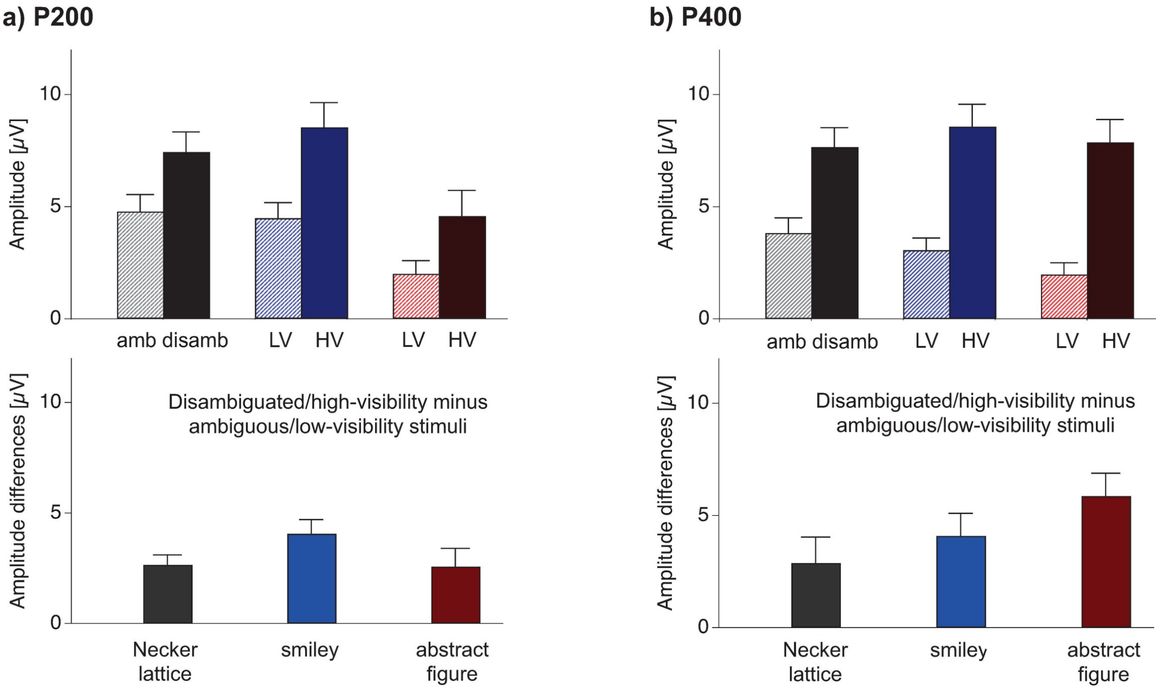

Fig 5. Grand mean P200 and P400 amplitudes. Top row: Grand mean amplitudes (±SEM) of the P200 (a) and P400 (b) ERP amplitudes are depicted for ambiguous (amb)/low-visibility (LV) and disambiguated (disamb)/high-visibility (HV) stimuli (upper row). Bottom row: Grand mean ERP amplitude differences for disambiguated/high-visibility minus ambiguous/low-visibility stimulus variants. All values result from the average around peak analysis (see methods section).

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should evoke N170 ERPs with larger (negative) amplitudes than the abstract figures. We tested whether this was the case in the present data.

Fig 6 displays the grand mean ERP data averaged across electrodes P7 and P8 and re-referenced to common average for the ambiguous/low-visibility (dotted lines, light colours) and disambiguated/high-visibility stimuli (solid lines, dark colours). Fig 6 (A) shows the ERP traces from high-visibility smileys (dark blue solid line) and high-visibility abstract figures (dark red solid line). Fig 6 (D) displays the grand mean data of low-visibility smileys (light blue dotted line) and low-visibility abstract figures (light red dotted line). The ERP traces in Fig (6A and 6D) show the same topology, with a positive deflection at around 150 ms, followed by a

Table 2. Effect sizes ERP effects.

	P200	P400
Necker lattices	1.36	0.97
Smileys	1.44	2.13
Abstract figures	0.71	2.08

Table 2 displays effects sizes (Cohen's d) for the difference between disambiguated/high-visibility and ambiguous/low-visibility conditions, separately for each stimulus type and ERP component (P200, P400).

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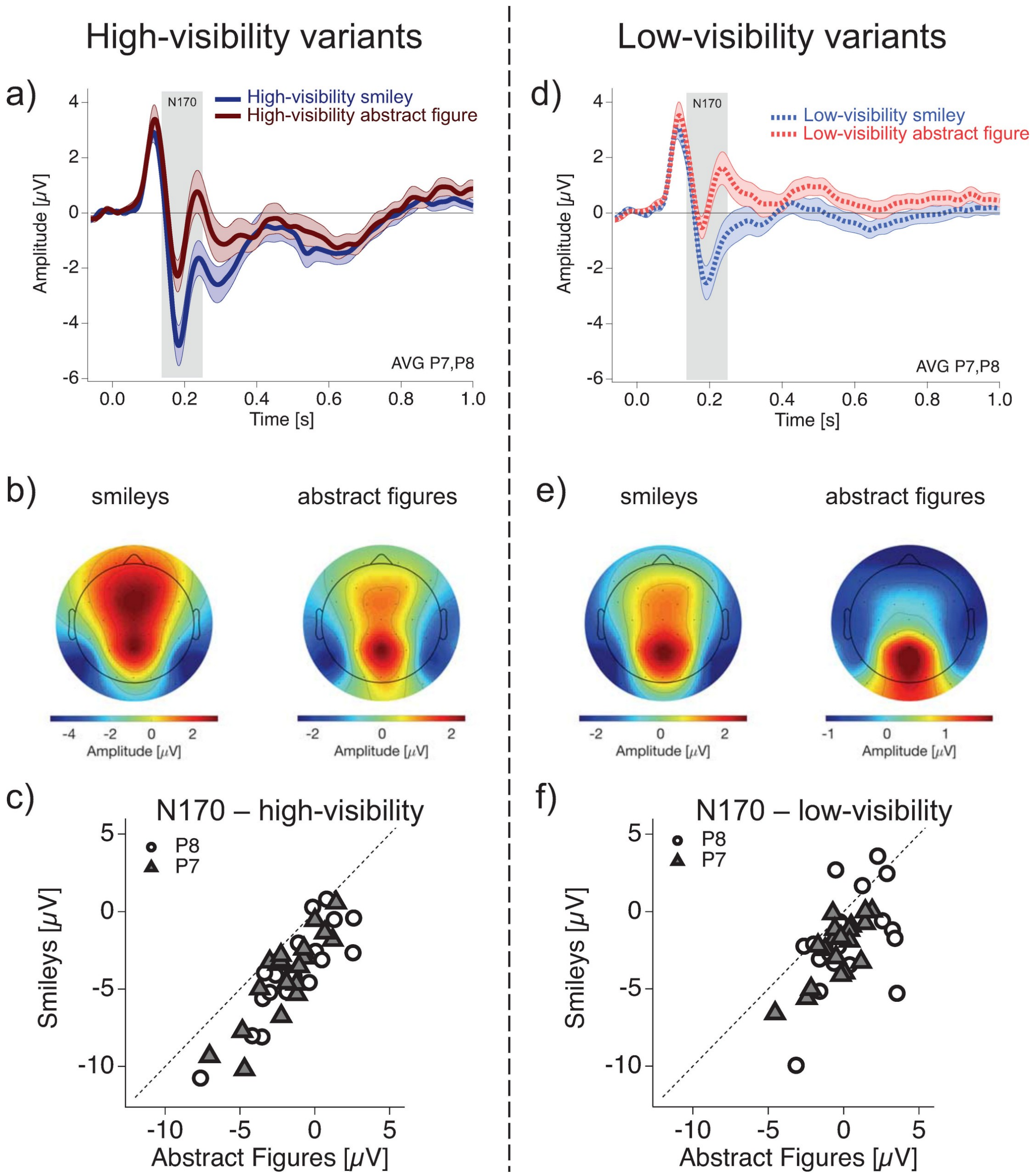

Fig 6. N170 for smileys and abstract figures. N170 effects (re-referenced to common average) in smileys and abstract figures. (a) and (d) depict the average of P7 and P8 grand mean data of smileys and abstract figures. (a) displays the ERP traces for the high-visibility variants (high-visibility smileys = dark blue solid line; high-visibility abstract figures = dark red solid line) and (d) for the low-visibility variants (low-visibility smileys = light blue dotted line; low-visibility abstract figure = light

red dotted line). (b) and (e) show the respective grand mean scalp maps of the N170. The scatter plots in (c) and (f) show the N170 amplitudes from individual participants for smileys (ordinate) versus abstract figures (abscissa) for high-visibility (c) and low-visibility (f) stimulus variants at electrodes P7 (filled triangles) and P8 (hollow circles) separately. For both visibility levels, the vast majority of data points are below the bisection line indicating larger (more negative) N170 amplitudes for smileys than for abstract figures. No hemispheric difference is indicated.

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negative deflection at around 180 ms (the N170). The maximal (negative) excursion of the N170 is around electrodes P7 and P8 for high-visibility smileys, high-visibility abstract figures, and for low-visibility smileys (see voltage maps in Fig 6B (left and right) and e (left)), which is in accordance with the literature [26]. The N170 of the low-visibility abstract figures shows the smallest negative excursions, staying close to zero. This may explain the different voltage distribution across electrodes for this condition as displayed in the voltage maps (Fig 6E right).

The rmANOVA of the N170 ERP amplitude showed a significant main effect of *stimulus* ($F(1,18) = 61.69$, $p = 9e\text{-}06$, $\eta_p^2 = 0.77$). The amplitude differences between smileys and abstract figures can be seen in Fig 6 (C) for high-visibility and in Fig 6 (f) for low-visibility stimulus variants.

The rmANOVA further showed a significant main effect of *sensory evidence* ($F(1,18) = 131.45$, $p = 3e\text{-}08$, $\eta_p^2 = 0.88$), while no main effect for the factor *electrode* ($F(1,18) = 1.32$, $p = 0.92$) indicated no detectable hemispheric difference. No interactions were indicated between none of the factors (for details see Table C in Supporting Information S2 File).

In summary, we found larger (negative) N170 amplitudes for smileys compared to abstract figures. We further found larger (negative) N170 amplitudes for high-visibility compared to low-visibility stimulus variants.

Discussion

The current study focused on two large ERP amplitude effects, labelled as the ERP Ambiguity Effects [16,17]: two ERP components (P200 and P400) show small amplitudes for ambiguous stimuli and large amplitudes for disambiguated stimulus variants. So far, these effects were found across very different lower (geometry, motion) and intermediate levels (Borings Old/Young Woman) of stimulus ambiguity. They have thus been attributed to stimulus ambiguity. In the present experiments, we investigated whether the ERP Ambiguity Effects can also be evoked by faces with high vs. low visibility of emotional expressions and in a control conditions with high and low visibility of low-level visual feature, namely the degree of curve bending.

We replicated these two ERP amplitude effects for Necker lattice stimuli and found similar effects for smiley faces and for abstract figures.

Perception of face stimuli is known to evoke larger N170 ERP components than non-face objects [26]. Larger (negative) amplitudes of the N170 ERP component for smileys compared to abstract figures thus indicate that the smileys were indeed processed as faces.

Median reaction times showed neither effects of sensory evidence (ambiguous/low-visibility, disambiguated/high-visibility) nor of stimulus type (Necker lattices, smileys, abstract figures). However, reaction times variability was overall larger for ambiguous/low-visibility than for disambiguated/high-visibility stimuli.

Can we really compare ambiguity in Necker lattices, smileys and abstract figures?

The term "ambiguity" is often used in the sense that one and the same sensory information is compatible with more than one interpretation. In the case of the classical ambiguous figures, like the Necker cube, the sensory information is most compatible with two interpretations and perception oscillates between them. We do not have this binary situation with two distinct perceptual experiences when looking at the low-visibility smileys. However, the results of our psychophysical pilot study, reported in the Supporting Information S1 File show that the smileys with low visibility of the mouth curvature (close to the inflection point of the sigmoidal function in Fig A in Supporting Information S1 File) can be sometimes perceived as happy and sometimes as sad. Further, the high visibility stimulus variants are most often perceived in accordance with the intended respective stimulus manipulation. The stimuli from the two categories are thus located an about comparable perceptual scales.

It is of course possible to execute the task of the smiley pilot study as well as the task in the subsequent EEG study simply by focusing on the mouth curvature, while ignoring the face information from the smileys. One obvious question is thus, whether the smileys are indeed processed as faces. Overall larger P200 amplitudes for smileys than for abstract figures indicate principle differences in their processing even though the low-level features, i.e. luminance and overall line length were identical. Further, the larger N170 ERPs for smileys than for abstract figures provide physiological evidence for face-specific processing in the former case. A detailed analysis of the N170, including independent component analysis (ICA), can be found in the Supporting Information S3 File. Additionally, several studies indicate that our perceptual system automatically interprets any information with an approximately face-like structure as a face [36–38]. Taken together, these arguments make it very probable, that the smileys are perceived as faces.

Assuming face-perception mechanisms for the smileys, a second question is whether perceptual uncertainty in the case of smiley stimuli occurs at the level of face-emotion decoding, or at the level of the mouth curvature processing, or both? Differences in the overall pattern of the P200 and P400 ERP Effects between smileys and abstract figures would provide evidence for the former. This, however, would not stand in line with the generality of the ERP Effects found so far [16,17].

In fact, we did find the same overall pattern of P200 and P400 ERP Effects in Necker lattice, smiley, and abstract figure stimuli, even though effect sizes differ between stimulus types (for further discussion see below). This finding is in line with the overall pattern of generality of the ERP Effects across stimulus types, indicating processing differences at an abstract level beyond lower-level stimulus-specific processing steps (see discussion below). Our N170 interpretation strongly indicates that smileys are processed in a face-like manner. But based on the present data we cannot say whether the curvature is perceptually resolved during an early visual processing step, or alternatively during a holistic, higher-level face and emotion processing step. Similarly, we do not know whether the ambiguity resolution in the Necker lattice takes place at the level of single lines or at the level of bound line object (= lattice).

Numerous studies about classical ambiguous figures as well as studies in the context of the predictive coding theory discuss perception as a decision process based on probabilities [39–41]. The perceptual decision task is thus about finding the most probable interpretation for the given sensory information with a given visibility and/or ambiguity level. The probabilities of perceptual interpretations in turn are influenced by a number of factors, like previous perceptual experiences on different memory time scales. Studies about priming and adaptation both in the ambiguous figure literature [e.g. 42–46] but also in the face perception literature [e.g. 47,48], the emotional face expression literature [49] and beyond [50,51] indicate influence of the immediate perceptual history on the present percept. Studies about an a priori bias e.g. in the case of the Necker cube [52] but also the face inversion effect [53,54] indicate the importance of longer-term memory. Perceptual probability values can further be influenced by the current context [55], by observers intents and goals, but also by task instruction in experiments about perception in the lab [e.g. 56,57].

In the case of classical ambiguous figures, the underlying probability distribution is discrete (mostly bimodal, almost binary) in nature. In the case of the Necker cube, for example, 90˚ interpretations are most probable, because we live in a world with many 90˚ angles, although many other perceptual interpretations are principally possible [see Fig 2C in 15]. The task of the current paradigm, asking for a binary perceptual decision, is compatible with this. The "natural" probability distribution for the low-visibility smiley is most probably not binary. The strategy of the current study was to "binarize" the probability distribution of the low-visibility smileys and of the low-visibility abstract figures with our choice of stimuli and with the binary task.

Ambiguity, probability, perceptual decision, and meta-perception–about the functional roles of the ERP effects

P200 and P400 in the literature. The currently investigated ERP Effects consist of amplitude differences in two ERP components, a centro-frontal P200 and a centro-parietal P400. The question is, what kind of neural processing do the P200 and the P400 amplitude effects reflect?

The results from the P200 time window in the current study indicate that there are two positivities at around 200 ms, one is a posterior P200, the other a more anterior P200 ERP component. The posterior P200 seems to be equally large as the anterior P200 for Necker lattice and smiley stimuli and even larger for the abstract figures (see voltage maps in Fig 4, right). The posterior P200 in the present data is most likely related to latest stages of sensory processing of the stimuli and probably related to posterior P200 components from the literature. In the literature, the posterior P200 is evoked by stimuli from different modalities [e.g. 58 for a visually evoked P200] although most studies used auditory stimuli [59]. Melloni et al. [60] modified the visibility of a letter embedded in varying levels of noise. They found a right-lateralized posterior P200, which was inversely related to letter visibility and depended on prior stimulus knowledge.

Only a few studies reported an anterior P200, similar to the present P200. Amongst these are Luck & Hillary [61], studying feature detection across visual dimensions, Taosheng et al. [62], studying modality-independent emotional salience, and Curran & Dien [63], studying the match of sensory input with memory contents [see also 64,65]. Kornmeier et al. [16,17] and a recent study [66] report a fronto-central P200 in the context of visual ambiguity (see also discussion below). These results about the anterior P200 provide evidence for its functional role beyond early sensory processing. In a recent study from our lab, we further found evidence for a functional separation between the P200, reflecting the ambiguity level of working memory information, and the P400, reflecting the integration of working memory content and sensory evidence [64].

The P400 is similar to the well-known P300 [specifically the P3b, see 67], which typically occurs in "oddball paradigms": the P300 occurs between 250 ms and 600 ms after onset of an infrequent and task-relevant target stimulus (the "oddball") or after infrequent omissions of a periodical stimulus. The P300 latency is negatively correlated with reaction times and its amplitude is negatively correlated with the target stimulus' frequency and positively correlated with stimulus discriminability [for recent reviews see 68,69]. One reason for our experimental block design, with either only ambiguous or only disambiguated stimuli, and for focusing only on stability trials and with this removing trials with oddball-like reversal events, was to avoid such an oddball P300 response. Delplanque et al. [70] investigated P300 ERPs evoked by oddball stimuli comprised of faces with unpleasant, pleasant or neutral emotional expressions. They found a typical P300 oddball effect with larger P300 amplitudes for faces with emotional valence compared to neutral faces. They assume a separate emotion-processing step on top of the oddball processing. The latter may be in line with our P400 findings in response to the smiley stimuli.

All of these arguments and observations indicate that the P400 cannot be reduced to the classical P300, although the two components may share some neural generators. In their former publication Kornmeier et al. [17] discuss this issue in more detail.

We recently found that the P200 and P400 ERP Effects are only present if the ambiguous and disambiguated stimuli are in the attentional focus [71,72]. This indicates that a certain relevance of the perceptual outcome, e.g. for the execution of a task, is a necessary precondition of the P200 and P400 ERP Effects. The processes underlying the ERP Effects are thus not executed automatically when the related sensory information is present. This is further evidence for higher-level processing steps related to attention and task-relevance.

Can reversal rates explain the ERP amplitude effects? The physical reversal rates for the disambiguated lattice stimuli as well as for low-visibility and high-visibility smileys and abstract figures were predefined to 30% by the stimulus program. This is about the rate of the typical reversal rates found for classical ambiguous figures, like the Necker cube [3,73]. As can be seen in Table 1 the perceptual reversal rates for the Necker lattice are in the expected range.

The perceptual reversal rates for the disambiguated lattice variants and the high-visibility smileys and abstract figures are in good confirmation with the predefined physical reversal rates. This result was expected because of the high visibility of the relevant curvature within the stimuli.

The perceptual reversal rates for the low-visibility smileys and abstract figures are roughly by factor 6 smaller than their predefined physical reversal rates of 30%. Given the low visibility of the curvature in these stimuli we expected a partial de-synchronization between physical and perceptual reversal events. However, the large decrease of reversal percepts translates into an increase of stability responses. This may indicate the influence of a priori perceptual biases (e.g. a preference for happy faces or upward bending), and/or perceptual priming evoked by the perception of immediately preceding stimuli. Further the large amount of stability responses may indicate that participants did not perceive the emotion/line bending as one of the two given options (e.g. smileys are perceived as neutral and neither as happy nor as sad) and a response strategy (e.g. preference for perceptual stability) would be the consequence. We did not collect information about individual strategies. Thus, we can neither analyse nor rule out the potential influence of such individual strategies to overcome low visibility and perceptual uncertainty on the ERP amplitude effects.

However, as already mentioned in the introduction there are qualitative differences between the perception of the ambiguous Necker lattice and the low-visibility smileys and abstract figures. At each moment we seem to have a clear and distinct 3D percept of the Necker lattice, which is one of the two most probable 90°-angle interpretations. The perceptual decision is thus an either-or decision. In the case of low-visibility smileys and abstract figures the perceptual decisions are rather a more-or-less decisions and the binarity only comes from the task constriction. This qualitative difference may be one reason for the quantitative difference in the perceptual reversal rates between the Necker lattices (close to 30%) and the low-visibility smileys and abstract figures (around 6%).

Given these and other differences it is even more remarkable that the ERP amplitude effects are that similar across stimulus types. The latter indicates that these effects reflect processes that are also beyond these differences, which we will discuss below.

Do the P200 and P400 ERP Effects reflect stability of neural representations underlying percepts? As already discussed above, because the sensory information is a priori incomplete, noisy and to varying degrees ambiguous, disambiguation, interpretation, and finally a perceptual decision become necessary. This decision is easy if a good quality of sensory information makes one interpretation highly probable compared to other theoretically possible interpretations. The resulting perceptual outcome will then be stable and reliable. In the case of ambiguity, and/or low visibility, perceptual decisions become more difficult and perceptual outcomes less stable over time, possibly resulting in spontaneous perceptual alternations as known from classical ambiguous figures.

It may be possible that the amplitude differences found for the P200 and P400 simply reflect differences in stability of neural representations. If this would be the case, we should expect that the neural representations of motion stimuli (e.g. the SAM), geometric cube stimuli (e.g. the Necker lattices) and face stimuli (e.g. the smileys) differ between each other, because they should be differently represented in the brain. However, the temporal and spatial patterns of our ERP Effects are surprisingly similar between these different stimulus categories. Further, the factor *stimulus* from the rmANOVA as well as the post-hoc t-tests did not indicate a significant difference of the amplitude effects between stimulus types.

Of course, it is not possible to make strong inferences from spatial distributions based on EEG voltage maps, and null-results from statistical tests do neither allow for far-reaching interpretations. Further, the significant interactions between the factors *stimulus* and *sensory evidence*, as indicated in the rmANOVAs, and differences in the sizes of the amplitude effects between stimulus categories (see Table 2) point to some differences. However, taking into account the large differences between stimulus categories (low-level features, but also conceptual differences), the identified ERP amplitudes are remarkably similar across stimulus categories.

EEG source analyses combined with fMRI data may resolve whether similarities on the scalp are based on the same underlying sources across stimuli. We are currently running an fMRI study investigating this question. Preliminary results indicate common sources across stimulus categories, making it less likely that the P200 and P400 ERP Effects reflect stability of perceptual / neural representations [74].

Do the P200 and P400 ERP Effects reflect meta-perceptual processing? An alternative interpretation of the present ERP amplitude effects is related to the recently discussed concept of meta-perception/ visual confidence. According to a definition given by Mamassian [41] meta-perception / visual confidence is "[. . .] the ability to estimate the accuracy of our visual decisions [. . .]", and with this it is "[. . .] a judgment on a judgment [. . .] ".

A closer look into the literature provides a rough time scale of visual processing and a very good guideline in this respect is the paper by Thorpe & Fabre-Thorpe [75]. Processing of objects and faces already takes place between 80 and 100 ms after stimulus onset and categorical judgements and decision making can be measured at about 120–160 ms after stimulus onset, as measured in monkeys. Values from humans may slightly differ and of course such values also strongly depend on stimulus identities. However, comparable values from humans indicate at least similar time scales [76–79]. Latencies of 200 ms (P200) and 400 ms (P400) thus indicate that the effects we found are most probably post-decision processes and may thus rather reflect estimations about the reliability of perceptual decisions.

We thus postulate that a secondary, meta-perceptual instance may evaluate the stability of neural/perceptual representations and the P200 and P400 amplitudes may reflect the evaluation result–or in other words–the certainty of our perceptual decision, with large amplitudes in the case of high reliability and vice versa. Assuming that this meta-perceptual instance is beyond sensory details—perhaps even beyond modalities—this approach may nicely explain the generality of our effects. In this case our results would present remarkably strong ERP correlates of meta-perceptual processing. It is important to add that meta-perceptual processing is not necessarily conscious processing. It is well possible and even probable that such meta-perceptual evaluations take place subconsciously in the majority of the cases and do not necessarily influence the quality of our conscious perceptual experience. Evaluations may only become conscious if their results involve substantial consequences for the current goals and the immediate behaviour.

Conclusion and outlook

The present results further extend the generality of the P200 and P400 ERP Effects across stimulus types, with larger amplitudes for disambiguated/high-visibility compared to ambiguous/low-visibility stimulus variants. Importantly the effects were not only shown for classical ambiguous figures, but also for stimuli with low visibility of certain stimulus features, i.e. curvature. In future experiments it would be interesting to investigate the ERP Effects in other modalities like audition and touch.

We currently interpret the generality of the ERP Effects as an indication for meta-perceptual evaluations beyond sensory details and categories, and thus as an indication of certainty or uncertainty of a perceptual decision. As an important next step on our agenda to test this interpretation, the present paradigm will be extended by a confidence judgement as a second task. It would be further support of our hypothesis, if one and the same ambiguous stimulus were to elicit P200 and/or P400 amplitude modulations as a function of confidence ratings. Another step could be to compare ERP results from one experiment with classical ambiguous stimuli and disambiguated stimulus variants with ERP results from a second experiment where the unambiguous stimuli embedded in high and low visual noise will be compared. Visual noise is another–ecologically reasonable–way to modulate stimulus visibility. Preliminary results from our lab indicate highly similar P200 and P400 amplitude effects with noise stimuli [80].

Stating that both, the P200 and the P400 effects correlate with meta-perceptual processing is still rather unspecific. The difference in latency between P200 and P400 of 200 ms, which is quite long on perceptual processing time scales, indicates at least two separate processing steps. An interesting question is thus about the functional difference between P200 and P400. An important aspect of our paradigm is, that a current stimulus needs to be compared with the percept of the previous one. Thus, access to working memory content is necessary in order to execute this task. Recent results from our lab provide evidence that the working memory stores the identity of a previously perceived stimulus along with its ambiguity level and/or a corresponding reliability label. We found that the P200 effect can be explained almost entirely by such a working memory effect [65]. This finding is in good confirmation with theories about meta-perceptual rating and predictive coding approaches [81,82] emphasizing temporal aspects (i.e. memory and prediction) of perception and meta-perception.

The P400 latency and the present reaction times have similar latencies. Ambiguous sensory input results in unstable and thus unreliable percepts and uncertain motor decisions during task execution, i.e. which key to press. The P400 might reflect processes at the intersection of perception, meta-perception and motor execution. However, uncertainty during motor execution should result in more variable and overall longer reaction times compared to certain situations. In response to ambiguous sensory input we found more variance but no increase in reaction times compared to unambiguous input, which puts this interpretation into question. More studies are necessary to further clarify the mechanisms underlying the P200 and the P400 effects.

In conclusion, we here report ERP Effects with a large degree of generalization across different stimulus material. These effects show exceptionally large effect sizes and are clearly visible in almost all participants, which is rather uncommon for ERP effects, because of the known a priori low signal-to-noise ratio of EEG [83]. This may make these effects interesting in clinical contexts and related studies are currently in progress. In view of what we know so far about the ERP Ambiguity Effects we favour explanations in the context of meta-perceptual confidence judgments and (un)certainty of perceptual decisions. If this direction of interpretation will be confirmed in subsequent studies, we need to think about re-labelling this effect from "ERP Ambiguity Effect" to "ERP Uncertainty Effect" or "ERP Confidence Effect".

Supporting information

S1 File. Psychophysical pilot study to identify low-visibility smileys.
(DOCX)

S2 File. ERPs—statistical results.
(DOCX)

S3 File. Face perception and the N170 ERP component.
(DOCX)

S1 Table. Reaction times—statistical results.
(DOCX)

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2.3 Supplementary Material 1

S1 File. Psychophysical Pilot Study to identify low-visibility Smileys.

The present study used ambiguous and disambiguated variants of Necker lattices and low-visibility and high-visibility stimulus variants of smileys and abstract figures. The perceptually ambiguous and disambiguated lattice stimuli were adopted from previous studies [1,2]. We used smileys with low-visibility of their emotional expression, in contrast, for the first time in this study. It was necessary to access the perceptual scale of visibility of the emotional expressions as a function of the stimulus variable 'mouth curvature'.

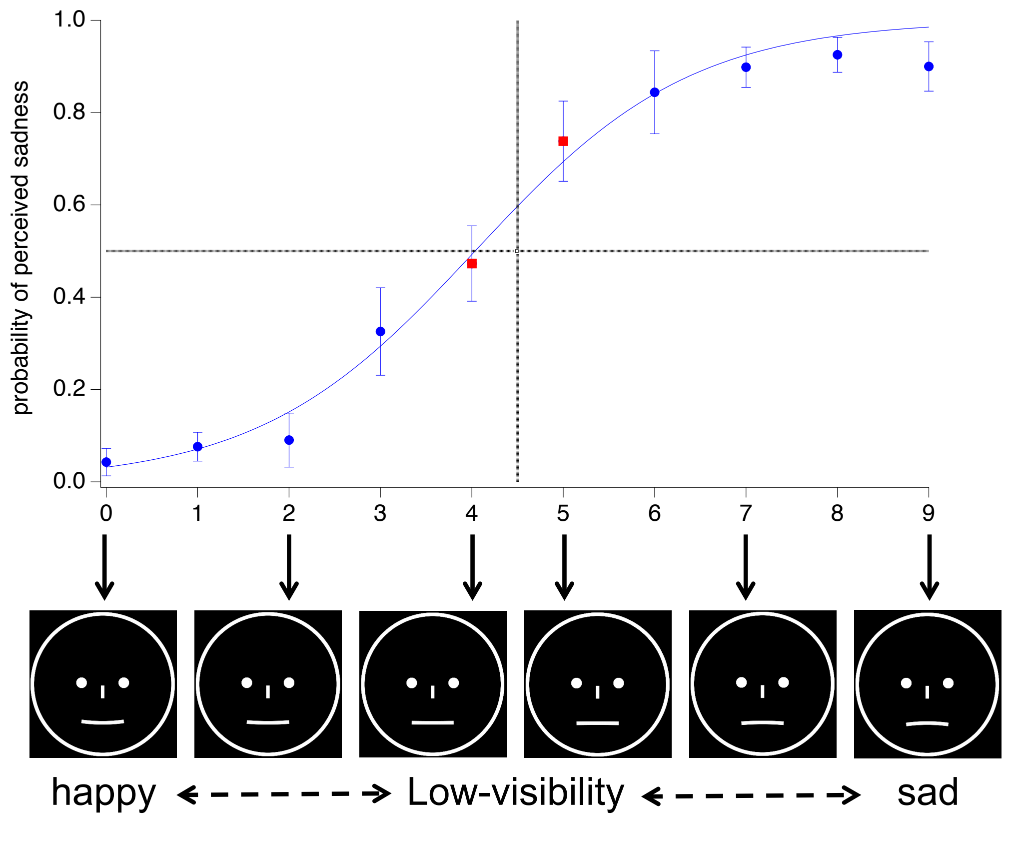
We thus conducted a pilot study with 7 participants to determine probabilities of happy and sad face percepts as a function of the parameter mouth curvature using the method of constant stimuli [3]. All participants gave their informed written consent. The study was approved by the ethics committee of the University of Freiburg and in accordance with the ethical standards laid down in the Declaration of Helsinki [4].

10 smiley variants were presented in random order 10 times for 800 ms each (ISI = 200 ms) and participants were asked to indicate for each smiley stimulus whether it was perceived as happy or sad. The smiley variants differed in their mouth curvature with radii of r = 11.237° VA (variants 0 and 9), r = 14.422° VA (variants 1 and 8), r = 20.193° VA (variants 2 and 7), r = 33.527° VA (variants 3 and 6), and r = 100.662° VA (variants 4 and 5) (see Methods section).

Psychometric functions were fitted to each participant's average responses (across the ten stimulus repetitions) and averaged across participants. Figure A depicts the psychometric function of the averaged data across participants (±SEMs). The sigmoid inflection point indicates the most low-visibility smiley variant, i.e. where both, happy and sad smiley percepts are equally likely.

One problem with the so identified low-visibility smiley stimuli is that they are not perceived in a binary manner as the ambiguous lattices. In the case of ambiguous lattice stimuli, observers typically alternate spontaneously between two perceptual interpretations with precisely defined spatial angles. In contrast there are typically no spontaneous alternations between a clearly happy and a clearly sad percept if a smiley variant around the inflection point is presented (e.g. smiley 4 in Supporting Information Fig. S1). Rather the emotional expression of smiley 4 (the identified low-visibility variant) is perceived as slightly happier or sadder or even as neutral. To circumvent this problem, we took the two smiley variants closest to the inflection point (smiley 4 and smiley 5 as low-visibility smiley variants in the main study (see also the Discussion section for further elaboration on this aspect) and used a task with only two response options (perceptual stability and perceptual reversals). To ensure clear percepts, the high-visibility smileys shown in the main study had a stronger mouth bending than the smileys variants 0 and 9 from this pilot study.

For the control experiment in the main EEG study we followed the above described logic to decide for appropriate stimulus variants and simply isolated the mouth variants of these four smiley variants and embedded them to newly created abstract figures.



Supporting Information File 1 - Fig A Pilot study to identify low-visibility mouth curvatures in smileys. The top row depicts the psychometric function of the grand means (across participants) displaying the probability of perceived sadness as a function of the randomly presented smiley variants (± SEM). At the bottom six examples of smiley variants are depicted (from left to right: smiley variants 0, 2, 4, 5, 7, 9). Smiley variants 4 and 5 were used as low-visibility (of the mouth curvature) variants. High-visibility smiley variants, used in the main study had even sharper mouth curvatures than smileys 0 and 9 to ensure clear percepts.

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2.4 Supplementary Material 2

S2 Table. Reaction times - statistical results.

Supporting Information Table S2. Reaction Time data - Wilcoxon tests

Dependent variable	Contrast	*Z* score (based on positive ranks)	Effect size *r*	*p*-value corrected (uncorrected)
Median	**Sensory evidence (ambiguous/low-visibility vs. disambiguated/high-visibility)**			
	Lattice	1.05	0.17	0.93 (0.31)
	Smiley	0.54	0.09	0.58 (0.58)
	Abstract Figure	0.85	0.14	0.93 (0.42)
	Stimulus type (collapsed across ambiguity/visibility levels)			
	Lattice vs. Smiley	1.01	0.16	0.91 (0.33)
	Lattice vs. Abstract Figure	1.65	0.27	0.72 (0.1)
	Smiley vs. Abstract Figure	0.77	0.12	0.85 (0.47)
Inter-quartile Range	**Sensory evidence (ambiguous/low-visibility vs. disambiguated/high-visibility)**			
	Lattice***	3.78	0.61	0.0002 (7e-06)
	Smiley**	3.7	0.6	0.0005 (2e-05)
	Abstract Figure**	3.54	0.57	0.002 (7e-05)
	Stimulus type (disambiguated/high-visibility stimuli)			
	Lattice vs. Smiley**	3.3	0.54	0.007 (0.0003)
	Lattice vs. Abstract Figure	2.05	0.33	0.44 (0.04)
	Smiley vs. Abstract Figure	2.13	0.35	0.41 (0.03)
	Stimulus type (ambiguous/low-visibility stimuli)			
	Lattice vs. Smiley	1.25	0.2	0.93 (0.23)
	Lattice vs. Abstract Figure	0.32	0.05	0.77 (0.77)
	Smiley vs. Abstract Figure	1.53	0.25	0.78 (0.13)

Bonferroni-Holm corrected (uncorrected p-values; Significance Codes: $p<0.05$*; $p<0.01$**; $p<0.001$***).

2.5 Supplementary Material 3

S3 File. ERPs - statistical results.

Supporting Information S3 File – Table A. ERP Effects - Repeated measures ANOVA on *ERP Amplitude* at electrode Cz.

	Factor	F-Value	p-value corrected (uncorrected)
P200	Stimulus	3.85	0.41 (0.03)
	Sensory evidence***	37.6	0.00023 (9e-06)
	Stimulus : Sensory evidence**	13.24	0.0011 (0.00005)
P400	Stimulus	0.81	0.91 (0.45)
	Sensory evidence **	27.15	0.0013 (5e-05)
	Stimulus : Sensory evidence***	40.97	1e-08 (5e-10)

Repeated measures ANOVA results for the amplitudes of the two ERP components P200 and P400 at electrode Cz with Bonferroni-Holm corrected (and uncorrected p-values). The factor *stimulus* has three levels: Lattice, Smiley, Abstract Figure. The Factor *sensory evidence* has two levels: disambiguated/high-visibility and ambiguous/low-visibility (Significance Codes: p<0.05*; p<0.01**; p<0.001***).

Supporting Information S3 File - Table B. Post-hoc t-tests for the interaction of *stimulus*sensory evidence*.

	Comparison	t-value	p-value corrected (uncorrected)	Cohen's d
P200 (D-A)	Lattice vs. Smiley	-2.28	0.42 (0.04)	0.52
	Smiley vs. Abstract Figure	1.91	0.62 (0.07)	0.44
	Lattice vs. Abstract Figure	0.09	0.93 (0.93)	0.02
P400 (D-A)	Lattice vs. Smiley	-1.19	0.92 (0.25)	0.27
	Smiley vs. Abstract Figure	-2.7	0.23 (0.01)	0.62
	Lattice vs. Abstract Figure	-2.84	0.19 (0.01)	0.65

Post-hoc t-tests for rmANOVA result of a significant interaction (*stimulus*sensory evidence*) at electrode Cz. Peak differences between disambiguated/high-visibility and ambiguous/low-visibility stimulus variants were calculated and p-values are Bonferroni-Holm corrected (and uncorrected p-values; Significance Codes: p<0.05*; p<0.01**; p<0.001***).

Supporting Information Table S3 File – Table C. N170 - Repeated measures ANOVA on *ERP Amplitude.*

	Factor	F-value	p-value corrected (uncorrected)
N170	Stimulus***	61.69	9e-06 (3e-07)
	Sensory evidence ***	131.45	3e-08 (1e-09)
	Electrode	1.32	0.92 (0.27)
	Stimulus : Sensory evidence	0.51	0.74 (0.49)
	Stimulus : Electrode	0.23	0.64 (0.64)
	Sensory evidence: Electrode	0.46	0.51 (0.51)
	Stimulus : Sensory evidence : Electrode	0.02	0.89 (0.89)

Repeated measures ANOVA results for the amplitudes of the N170 ERP component with Bonferroni-Holm corrected p-values (uncorrected p-values). The factor *stimulus* has two levels: Smiley, Abstract Figure. The factor *sensory evidence* has two levels: disambiguated/high-visibility and ambiguous/low-visibility. The factor *electrode* has two factors: P7 and P8 (Significance Codes: p<0.05*; p<0.01**; p<0.001***).

2.6 Supplementary Material 4

S4 File. Face Perception and the N170 ERP Component.

Background

One of the major foci of the present experiments was to study ERP correlates of visibility of the emotional content of smiley face stimuli. We manipulated emotion by varying the smileys' mouth curvatures. One problem of this approach is that participants could simply distinguish between upward and downward oriented (mouth) curvatures to execute the task. Face perception is in principle not necessary.

To clarify whether the smileys were really perceived as faces, we presented the same mouth curvatures in the context of abstract figures as a control condition.

Face perception is known to evoke larger N170 ERP components than objects [5]. If smileys were perceived as faces, they should evoke N170 ERPs with larger amplitudes than the abstract figures.

Analysis overview

The Independent Component Analysis (ICA) was applied to isolate an independent EEG component that most probably represents the N170. The amplitudes of the respective components from smiley and abstract figure stimuli were then compared with each other. The basic steps were the following:

- ICA on each individual dataset
- Isolation of independent components (ICs) most likely representing the N170 ERP component
- Back-projection of the identified components into the electrode domain.
- Determination of how much of the originally found N170 ERP components can be explained by those components.

Analysis details

(A) Calculating ICA

For each participant and visibility level (low-visibility and high-visibility) the following pre-processing steps were realized:

- Pooling smiley and abstract figure data
- Down-sampling data to 250 Hz
- Selecting data from 60 ms before to 1000 ms after stimulus onset (only stability trials; see Methods for their definition)
- Rejecting artefacts (± 100 µV threshold)
- Concatenating single trials

On this pre-processed data an AMICA [6] was conducted using the implementation provided by the Matlab toolbox EEGLAB [7].

In the ICA the number of electrodes (here 32) determines the maximal number of identifiable independent components (ICs). The difference between low-visibility and high-visibility stimuli is prominent in the data and importantly, detected by the ICA. To not "loose" available ICs to the ERP difference related to stimulus visibility, but to extract the N170 related ICs, we decided to calculate separate ICAs for low-visibility and high-visibility stimuli.

(B) Selection of ICs related to the N170

The ICA provided 32 ICs per participant. The ICs that most likely contributed to the N170 component were selected as follows:

(B1) Rejection of ICs representing eye artefacts: ICs related to eye artefacts were identified with a cluster analysis based on dipole locations of the ICs close to the eyes and artefact typical activations [8]. Those ICs were excluded.

(B2) Selection steps for N170-related ICs:

- Selection of ICs with maximal activity located in the posterior hemisphere (TP9, CP5, CP1, CP2, CP6, TP10, P7, P3, Pz, P4, P8, PO9, O1, Oz, O2, PO10)
- Back-projection of the selected ICs into the electrode domain
- Selection of those ICs whose back-projection explained at least 5 % of artefact-free data (sum of the squared amplitude values) at the N170-specific electrodes P7 and P8 (spatial ROI) in a time-window from 170 to 220 ms (temporal ROI)

Results

Between 2 and 7 (median = 4) ICs per participant were found for the low-visibility and for the high-visibility stimuli related to the N170 ERP component. The sum of those ICs explained on average 61.5 % (median, range = 35.6-80.2 %) for the low-visibility stimuli and 72.5 % (median, range = 56.3-83.3 %) for the high-visibility stimuli of the originally found N170 amplitudes related to smileys and abstract figures.

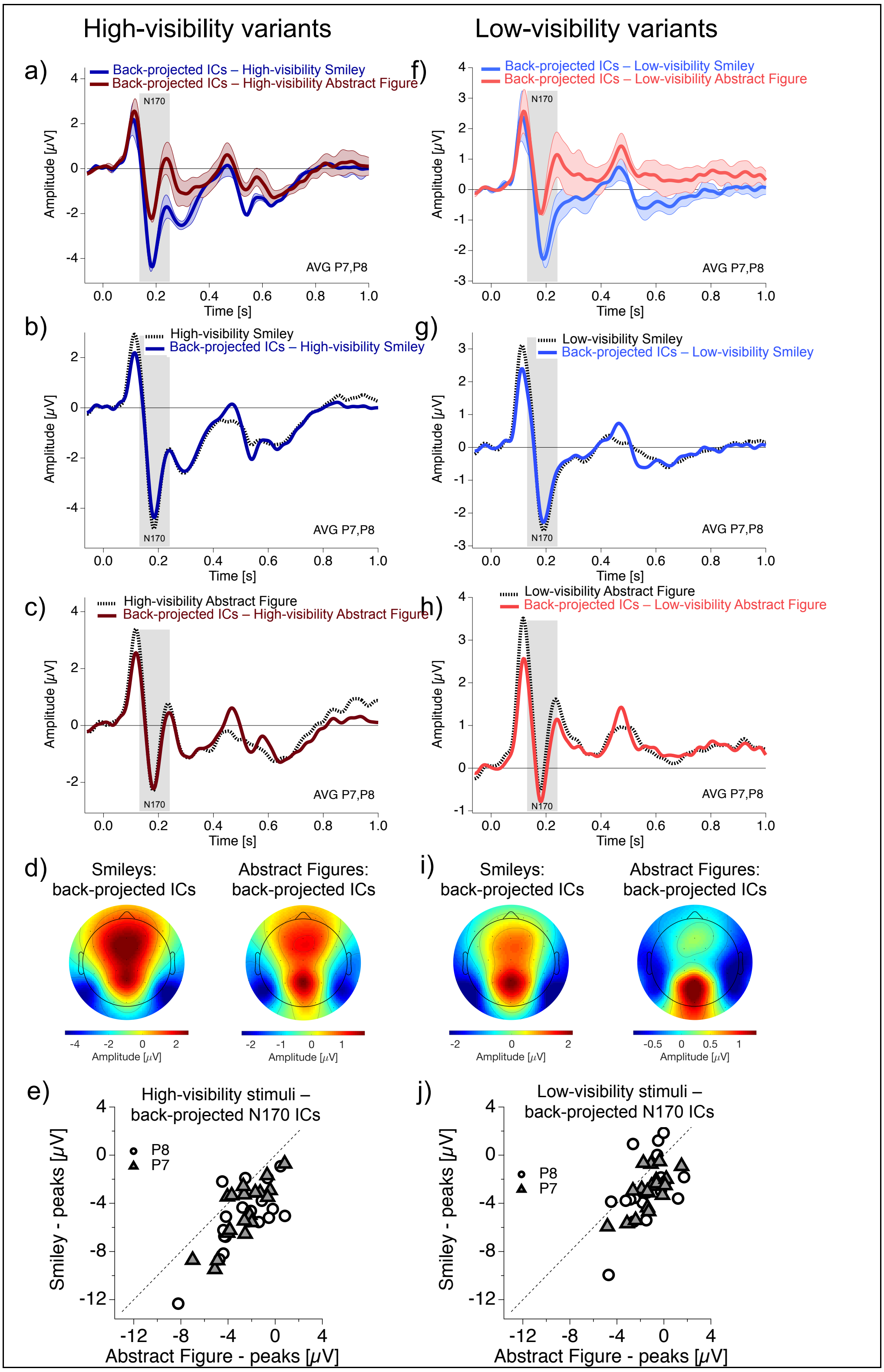
As can be seen in the graphical illustration of the results (Fig A a-c and f-h), the modulation of the N170 (smileys vs. abstract figures) is almost identical between the original ERPs and the back-projected N170 related independent components. Importantly, the effect of larger N170 amplitudes of smileys compared to abstract figures is conserved in the back-projected N170 components from the IC analysis.

Discussion:

The P200 ERP and the N170 are in relatively close temporal vicinity. It is thus theoretically possible that the modulation of one of those ERP components as a function of stimulus type and / or visibility level may be also reflected in the other component due to volume conduction.

We applied the ICA in order to disentangle the two components and therewith isolate ERP specific effects. In particular we were interested in whether the N170 component shows face specific modulations with the smiley stimuli. We further aimed to check whether such a modulation is really related to the N170 or alternatively influenced by the P200 modulation.

We identified N170-specific independent components that show – after back-projection - the same face specific modulation as the originally identified N170. We regard this as evidence for face-specific processing of the smiley stimuli.


High-visibility variants
Low-visibility variants
a)
Back-projected ICs – High-visibility Smiley
Back-projected ICs – High-visibility Abstract Figure
N170
Amplitude [µV]
AVG P7,P8
Time [s]
f)
Back-projected ICs – Low-visibility Smiley
Back-projected ICs – Low-visibility Abstract Figure
b)
High-visibility Smiley
Back-projected ICs – High-visibility Smiley
g)
Low-visibility Smiley
Back-projected ICs – Low-visibility Smiley
c)
High-visibility Abstract Figure
Back-projected ICs – High-visibility Abstract Figure
h)
Low-visibility Abstract Figure
Back-projected ICs – Low-visibility Abstract Figure
d)
Smileys: back-projected ICs
Abstract Figures: back-projected ICs
i)
Smileys: back-projected ICs
Abstract Figures: back-projected ICs
Amplitude [µV]
e)
High-visibility stimuli – back-projected N170 ICs
P8
P7
Smiley - peaks [µV]
Abstract Figure - peaks [µV]
j)
Low-visibility stimuli – back-projected N170 ICs

Supporting Information S4 File Fig B. Back projected ICA components - N170 Smiley vs. Abstract Figure. Back projected N170 independent components in smileys and abstract figures, analysed separately for high-visibility and low-visibility stimuli. (a) depicts the grand mean back-projected ERP traces averaged across electrode P7 and P8 of smileys (blue) and abstract figures (red) for the high-visibility (solid lines) stimulus variants and (f) for the low-visibility (dotted lines) stimuli. Sub graphs (b, c, g, h) show the back-projected IC ERPs together with the original ERPs. The grand mean data was averaged across electrodes P7 and P8. Sub graphs (d) and (i) show the grand mean scalp maps of the N170. Sub graph (e) and (j) depict scatterplots of the N170 peak amplitudes from the back-projected data of individual participants by plotting smileys (ordinate) versus abstract figures (abscissa) for electrodes P7 (filled triangles) and P8 (hollow circles) separately. The vast majority of data points are below the bisection line, showing larger N170 amplitudes for smileys than for abstract figures. This indicates face-specific processing of the smileys.

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3. Preliminary PhD article No. 2: Perceptual uncertainty effects in Schizophrenia Spectrum Disorder

3.1 Summary

Schizophrenia Spectrum Disorder (SSD) represents a complex set of neurodevelopmental disorders with severe implications for the lives of patients and their families. Diagnostics are based on behavioural parameters (American Psychiatric Association, 2013), while reliable physiological markers so far do not exist.
Patients with SSD show altered perceptual processing (Silverstein et al., 2015) and impairments in the integration of bottom-up with top-down information (Notredame et al., 2014; van Assche and Giersch, 2011). This might cause a different handling of the perceptual inference problem in patients with SSD compared to controls. The ERP Uncertainty Effects (Kornmeier and Bach, 2009; Kornmeier et al., 2016; Joos et al., 2020b) are proposed to reflect a reliability estimation of the perceptual outcome, which grounds on solving the perceptual inference problem. The ERP Uncertainty Effects are thus hypothesised to being altered in patients with SSD. Further, patients with SSD show deficits in the processing of emotions (Dlabac-de Lange et al., 2018; Turetsky et al., 2007; Kohler et al., 2003). Therefore, the paradigm and emotional stimuli from chapter 2 (Joos et al., 2020b) were applied to patients with SSD in the current project. The ERP effects have large effect sizes and are visible in individual participants, which make them promising candidates to reliably differ between patients with SSD and controls. Due to the Corona pandemic, I was not able to finish data collection during the time of my PhD. For the EEG analysis, I was able to include 11 patients and 12 controls. Data collection will remain on-going until a sample size of N = 20 per group is reached. Due to the fact that this study is statistically underpowered at this point in time, the current findings may change with more data and the interpretations derived from the current data should be made cautiously.
The ability to identify poorly visible emotional expressions was expected to reveal a large inter-individual variability and was thus determined for each participant separately. In order to do so, a range of smiley stimuli with different levels of visibility were presented in behavioural Experiment 1. For each individual, those stimuli that evoked the highest perceptual uncertainty

were determined. The selected stimuli did not systematically differ between the groups. Controls revealed longer reaction times in response to less visible stimuli and shorter reaction times to the more clearly visible stimuli. Patients, on the other hand, revealed (1) generally long reaction times irrespective of stimulus visibility and (2) reaction times were very similar to those of the controls in response to the less visible stimuli.
In electrophysiological Experiment 2, the low-visibility stimuli determined in Experiment 1 were presented in one experimental condition. In another experimental condition high-visibility smiley stimuli were presented. Contrasting results of the two conditions revealed that the ERP Uncertainty Effects were replicated (see Joos et al., 2020b) with large ERP amplitudes in the case of high-visibility of the emotional expressions within smiley faces and small ERP amplitudes in the case of low-visibility. There was an observable tendency for smaller ERP Uncertainty Effects in patients with SSD compared to controls, but this difference did not reach statistical significance. In an exploratory analysis of Experiment 2, differences in perceptual processing in response to perceptual (un)certainty between patients and controls were investigated by means of topographic differences. To this end, a data-driven microstate analysis was conducted. Microstate Uncertainty Effects were found to differ between patients with SSD and matched controls. Interestingly, the microstates that differed between groups were only present in subsets of the groups, possibly suggesting sub-groups within the patient and the control group. Additionally, the earliest time point after stimulus onset at which processing of perceptual (un)certainty differed between patients with SSD and controls was found to occur as early as 115 ms after stimulus onset at occipital electrode sites.
The study underlying the unpublished manuscript "Uncertainty Effects in Schizophrenia Spectrum Disorder - an EEG study" indicates that processing of (un)certainty is altered in patients with SSD compared to controls. The underpinnings of the sub-groups, as indicated by the Microstate Uncertainty Effects, are currently not clear and can only be determined with more data sets. Furthermore, it will be interesting to unravel the anatomical sources of the differing microstates in future studies (optimally including anatomical MRI scans to facilitate the inverse solution for EEG source analysis) and thus learn more about the functional role of those microstates. The finding that patients reveal similar reaction times for a range of different stimuli in Experiment 1 suggests a generally higher level of uncertainty in patients compared to controls. Moreover, Schizophrenia Spectrum Disorder is typically regarded as a high-level cognitive disease. In contrast, the very early EEG difference between groups (N115) additionally indicates low-level alterations in patients with SSD compared to controls. Ultimately, previous studies showed that patients with SSD reveal altered predictive mechanisms (Notredame et al., 2014). Altered predictive mechanisms might result in altered reliability attributions to the perceptual outcomes and thus might cause the altered behavioural and neural responses to (un)certainty as found in the current study in patients with SSD.

Contribution to the paper I was part of the funding acquisition, as well as the conceptualisation and administration of the project. I was responsible for data curation, formal analysis, investigation, methodology, software, validation, visualisation, writing the original draft and reviewing and editing the manuscript.

3.2 Main Manuscript

Preliminary manuscript: Perceptual uncertainty effects in Schizophrenia Spectrum Disorder – an EEG study

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Preamble

The following preliminary manuscript presents a data set, which is not fully collected yet and the whole study is currently underpowered. Data collection had to be stopped completely between March and June 2020 due to restrictions during the Corona pandemic. Since then no one participated in my study. The reported results are thus preliminary and they might change with more data.

The currently small data set, unfortunately, does not allow calculating reliable correlational analyses between the behavioural and physiological variables collected from the experiment and clinical symptoms of the patients. Once the data set is completed, we will correlate the findings with the symptoms and properly introduce and discuss this issue.

Abstract

The information available to our senses is noisy, incomplete, and to varying degrees ambiguous. The perceptual system has to create stable and reliable percepts out of this restricted information by integrating the sensory information (bottom-up) with endogenous information (top-down). Current theories explain both social and perceptual impairments in patients with Schizophrenia Spectrum Disorder (SSD) with deficits in this integration process. Diagnostics of SSD are so far based on behavioural parameters, while reliable physiological markers do not exist.

Recent studies compared the ERP signatures evoked by ambiguous/low-visibility with unambiguous/high-visibility stimuli. They found large ERP differences between these stimuli and interpreted them as "ERP Uncertainty Effects", resulting from the differential integration of sensory with endogenous information. The large size of these effects and their visibility in individual participants make them promising tools to study the underpinning of SSD.

In two experiments, we compared behavioural and electrophysiological correlates of (un)certainty in patients with SSD and matched control participants. We evoked uncertainty by low-visibility of emotional expressions in smiley faces and certainty by high-visibility of emotional expressions in smiley faces.

In Experiment 1, we presented a range of stimuli with different visibility levels in random order and participants indicated for each stimulus whether they perceived a happy or a sad emotional expression. We found that stimulus visibility modulates reaction times differently for patients with SSD compared to controls. In Experiment 2, we recorded EEG while presenting those two smiley stimuli with the lowest visibility of happiness and sadness, as determined on the individual level by Exp. 1. In another experimental condition, we presented two smiley stimuli with high-visibility of happiness and sadness. We replicated the ERP Uncertainty Effects from previous studies with larger ERP amplitudes in response to high-visibility stimuli compared to low-visibility stimuli. An observable tendency for smaller ERP Uncertainty Effects in patients compared to controls did not reach statistical significance. In an additional exploratory part of the data analysis, we performed a microstate analysis and found qualitative differences between patients and controls in the time window of the ERP Uncertainty Effects. Further, EEG differences between the two groups already start during lower-level visual processing at around 115 ms after stimulus onset at occipital electrode sites.

The results indicate similarities but also principle differences in the processing of (un)certainty between patients with SSD and controls. Altered predictive coding mechanisms as already reported in patients with SSD might evoke this altered processing of (un)certainty. This might be reflected in early occipital alterations and qualitatively different EEG microstates and it might result in a less stimulus-specific reaction time pattern in patients compared to the matched controls.

Introduction

Schizophrenia Spectrum Disorder (SSD) is a complex set of neurodevelopmental disorders with a prevalence in the population of around 1% [1]. The disorder has severe consequences for the social lives of patients and their families, along with considerable socioeconomic burden. Diagnostics are based on behavioural parameters [2], while reliable physiological markers do not exist so far.

Fundamental deficits in the process of perception [3–5] have since long been described in Schizophrenia Spectrum Disorder. This may be explained by the difficulties inherent to visual perception. Under normal circumstances, the perceptual experience is stable and reliable and permits a smooth interaction with the external environment. However, the information available to our senses (bottom-up) is always restricted, noisy and to varying degrees ambiguous. To provide a stable and reliable representation of the external world, the perceptual system complements the incomplete exogenous information (bottom-up sensory input) with endogenous information [top-down, e.g. memorized concepts; 4,5]. The quality of the exogenous information and the precision of endogenous information determine the relative contribution of the two types of information to the perceptual outcome. Consequently, our perception does not represent the external world exactly as it is, but is always biased through endogenous information. Patients with SSD show impairments in the integration of sensory information with memorized concepts [8] and spatial and temporal context [9]. Typical cognitive symptoms of SSD, like disorganized thoughts and memory deficits, but also the lower susceptibility to certain perceptual illusions in patients with SSD have been linked to this imbalance during the perceptual process [1,8,10].

It has been proposed that studying ambiguity resolution in patients with SSD provides a promising tool to investigate the underpinnings of the disorder [1,8,11,12] as a way to understand how patients integrate bottom-up with top-down information. The Oxford English Dictionary defines ambiguity as the: "Capability of being understood in two or more ways […]" [13]. The available sensory information is thus equally compatible with different interpretations. Ambiguity resolution refers to the perceptual decision between these alternative interpretations and strongly involves the integration of top-down processes. In the case of ambiguous sensory information, the perceptual decision is difficult and uncertain, while disambiguated sensory information leads to an easy and certain perceptual decision.

Interesting in this context are results from the group of Kornmeier [14–16]. They found remarkably large EEG differences (Cohen's d = 0.8-2.1) that are visible on the individual level when contrasting classical ambiguous figures with their disambiguated variants. They found two event-related potential (ERP) components, 200 and 400 ms after stimulus onset, with large amplitudes in response to disambiguated and small amplitudes in response to ambiguous stimulus variants. Importantly, they found these effects for very different classical ambiguous figures (geometry: Necker lattice, a variant of the Necker cube [17]; motion:

SAM/"motion quartet" [18]; Gestalt perception: Borings Old/Young Woman [19]) and their respective disambiguated stimulus variants [14,15]. Further, they found highly similar ERP differences when contrasting highly visible emotional facial expressions with less visible emotional facial expressions [16]. The generality of these ERP effects together with the late occurrences (in visual processing times) of the related ERPs indicate processing steps beyond low-level visual processing. According to the current interpretation, perceptual outcomes (integration of exogenous with endogenous information) are automatically generated by the perceptual system and the certainty about the perceptual outcome is rated by a meta-perceptual evaluation instance. The ERP effects might reflect this evaluation with large amplitudes in the case of high reliability of the perceptual outcome resulting in a state of certainty and with small amplitudes in the case of low reliability of the perceptual outcome resulting in a state of uncertainty. Therefore, they labelled their effects accordingly the "ERP Uncertainty Effects" [16].

It has been found that patients with SSD reveal a different processing of classical ambiguous figures compared to controls [8,20,21]. Further, patients with SSD have problems to disambiguate stimuli with emotionally ambiguous content [22] and show impairments in estimating emotional states from facial expressions [23–25].

If the available bottom-up sensory information is of sufficient quality, the perceptual system can successfully integrate it with top-down information. This results in an adequate perceptual interpretation and additionally in an adequate rating of its reliability. Kornmeier et al. interpret large P200 and P400 amplitudes as correlates of high perceptual reliability [14–16]. If the sensory information, in contrast, is of low quality, e.g. if it is ambiguous or if it is of low visibility, perceptual interpretations become less reliable and the P200 and P400 ERPs show respectively small amplitudes.

In patients with SSD the integration of bottom-up with top-down information is supposed to be altered [e.g. 8,9]. Altered integration mechanisms may result in erroneous reliability estimations of the perceptual outcome. This in turn should result in distorted ERP Uncertainty Effects. The reasons why these effects provide a promising tool to find reliable physiological differences between patients with SSD and healthy controls are threefold: (1) the large effect sizes of the ERP Uncertainty Effects, (2) their visibility in individual participants, and (3) the ERP effects were found for different degrees of visibility of emotional facial expressions and patients with SSD are known to have difficulties to estimate emotional states from facial expressions [23–25].

In the current study, the ERP Uncertainty Effects introduced by Kornmeier et al. [14–16] are compared between patients with SSD and control participants, matched in age, sex, and education level. The ERP Uncertainty Effects in this study are evoked by face stimuli with different degrees of visibility of their emotional expressions (methodology adapted from Joos et al. [16]). The ability to identify the emotional state of a person depends on low-level visual features in the observed person's face but also on the existence of a reference system for emotionality, including theory-of-mind aspects. We expected a large inter-individual variability in this ability and thus determine the individual low-visibility stimulus variants separately for each participant.

In the subsequent main experiment we compare the perceptual processing of low- and high-visibility emotional stimuli within participants to study the ERP Uncertainty Effects. We further compare these ERP Uncertainty Effects between patients with SSD and healthy controls. The specific type of modulation between patients and controls will reveal alterations in the underlying perceptual processes in patients with SSD. If, for example, the absolute amplitudes of the low-visibility traces are altered in patients with SSD, this might be related to the task difficulty. If, on the other hand, the absolute amplitudes of the high-visibility traces are different in patients with SSD, this might reflect a fundamental impairment in perceptual processing, not related to the difficulty of the task.

It is also possible that patients with SSD process (un)certainty in a different way compared to controls. Different processes should be located in other brain areas and thus should evoke different topographic maps. We therefore investigate differences in the topographic maps in an explorative and data-driven microstate analysis. We will label the resulting effects "Microstate Uncertainty Effects".

The Uncertainty Effects start to develop 200 ms after stimulus onset. However, several studies have shown that earlier ERP components differ between patients and controls [26,27]. In addition to the investigation of higher-level processes such as the Uncertainty Effects, we are interested in possible differences between patients and controls during the early perceptual processing of the sensory information. We thus identify the earliest significant difference between the groups at occipital electrodes.

Methods

Participants

Participants are divided into two groups. The patient group consists of 14 stabilized chronic outpatients (3 woman, 11 men; mean age = 38.6 years, SD = 9.1; mean level of education = 13.1 years, SD = 2.0) and the control group consists of 12 matched controls (3 woman, 9 men; mean age = 37.8 years, SD = 8.2; mean level of education = 13 years, SD = 1.7). Patients were recruited in the University of Strasbourg Psychiatry Department and controls were recruited by advertisement. Controls are individually matched with patients on sex, level of education, and age. One patient with SSD had to be excluded from analysis, because this person left after 1/3 of the experiment.

All participants gave their informed written consent. The study was approved by the ethics committee CPP Est IV and performed in accordance with the ethical standards laid down in the Declaration of Helsinki [28]. All participants have normal or corrected-to-normal visual acuity as measured with the Freiburg Visual Acuity Test [FrACT 29].

Two senior psychiatrists from the University Psychiatry Department diagnosed the patients with SSD using the Mini International Neuropsychiatric Interview. Criteria for the diagnosis of SSD are in accordance with the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*. Symptoms were assessed with the help of the Scales for the assessment of Positive Symptoms (SAPS) [30] and Negative Symptoms (SANS) [31]. The mean score for the SAPS is 21.77 (SD = 22.77) and the mean score for the SANS is 33.54 (SD = 24.64).

The mean age at onset of SSD symptoms was 23.23 years (SD = 8.73), the mean disease duration is 16.62 years (SD = 13.94), and the median number of hospitalizations is 3 (inter-quartile range from 1 to 3). 11 patients receive atypical antipsychotic treatment, one receives typical antipsychotic treatment, and one receives both atypical and typical treatment. The mean standard dose is 300.2 mg/day (SD = 198.7) of chlorpromazine or chlorpromazine equivalents. Another participant receives anti-epileptic drugs (Depakote 1250 mg/d) and another an anti-parkinsonian agent (Lepticur 10 mg/d).

We measured the verbal fluency as an indicator of intellectual ability using the French National Adult Reading Test [32]. We calculated the WAIS-R scores according to Mackinnon et al. [33]. Patients have a mean WAIS-R full scale score of 109.04 (SD = 6.74) and controls have a mean score of 110.71 (SD = 5.74). The mean WAIS-R verbal score was 109.2 (SD = 8.49) for patients and 113.24 (SD = 7.23) for controls. The mean WAIS-R performance score was 105 (SD = 3.72) for patients and 106.77 (SD = 3.17) for patients. We did not find differences in those scores between patients with SSD and matched controls.

General information

Stimuli were generated and presented using PsychoPy v1.82 [34] and presented on a Sony CPD-520GS Trinitron monitor with a refresh rate of 60 Hz. Experiments were performed in a room with reduced illumination. The analyses were conducted in Igor Pro 6.3 (Wavemetrics, Inc.) and statistics were done in SPSS (IBM SPSS Statistics for Macintosh, Version 24.0).

Experiment 1

Stimuli

In the electrophysiological Experiment 2, smiley stimuli with high-visibility of their emotional expressions are compared with smiley stimuli with low-visibility of their emotional expressions. The perception and classification of poorly visible emotional expressions is highly subjective and was thus determined for each participant separately. In a behavioural Experiment 1, we determine those smiley stimulus variants that evoke the highest perceptual uncertainty, i.e. those stimulus variants that are about equally often rated as being happy and sad.

Ten different smiley stimuli with low-visibility of the respective emotional expressions (see Fig 1, stimulus specifications adopted from Joos et al [16]) were presented in random order using the method of constant stimuli [35]. The emotional expressions of the smiley stimuli were either happy or sad and it was only evoked by one parameter, i.e. the mouth curvature. The smiley variants have mouth curvatures with radii of r = 11.237°VA (stimulus variants S1 and S10), r = 14.422°VA (variants S2, S9), r = 20.193°VA (variants S3, S8), r = 33.527°VA (variants S4, S7), and r = 100.662°VA (variants S5, S6). The face border is described by a white circle with a diameter of d = 4° VA on a black background. The eyes are two filled white circles with a diameter of 0.214° VA and a distance to the vertical face symmetry axis of 0.611° VA to the left and right respectively. The nose is indicated by a simple vertical line with 0.377° VA length and 0.102° VA width, located on the vertical face symmetry axis at 2.076° VA distance from the upper central face border.

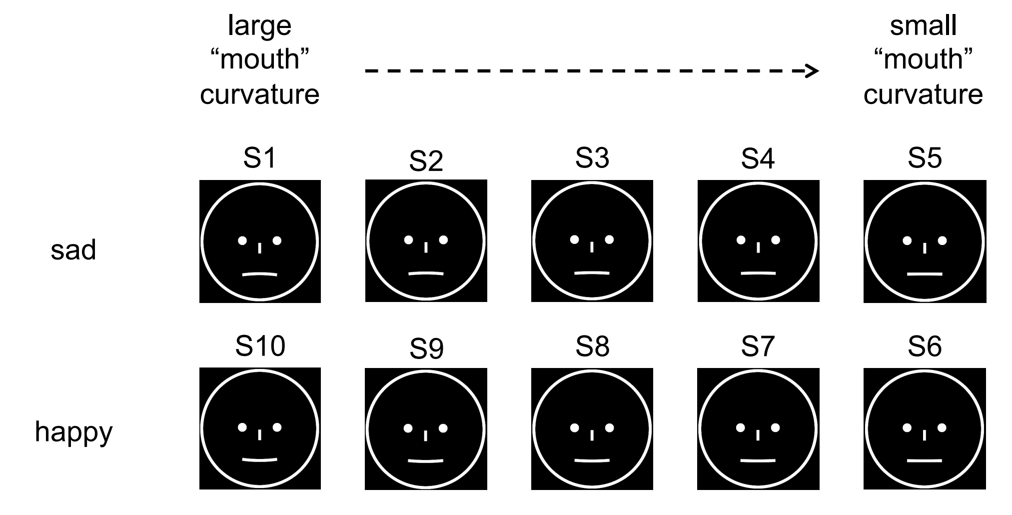

Figure 1 10 smiley stimulus variants (S1-S10) were presented in Experiment 1. The emotional expression of the smiley stimuli is only created through different mouth curvature radii and was either happy (S1-S5) or sad (S6-S10).

Procedure

The ten smiley variants (see Fig 1) were presented in random order for 1000 ms each (inter-stimulus interval = 400 ms). Each stimulus variant was repeated 20 times. The fixation point was the nose of the smiley stimuli. Only the line representing the nose was presented during the ISI in order to not disrupt fixational efforts. Participants were asked to indicate for each smiley stimulus whether it was perceived as happy or sad by pressing separate keys.

Behavioural analysis

Emotion perception

We first sorted the smiley stimuli from maximal sad (S1) over neutral (S5, S6) to the maximal happy expressions (S10, see Fig. 1). Subsequently, psychometric functions (sigmoids) were fitted to each participant’s average responses (across the 20 stimulus repetitions). The individual sigmoid inflection point indicates the theoretical smiley variant, where the perception of both happy and sad smiley percepts is equally likely. Using Mann-Whitney U tests we compare the two sigmoid function parameters (inflection point and rate) between patients with SSD and matched controls. Further, we computed the explained variance (R^2) of the sigmoidal fit to the responses.

Two patients with SSD did not respond to stimulus variant S5 at all. We substituted the non-existing response with the hypothetical response value obtained through the sigmoidal fit.

Manual responses

We identified the number of manual responses separately for each stimulus variant on the individual level. We then compared these response frequencies between the groups using Mann-Whitney U tests for each stimulus variant separately in order to test for general response biases. Further, we calculated the median reaction times for each stimulus variant on the individual level. We tested the median reaction times between the groups using separate Mann-Whitney U tests for the different stimulus variants. In order to check for reaction time differences between the different stimulus variants within groups, we logarithmised the individually determined median reaction times and performed a repeated-measures ANOVA (rmANOVA) with the stimulus identity as within-participant factor. Additionally, we fitted for each of the ten stimulus variants Gaussian distributions to the individual median reaction times. To this end, we (1) normalized the median reaction times (individual level) to range between 0 and 1 and (2) set the maximal possible mode of the Gaussian function to 1 in order to account for general reaction time differences between participants. Further, (3) we restricted the minimal variance of the Gaussian to 0.85, resulting in a width that must comprise at least two stimulus variants in order to prevent the Gaussian fit from peaking at an outlier response. We then computed for each participant the explained variance (R^2) of the Gaussian fit to the reaction time data.

Two patients with SSD did not respond to stimulus variant S5 at all (as already mentioned above). We averaged the reaction times in response to the immediate neighbouring stimulus variants (S4 and S6) and substituted the non-existing response with this mean reaction time for the rmANOVA and goodness of fit analyses. *P*-values of response frequencies and reaction time analyses were correct for multiple testing using the Bonferroni-Holm correction with an alpha of 0.05 [36].

Identifying low-visibility smiley stimuli for Experiment 2

We determined the appropriate low-visibility stimulus variants for each participant in order to use them for the electrophysiological part of the study (Experiment 2). The values of the individually determined inflection points, however, were most often not integers and thus did not match one of the presented stimulus variants (S1-S10). Therefore, we chose two stimulus variants for each participant, namely those that were closest to the inflection point (i.e. the left and right immediate neighbours). If, for example, the calculated inflection point has an x-value of 5.5 then stimulus variants S5 and S6 are labelled as the two most low-visibility smiley stimulus variants for this participant.

Experiment 2

Stimuli

In the electrophysiological Experiment 2 high-visibility smiley variants are compared with low-visibility smiley variants. Both visibility levels contained a happy and a sad smiley and thus consisted of two stimulus variants each. This results in a total of four stimulus variants, i.e. happy high-visibility stimulus, sad high-visibility stimulus, happy low-visibility stimulus, and sad low-visibility stimulus.

The low-visibility smiley variants were determined for each participant individually (see Methods "Experiment 1"). The high-visibility smiley variants were chosen such that their emotional expression was easily detectable for all participants (see Fig. 2). We therefore presented the same high-visibility stimuli to all participants. The stimuli themselves have the same features as described previously, but their mouth curvatures has a radius of r = 4.601°VA for both happy and sad smiley variants (see Fig 2).

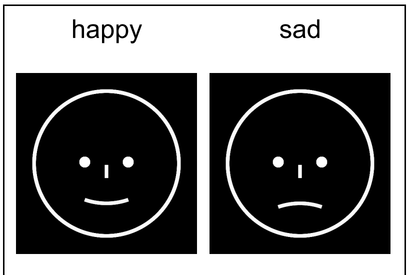

Figure 2 The two high-visibility smiley stimulus variants.

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Procedure

We presented two separate experimental conditions with either only high-visibility smiley stimuli or only low-visibility smiley stimuli. Experimental blocks lasted for seven minutes and were repeated two times in a pseudo-randomized order. Within the high-visibility and low-visibility stimulus conditions, the two respective stimulus variants (happy and sad) were alternated pseudo-randomly and had a reversal probability of 50%.

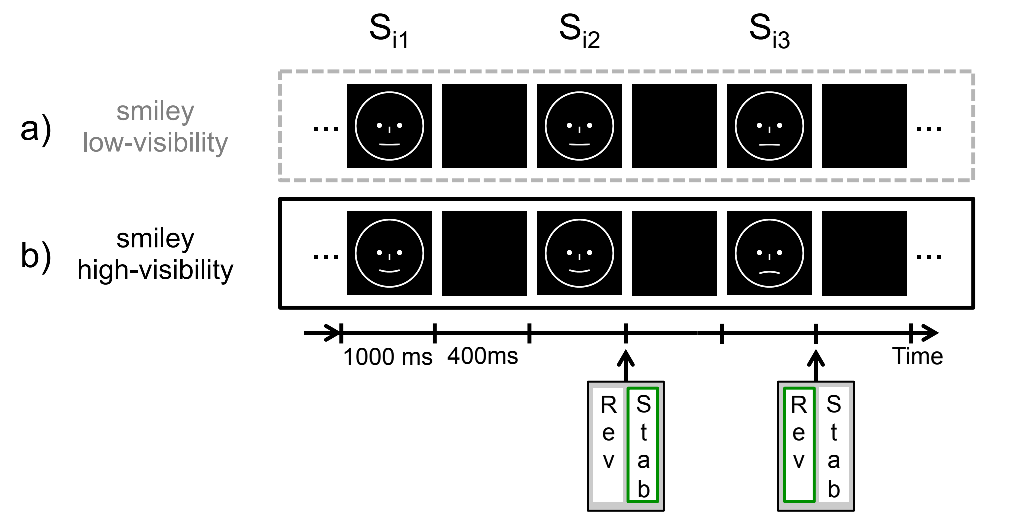

Figure 3 Experimental paradigm. Stimuli were presented discontinuously for 1000 ms with an ISI of 400 ms. Participants compared the current stimulus with the immediately preceding one. In case of identical percepts across two consecutive stimuli, participants indicate perceptual stability (stab) and in case of a change from one stimulus to the next, participants indicated perceptual reversal (rev). Within one experimental condition the visibility level stayed unchanged. The specific sequences of stimuli (Si1, Si2, Si3) in (a) and (b) are for demonstration purposes.

Stimuli were presented discontinuously for 1000 ms with a blank inter-stimulus interval (ISI) of 400 ms (see Fig 3 and [14–16]). According to the paradigm used in previous studies reporting the ERP Uncertainty Effects [14–16], participants were instructed to compare their current percept to the immediately preceding percept and to indicate perceptual reversals (change from one percept to the other) or perceptual stability (identical percepts across two consecutive presentations) for each stimulus (Fig 3) by pressing different keys. We used a standard keyboard on which the keys "F" and "J" were associated with either perceptual stability or perceptual reversal (the other keys on the keyboard were not used). Keys were pressed using the two index fingers and the stability and reversal assignment to the left ("F") or right ("J") index finger was counterbalanced between participants.

In the low-visibility condition, participants very often responded incorrectly and/or did only perceive very few reversal trials. Therefore, we will only analyse perceptual stability trials.

Data analysis

Eye tracker recording and processing

Eye tracking data (left eye) was measured using EyeLink CL 1000 (SR Research) with a sampling rate of 1000 Hz. A 9-point grid was used to calibrate the eye tracker before the experimental conditions and participants' heads were stabilized using a chin-rest.

In order to check whether patients and controls fixated similarly on the nose of the smileys, we analysed fixations and compared them between patients with SSD and healthy controls. Fixations are defined as stable eye position coordinates when lasting between 90 ms and 1000 ms. Only data sets (one participant, one experimental condition) with at least 30 fixations were included in the analysis. Due to problems during eye tracking data acquisition we could only include 7 patients with SSD and 8 matched controls in the analysis of the eye tracking data.

To analyse the fixations and find possible differences between patients with SSD and matched controls, we first clustered the fixations within one participant, within one experimental condition (high-visibility or low-visibility), and within one emotion (happy or sad) using a hierarchical cluster analysis with the Euclidean distance as metric and complete-linkage as fusion algorithm. The advantage of hierarchical clustering is that it does not need predefined parameters for building clusters (like number of clusters, critical value for the Euclidean distance, etc.). The output of the hierarchical clustering is a ranking of fixations based on their Euclidean distances. The clustering algorithm, however, does not return a threshold of Euclidean distance between fixations, which would allow distinguishing between clusters. Thus, the algorithm does not define how many clusters can be found within the data set. The experimenter has to define criteria to differ between groups of fixations that belong together and thus form a cluster. We aimed at having clusters with the following criteria:

(1) The cluster centroids had at least a distance of 0.7°VA (smallest distance between nose and mouth) between each other in order to being able to differ groups of fixations centred on the nose from groups of fixations centred on the mouth

(2) The number of fixations within a cluster had to at least comprise 10% of the data set in order to exclude outliers and/or very short fixation periods

We applied these criteria starting from the least possible amount of clusters, continued with increasing cluster number, and stopped at the largest number of clusters that still fulfilled the above-mentioned criteria.

The so identified clusters and their respective centroids were then compared between the two groups (patients with SSD and matched controls) individually for conditions (high-visibility or low-visibility) and emotions (happy or sad) using the following variables:

(1) *Number of Clusters*: We counted the number of cluster centroids per participant, condition, and emotion. This is a measure of spatial fixation variability between participants over the time of the experiment.

(2) *Spatial Variance*: We calculated the variance of the x- and y-distributions of the fixations within clusters. This is a measure of spatial variability within clusters. In the case that several clusters were found for one participant, one condition, and one emotion, we averaged the spatial variances across individual clusters.

(3) *Distance to Fixation Target*: We calculated the spatial distance between cluster centroids and the fixation target, i.e. the nose of the smiley stimuli. This is a measure of how well participants could follow the instruction of fixation on the nose. In the case that several clusters were found for one participant, one condition, and one emotion, we averaged the spatial distances to the nose of the multiple clusters respectively.

We calculated a rmANOVA with the between-participants factor *group* (patients with SSD or matched controls) and the within-participants factors *visibility level* (high-visibility or low-visibility) and *emotion* (happy or sad) for the variables *Number of Clusters*, *Spatial Variance*, and *Distance to Fixation Target*.

Key press analysis

We calculated the number of correct responses and median reaction times separately for both groups (patients with SSD or matched controls) and for both visibility levels (high-visibility or low-visibility).

In response to high-visibility stimuli, manual responses were regarded as valid if the following two criteria were fulfilled: (1) the response had to match the actual sensory information (stability trials) and (2) the response had to be given between 150 ms after stimulus onset and the next onset of a stimulus, i.e. 1400 ms after stimulus onset. Low-visibility stimuli were chosen such that those stimuli are equally likely to being perceived as happy and as sad (see "Experiment 1"). As a consequence, there are no "correct" and "false" responses to those stimuli and valid responses only had to fulfil the criterion that the response was given between 150 ms and 1400 ms after stimulus onset. The number of valid responses was compared using a two-tailed Mann-Whitney-U-Test to test between groups and a two-tailed Wilcoxon signed-rank test to test between visibility levels.

The above-described valid responses (low-visibility: perceived stability; high-visibility: correctly identified stability) were further considered in the reaction time and ERP analysis. Reaction times were measured as the time between stimulus onset and the key press. Median reaction times were compared using two-tailed Mann-Whitney-U-Tests to test between groups and two-tailed Wilcoxon signed-rank tests to test between visibility levels.

For both behavioural analyses (number of correct responses and reaction times), (1) the effect size r was calculated by dividing the Z-score by the root of the total number of observations [37], (2) resulting p-values were corrected for multiple testing using the

Bonferroni-Holm correction with an alpha of 0.05 [36] , and (3) we could include 13 patients with SSD and 12 matched control participants.

EEG recording and pre-processing

EEG was recorded with 64 active silver/silver chloride electrodes at scalp locations according to the 10-20 system [38] using Biosemi's Active Two system. EEG data were digitized with 2048 Hz and online low-pass filtered with 0.01-417 Hz. Data analysis was executed in Igor Pro 6.3 (Wavemetrics, Inc.). The data were down sampled to 1000 Hz and band-pass filtered offline at 0.01-25 Hz.

Trials exceeding an artefact threshold of ±150 µV were excluded from analysis. The baseline was defined as the average from 60 ms before to 40 ms after stimulus onset. For each group and visibility level, the EEG data was averaged separately for each participant and electrode. The trials started 60 ms before stimulus onset and were analysed until 1000 ms after onset, i.e. until the end of the stimulus presentation.

Uncertainty Effects

ERP Uncertainty Effects: Hypothesis-driven amplitude analyses

This ERP analysis focused on the previously described ERP Uncertainty Effects [14–16] showing positive deflections 200 and 400 ms after stimulus onset with high amplitudes in response to disambiguated/high-visibility stimuli and low amplitudes in response to ambiguous/low-visibility stimuli. Following these previous studies, we re-referenced the data to the averaged mastoid channels. Further, we focused on electrode Cz as spatial region of interest (ROI) for both ERP components and on temporal ROIs from 140 to 300 ms for the P200 and 300 to 600 ms for the P400.

We identified the individual peak amplitudes in the respective spatial and temporal ROI and measured the average voltage in a ±30 ms time window around the peak [39]. Two patients with SSD had to be excluded due to massive EEG artefacts. Thus, 11 patients with SSD and

12 matched controls with at least 30 valid trials per condition were included in the statistical analysis.

We conducted a rmANOVA with the within-participants factor *visibility* (high-visibility vs. low-visibility) and the between-participants factor *group* (patients vs. controls) separately for the P200 and for the P400 ERP component.

Microstate Uncertainty Effects: Exploratory topographical analysis

In this exploratory part of the Uncertainty Effects analysis, we investigated topographic effects using a modified microstate analysis. For some participants not all channels were available due to massive EEG artefacts. We thus had to perform the whole microstates analysis on those channels that were usable for all participants. In total this analysis was based on 48 channels, while we had to exclude channels Fp1, AF7, F7, T7, P7, P9, PO3, Iz, Fpz, Fp2, AF8, P2, P10, PO8, PO4, O2.

We investigated Microstate Uncertainty Effects in the following way:

(1) We re-referenced the data to common average.

(2) We calculated the difference ERPs (dERPs) between high-visibility and low-visibility conditions to isolate the ERP Uncertainty Effects, for each participant separately.

(3) The time span of the P200 and P400 temporal ROIs, i.e. 140 ms to 600 ms after stimulus onset, was selected for further analysis.

(4) We applied normalization on the individual level to make the amplitude range comparable between participants, while keeping the individual topographical patterns.

(5) Cluster analysis:

   a. We applied a hierarchical cluster analysis on the selected data for each individual, with the Euclidean distance as metric and complete-linkage as fusion algorithm. This hierarchical clustering was thus performed on amplitude maps as a function of time points (sampling frequency = 1000 Hz).

b. The detection of clusters within the resulting dissimilarity values was determined by applying a modified elbow method. The elbow method represents the intra-cluster sum of squared distances (residual variance) as a function of the number of clusters and usually one can detect a clear “elbow” or “knee of a curve” (i.e. a sudden drop of residual variance from one given number of clusters to the next larger one), which is then set to be the optimal number of clusters. In the current results, however, no clear elbow was detectable. Thus, we plotted the residual variance as a function of the number of clusters, fitted a psychometric curve to the residual variance, and calculated the slope for this fit. The threshold for the optimal number of clusters was then determined as the standard deviation of the slope of the residual variance fit. The smallest number of clusters with a higher slope value than the threshold was chosen.
c. In order to compare clusters between participants and between groups we conducted a "meta-clustering". This meta-clustering was performed on all of the individually determined clusters with the same setting as previously described. In the following, the resulting meta-clusters will be labelled as "microstates", because they represent topographic patterns of EEG activity that are stable over short time periods and that are present in the majority of the participants.
d. The resulting microstates were back projected onto the individual dERPs and thus a comparison between groups was possible.
    i. We compared the *number of occurrences* for each microstate between patients and controls. In case that a microstate occurred with the same frequency in both groups, we compared the mean *duration* of this

microstate and the *coverage*, i.e. fraction of the total time that a microstate was dominant, between the groups.

ii. Similarity within groups and between groups: One stimulus presentation lasted for 1000 ms. At every time point we collected one data point vector containing the voltage information of all 48 channels. For each data point vector we identified the microstate topography. In order to compare the similarity of the sequence of microstates between two participants within these 1000 ms, we calculated for each time point correlation coefficients between the microstates topographies of two participants. Each resulting correlation coefficient is thus a measure of similarity of microstates between the two participants at this specific time point. We calculated the average of these correlation coefficients as a measure of similarity across the 1000 ms of stimulus presentation. We did this for each possible pair of participants within an experiment group (within similarity) and separately, for each possible participant pair between groups (between similarity).

The statistical analyses of the Microstate Uncertainty Effects were performed using permutation tests with 10000 repetitions. Because this is the exploratory part of the analysis and the study in general is underpowered, we did not correct for multiple testing.

Early occipital differences

In this exploratory part of the analysis, we aimed to identify the earliest differences between patients with SSD and matched controls. The data was re-referenced to the averaged mastoid channels. We calculated the difference between high-visibility and low-visibility conditions in order to isolate effects related to the visibility of the stimuli on the individual level. Then we compared the isolated effects between patients with SSD and matched controls and identified the earliest deviation between the two groups using a running t-test. We found a significant difference between the groups already 115 ms after stimulus onset at electrode Oz (see Fig. 10 a). This finding is of an exploratory nature and we did not correct for multiple testing in this part of the analysis.

In order to systematically evaluate this effect on the individual level we performed a peak analysis based on the above-mentioned findings. We chose 100 ms to 130 ms after stimulus onset as the temporal ROI and electrode Oz as the spatial ROI. We identified the individual peak amplitudes in the respective spatial and temporal ROI and measured the average voltage in a ±30 ms time window around the peak [39]. As described in the previous analysis part, we included the same 11 patients with SSD and 12 matched controls in the statistical analysis. We conducted a rmANOVA with the within-participants factor *visibility* (high-visibility vs. low-visibility) and the between-participants factor *group* (patients vs. controls).

Correlation SAPS/SANS with the results of Experiment 2

We investigated possible relations between the symptoms of patients and their behavioural and neural responses. To this end, we calculated Spearman correlations between SAPS and SANS results and the previously mentioned measures of Experiment 2, i.e. key presses, reaction times, hypothesis-driven amplitude analysis (for P200 and P400 separately), exploratory topographical analysis, and the early occipital differences.

Results

Experiment 1

Emotion perception

In a first step, each participant was randomly presented with 10 smiley stimulus variants, differing in their degree of visibility in order to determine those variants that are equally likely perceived as happy and as sad. Psychometric curves were fitted to the individual data. The grand mean data can be inspected in Figure 4 top row. We do not find differences between patients with SSD and matched controls for neither the value of the inflection point, nor for the rate of the sigmoidal fit. We further estimated the goodness of the sigmoidal fit on the individual level, depicted in the bottom row of Figure 4. We find that the sigmoidal fit explains more than 90% of the variance in 10 out of 11 patients and in 12 out of 12 controls.

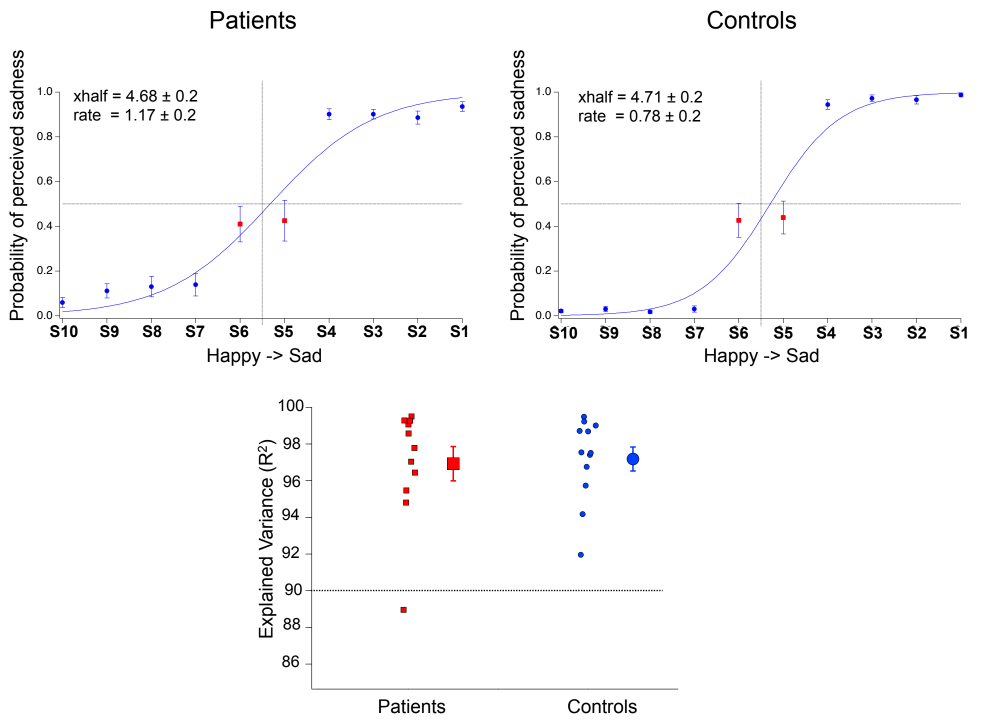

Figure 4 Emotion perception in Experiment 1. Top row: Averaged responses of perceived sadness (blue circles ± SEM depicted as error bars) for the stimulus variants S10-S1 (see Figure 1 for display) of patients with SSD (left graph) and matched controls (right graph). A psychometric curve is fitted (blue line) and values for the inflection point (xhalf) and the rate of the function are provided for both groups. Red squares indicate the group average of stimulus variants neighbouring the inflection point. The Bottom row depicts how well the sigmoidal functions fit the individual data (explained variance more than 90% in 10/11 patients and in 12/12 controls).

Response Frequencies

Table 1 presents the mean number of valid responses (± standard deviation), separately for the different stimulus variants (S10-S1) and groups (patients with SSD and controls). Patients with SSD showed significantly less manual responses for stimulus variants S10 ($Z = 2.88$, $r = -0.6$, $p = 0.04$), S8 ($Z = -2.87$, $r = -0.6$, $p = 0.04$), S4 ($Z = -2.83$, $r = -0.59$, $p = 0.04$), and S2 ($Z = -2.73$, $r = -0.57$, $p = 0.04$).

Reaction times

In Figure 5 reaction times can be inspected on the grand mean level (top row) and on the individual level (middle row). Controls (right column, blue colour) clearly show longest reaction times in response to stimulus variants S6 and S5 with the least visibility (see also Fig. 1, right), while patients with SSD (left column, red colour) seem to have the same reaction times in response to all stimulus variants. Mann-Whitney-U tests show that reaction times are (marginally) significantly smaller in patients compared to controls for stimulus variants S10 (Z = -2.4, r = -0.5, p = 0.09), S9 (Z = -2.4, r = -0.5, p = 0.08), S8 (Z = -2.28, r = -0.48, p = 0.09), S4 (Z = -2.5, r = -0.51, p = 0.09), S3 (Z = -3.2, r = -0.67, p = 0.009), S2 (Z = -2.65, r = -0.55, p = 0.06), and S1 (Z = -3.2, r = -0.67, p = 0.01). The rmANOVA of the within group comparison reveals that controls show a significant effect for the factor *stimulus* ($F(1,9)$ = 30.64, p = 7e-25, η_p^2 = 0.74), but patients do not ($F(1,9)$ = 0.7, p = 0.7, η_p^2 = 0.07). In order to account for the different dynamics of reaction times in controls compared to patients, we fitted Gaussian distributions on the individual reaction times as a function of stimulus identity. We calculated the explained variance (R^2), which can be seen in the bottom graph of Figure 5. The Gaussian distribution can explain more than 90% of the reaction time data variance in 10 out of 12 controls and only in 5 out of 11 patients.

Stimulus variant	Patients with SSD	Controls
S10	19.2 (±1.1)	20 (±0)
S9	18.4 (±2.1)	19.9 (±0.3)
S8	17.6 (±3.1)	20 (±0)
S7	17.6 (±4)	19.9 (±0.3)
S6	14.9 (±6.7)	17.3 (±5.5)
S5	13.8 (±8.2)	19.9 (±4.9)
S4	16 (±5.1)	19.9 (±0.3)
S3	18.8 (±2.3)	20 (±0)
S2	19 (±1.7)	19.9 (±0.3)
S1	19.4 (±1)	19.9 (±0.3)

Table 1. Mean number of valid responses (± standard deviation) in Experiment 1.

Identifying low-visibility smiley stimuli for Experiment 2

We calculated the inflection point for each participant and therewith individually determined the low-visibility stimulus variants that were used in Experiment 2.

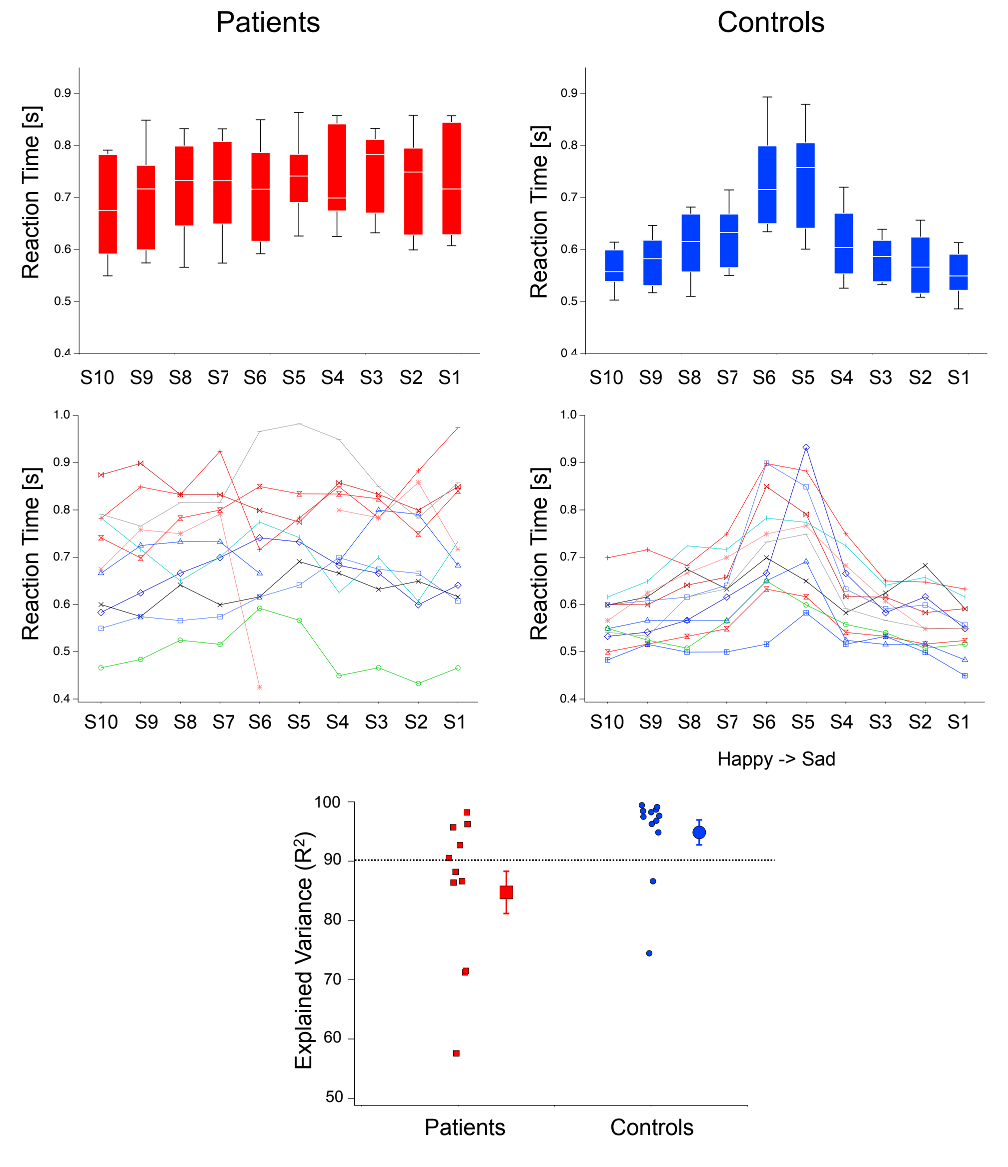

Figure 5 Reaction times in Experiment 1. The right column depicts data of controls (blue) participants and the left column depicts data of patients with SSD (red). The top row shows the median reaction times on the group level for the ten stimulus variants (S10-S1, see also Fig 1). Control participants clearly exhibit longer reaction times in response to stimulus variants S6 and S5, i.e. the most neutral stimuli, whereas patients show larger and also more similar responses to all stimulus variants. The middle row shows the median reaction times on the individual level, i.e. every line (specific colour and specific icon) represents one participant. We fitted Gaussian distributions on the individual reaction times as a function of stimulus identity and calculated the explained variance (R^2), which can be seen in the bottom graph. The Gaussian distribution can explain more than 90% of the reaction time data variance in 10 out of 12 controls and only in 5 out of 11 patients.

Experiment 2

In the second part of the study, we compare a condition presenting high-visibility stimuli with a condition presenting low-visibility stimuli (as determined on the individual level in Exp. 1). We had a 2x2 design with the between-participants factor *group*, i.e. patients with SSD vs. matched controls, and the within-participants factor *visibility*, i.e. high-visibility vs. low-visibility stimulus variants.

Behavioural Results

Eye tracker data

Analyses of the eye tracking data do not reveal any significant differences. The variables *Number of Clusters*, *Spatial Variance*, and *Distance to Fixation Target* are unaffected by the between-participants factor *group* and also unaffected by the within-participants factors *visibility level* and *emotion.* Across both within-participants factors as well as across the between-participants factor *group* the mean number of cluster per participant is 3.1 (SD: 1.2), the mean spatial variance of each cluster is 9.15°VA (SD: 2.98°VA), and the mean distance of the average cluster centroid to the nose (fixation target) is 1.29°VA (SD: 0.73°VA). In Fig 6 one exemplary data set is displayed.

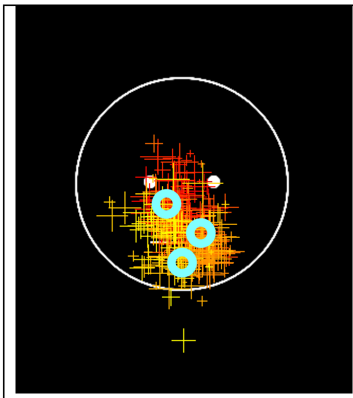

Figure 6 Exemplary eye tracking data (one data set). Each cross represents one fixation, with the size indicating the duration of this fixation (small = short duration, large = long duration) and the colour indicating the time-course of the fixations (light colour = beginning of the measurement, dark colour = end of the measurement). The blue circles represent the cluster centroids found for this data set.

Key presses

The mean number of valid responses for high-visibility stimuli is 322.62 (SD: 148.4) for patients and 521.92 (SD: 81.05) for controls. The mean number of valid responses for low-visibility stimuli is 385.3 (SD: 154.9) for patients and 509.2 (SD: 78.7) for controls. We find

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that the number of valid responses does not differ between visibility levels and they do not differ between the groups in response to low-visibility stimuli. We do, however, find that controls show significantly more correct responses for high-visibility stimuli compared to patients (Z = -3.4, r = -0.68, p = 0.008). Further, we find that controls reveal significantly more valid responses to high-visibility stimuli compared to low-visibility stimuli (Z = -3.06, r = -0.88, p = 0.02).

Median reaction times for patients with SSD are 683 ms (IQR: 533-733 ms) in the high-visibility condition and 666 ms (IQR: 567-666 ms) in the low-visibility condition. Median reaction times for matched controls are 575 ms (IQR: 516-620 ms) in the high-visibility condition and 641 ms (IQR: 541-700 ms) in the low-visibility condition. This can be inspected in Figure 7. The median reaction times neither differ significantly between groups nor between visibility levels.

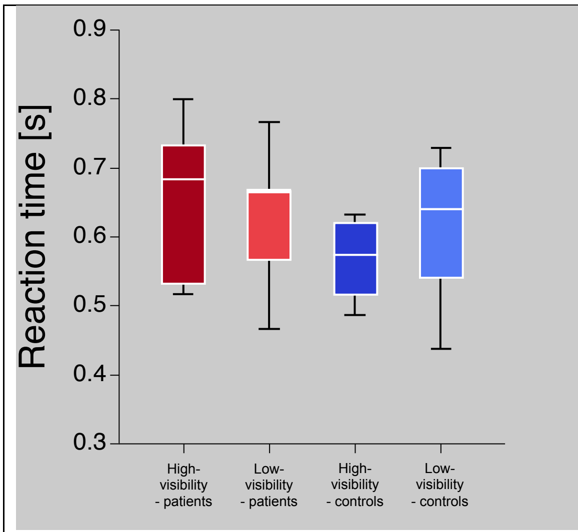

Figure 7 Median reaction times for the two visibility levels (high-visibility dark colours, low-visibility light colours) and the two groups (patients red, controls blue). The median of the individual median reaction times is the white line (low-visibility patients: white line is above the red square) and the whiskers depict the interquartile ranges of the reaction times.

Uncertainty Effects

ERP Uncertainty Effects: Hypothesis-driven amplitude analyses

We replicate the previously found ERP Uncertainty Effects in response to smiley stimuli. In Fig 8 (a) larger amplitudes for high-visibility (solid line) compared to low-visibility (dashed line) stimuli can be inspected. The rmANOVA indicates a significant main

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effect of *visibility* for both the P200 ($F(1,21) = 10.13$, $p = 0.005$, $\eta_p{}^2 = 0.325$) and the P400 ($F(1,21) = 20.88$, $p = 0.0002$, $\eta_p{}^2 = 0.499$).

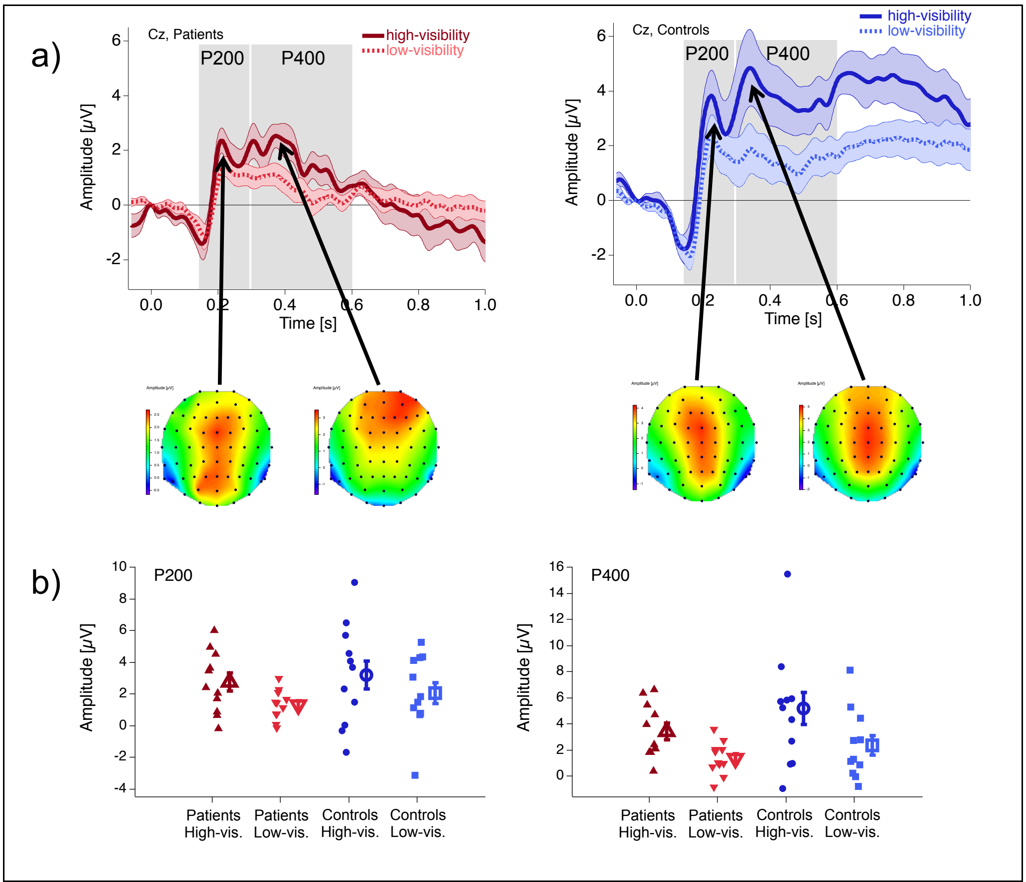

Figure 8 P200 and P400 ERP Effects in patients with SSD and matched control participants. In (a) the grand mean ERP traces (upper part) in response to high-visibility (dark colours, solid lines) and low-visibility (light colours, dotted lines) stimuli are depicted for patients (red, left graph) and controls (blue, right graph). The bottom part shows the voltage maps at peak latencies of the high-visibility conditions of the grand mean ERPs. In (b) the P200 (left graph) and P400 (right graph) amplitudes of individual participants (small icons) are depicted for both groups and both visibility levels along with the mean amplitudes and the SEM (large icons and error bars, respectively).

One aim of the current study was to investigate possible amplitude differences of the ERP Uncertainty Effects between patients with SSD (Fig 8 a, left graph, red colours) and control participants (Fig 8 a, right graph, blue colours). In Fig 8 (a) it seems that the difference between high- and low-visibility responses would be less in patients than in controls. Further, two clear P200 and P400 peaks can be identified for control participants with a spatial distribution ranging from frontal to parietal electrodes (see also voltage maps below the grand mean ERP graph), while there seems to be three peaks in the patient data. The ERPs seem to differ between the groups in terms of their spatial distributions and the temporal development of the ERP traces (see Fig 8 a). The statistical analysis, however, shows no significant difference between *groups* for neither the P200 nor the P400.

Microstate Uncertainty Effects: Exploratory topographical analysis

In the previous paragraph, we investigated the Uncertainty Effects in terms of amplitude (ERP Uncertainty Effects). Comparing amplitude differences between patients and controls is justified under the assumption that the same processes occur with different strengths. However, a difference in underlying processes is not captured with this analysis. Different underlying processes should have different locations in the brain and should thus result in different topographies (for further elaboration see the discussion section). We therefore investigate topographic differences in the processing of perceptual (un)certainty by means of a data-driven microstate analysis, i.e. the Microstate Uncertainty Effects. With this analysis we again focus on the differential processing of low- vs. high-visibility of the smiley stimuli and therefore calculated the difference between high- and low-visibility conditions for each participant. We performed a cluster analysis on the individual level in the time range of the P200 and the P400. We then clustered all of those resulting clusters again in a "meta-clustering" across patients and controls as described in the methods section. We back-projected those meta-clusters onto the individual time-series and investigated possible differences in the resulting microstates between patients with SSD and controls.

In Figure 8 the dominant microstates within the temporal ROI are depicted for each individual, with patients data shown in the left column and controls data shown in the middle column. In the right column the related microstate topographies are depicted. There are two colour codings: (1) the colours depicted in the left and middle column code for the identity of the respective microstate and are presented in the right column as headings of the microstate topography. (2) The colours depicted within the microstate topography indicate the strength of activation and range from red, i.e. the highest activation, to blue, i.e. the lowest activation. The spatial distributions of the microstate (right column in Fig 9) reveal that the positive activations are mainly located at frontal electrodes (Microstates C, D, E, F, G, H, L) or at central electrodes (Microstates A, B, J, K).

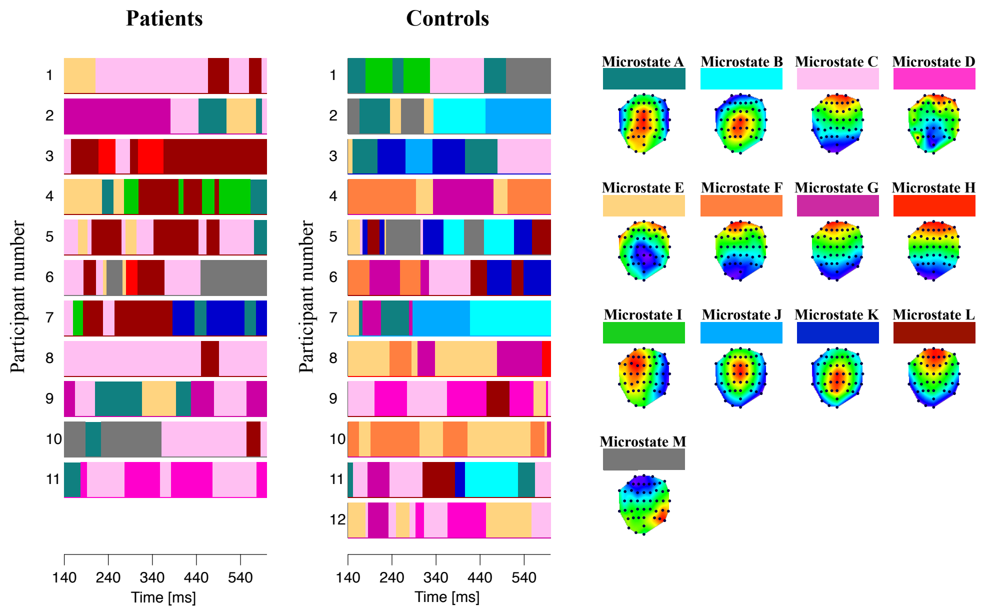

Figure 9 Microstate Uncertainty Effects in the P200-P400 time range. For all participants (rows) of both groups (patients left column, controls middle column) the dominant microstates are depicted in different colours. In the right column the colours are associated with the respective graphical illustration of the microstate topography (colours within the graphs: red = highest values, blue = lowest values). Note that the underlying data is the difference between high-visibility and low-visibility conditions.

The *occurrence frequency* is higher for controls compared to patients with SSD for microstate B (light blue; $p = 0.0002$), microstate F (dark orange; $p = 0.0002$), and microstate J (middle blue; $p = 0.0002$). Microstate L (dark red) is more frequent in patients than in controls ($p = 0.02$). For those microstates that occur similarly frequent in patients and controls we further investigate the *duration*, i.e. temporal length of dominance of one microstate, and the *coverage*, i.e. fraction of the total time that a microstate is dominant. We do not find any significant differences between groups for the variable *duration*. Microstate C (light pink), however, shows significantly more *coverage* in patients compared to controls ($p = 0.03$).

We further investigate the similarity of the temporal evolution of dominant microstates within and between the two groups by means of linear correlations. Within patients the average correlation coefficient is 0.58 (SD = 0.21) and within controls it is 0.54 (SD = 0.18). Between the two groups the average correlation coefficient is 0.58 (SD = 0.04). We do not find any significant differences of correlation coefficients between the within patients design, the within controls design, and the between groups design.

Early occipital differences

The previous ERP effects concerned the higher-level ERP Uncertainty Effects. In this section, the earliest differences between patients with SSD and matched controls are identified at electrode Oz. These results are of an exploratory nature and yield interesting effects for future analyses.

In Figure 10 (a) the grand mean differences between high-visibility and low-visibility conditions are depicted separately for patients (red) and controls (blue). A running t-test shows that the earliest significant differences between the groups are present between 100 ms and 130 ms after stimulus onset (see Figure 10 (a)). We then applied the so-identified region of interest in a regular peak analysis (for details see the methods section). In the top graphs of Figure 10 (b) the grand mean ERP traces can be inspected for high-visibility conditions (left graph, dark colours solid lines) and low-visibility conditions (right graph, light colours, dotted lines). Patients (red) and controls (blue) show different amplitude values of the negative deflections within the temporal ROI (grey bar). The voltage maps (bottom part of (b)) reveal a negative deflection at central occipital electrode sites in controls. This negativity seems to be absent for the patients. The individual data is depicted in Figure 10 (c) and shows generally larger negative ERP amplitudes for controls compared to patients. The rmANOVA indicates a significant main effect of the between factor *group* ($F(1,21) = 6.51$, $p = 0.02$, $\eta_p{}^2 = 0.24$). Further, we find a significant interaction between *group* and *visibility* ($F(1,21) = 4.7$, $p = 0.04$, $\eta_p{}^2 = 0.18$). We do not find a significant main effect for the factor *visibility*.

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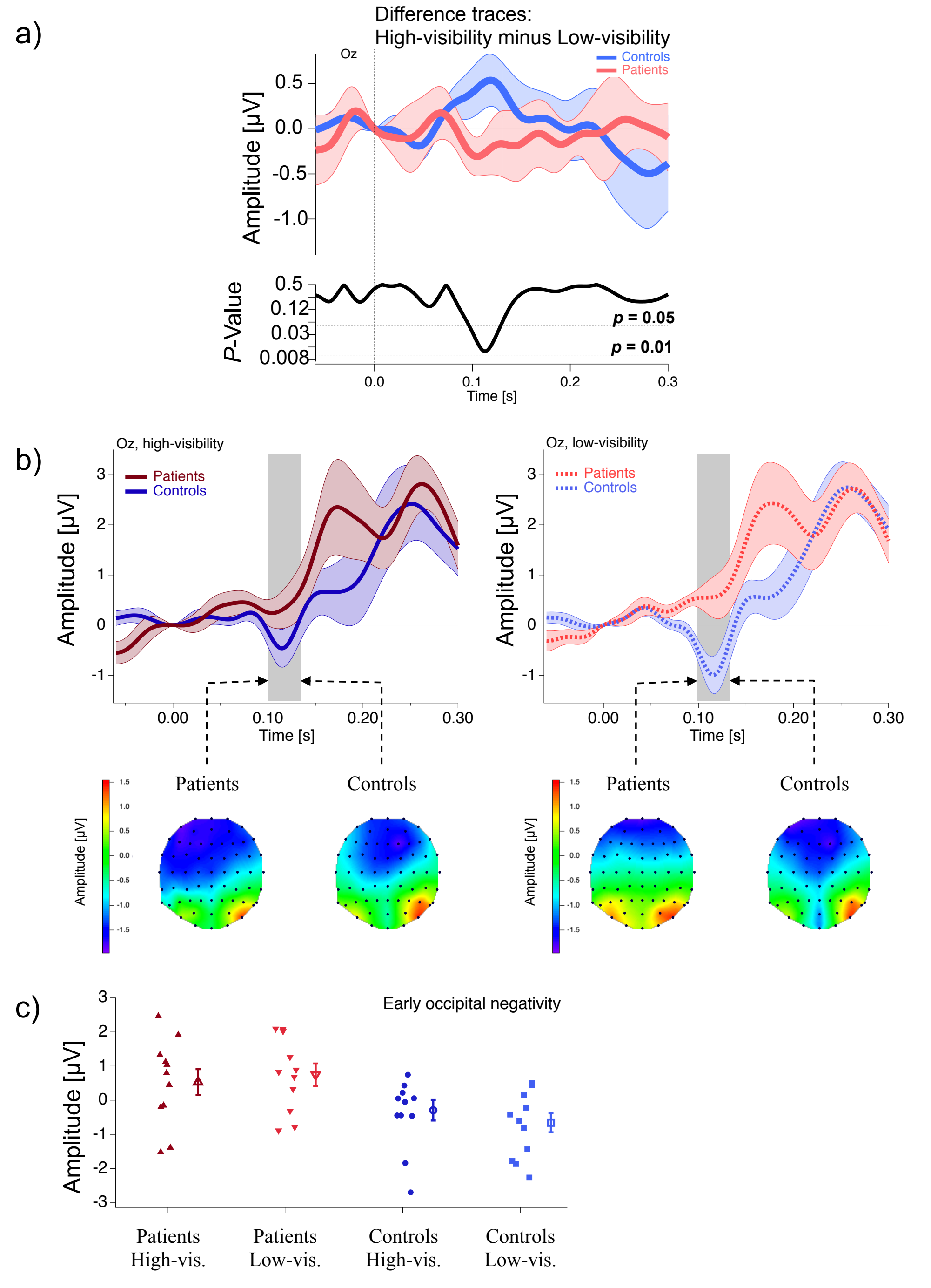

Figure 10 Occipital ERP effects at around 115 ms after stimulus onset in patients with SSD and matched control participants. In (a) the grand mean difference between high-visibility and low-visibility conditions is depicted for controls (blue) and patients (red). A running t-test was performed and revealed that significant differences between the groups are present in the time-range of roughly 100 ms to 130 ms after stimulus onset. In (b) the grand mean ERP traces (upper part) are depicted for patients (red) and controls (blue) in response to high-visibility (dark colours, solid lines) in the left graph and in response to low-visibility (light colours, dotted lines)

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in the right graph. The grey bar indicates the temporal ROI. The bottom part shows the voltage maps at peak latencies of the respective condition. There is a small difference between patients and controls in the high-visibility conditions and a clear difference between groups in the low-visibility conditions. In (c) the individual amplitudes (small icons) are depicted for both groups and both visibility levels along with the mean amplitudes and the SEM (large icons and error bars, respectively).

Correlation SAPS/SANS with the results of Experiment 2

We find no significant correlations between the SAPS/SANS scores and the measures of Experiment 2.

Discussion

The present study is divided into a hypothesis-driven data analysis part and a separate exploratory analysis part. In the hypothesis-driven part, we postulated highly similar steps but different intensities in (un)certainty processing between SSD patients and controls. To this end, we adopted spatial and temporal ROIs from previous studies [14–16] describing the ERP Uncertainty Effects. These effects show large ERP amplitudes in response to stimuli that evoke certainty (e.g. highly visible stimuli) and small ERP amplitudes in response to stimuli that evoke uncertainty (e.g. less visible stimuli). Stable and reliable percepts result from an integration of bottom-up sensory with top-down endogenous information. According to the current interpretations, the ERP Uncertainty Effects reflect how certain an observer is about her/his perceptual interpretation of the sensory information [14–16,40]. Perceptual integration functions are proposed to be altered in patients with SSD [1,8–10]. As a consequence, certainty estimations should be inadequate and thus result in an altered ERP Uncertainty Effects pattern. In the current experiments, we tested this hypothesis by comparing EEG data from patients with SSD with that of matched controls in response to (un)certainty.

In a behavioural Experiment 1, we first determined those smiley stimuli that evoked the highest uncertainty for each individual separately. We presented 10 stimulus variants differing in the degree of visibility of the happy and sad expression in random order and participants indicated whether they perceived them as happy or sad. The selected stimuli do not systematically differ between the groups. We do, however, find differing numbers of manual responses between patients and controls and a strikingly different pattern of reaction time results between the two groups in response to the randomly presented low-visibility smiley stimuli.

In Experiment 2, behavioural and neural responses to high-visibility stimuli are compared with those to low-visibility stimuli. All participants were instructed to fixate a central fixation target during the EEG experiment in order to minimize artefacts induced by eye-movements. We analysed the fixation behaviour and find no difference between the groups. Further, reaction times in this EEG experiment do not differ between the groups. For the high-visibility stimuli, however, we find more correct responses in controls than in patients with SSD.

In the hypothesis-driven analysis of the ERP Uncertainty Effects, we replicate those effects for controls and also find them for patients with SSD, with larger amplitudes of the P200 and the P400 ERP components in response to high-visibility compared to low-visibility stimuli. The observable tendency for smaller ERP Uncertainty Effects in patients compared to controls does not reach statistical significance. In the exploratory analysis we kept the temporal ROI of the ERP Uncertainty Effects but took into account the possibility of qualitative differences in processing steps, potentially resulting in different spatial patterns of the ERP signals between patients with SSD and controls. We therefore performed a microstate analysis on the Uncertainty Effects data and find differences between the groups. Three of the identified microstates occur more frequently in controls than in patients and one microstate occurs more frequently in patients than in controls. Another microstate is dominant for an overall longer time in patients than in controls. Degrees of similarity in the temporal microstate evolution within and between groups were investigated by means of correlation coefficients. These temporal evolutions of microstates are about equally similar between participants within groups and between groups.

Additionally, we explore the earliest time point after stimulus onset at which the ERP traces for low-visibility smiley stimuli are different from those evoked by the high-visibility smileys and compared the EEG data around these time points between groups. We identify an early ERP negativity in the difference traces (high-visibility traces minus low-visibility traces) at 115 ms after stimulus onset, which is most prominent at electrode Oz. This negativity shows larger amplitudes in controls compared to patients.

Limitations of the study

The present study is part of the dissertation project of the first author Ellen Joos. Due to the Corona pandemic we had to stop measurements at a time point of the study when we had a bit more than half of the planned number of participants (N = 20 per group). The study is at its current state thus strongly underpowered with usable EEG data from 11 patients with SSD and 12 controls. The results are preliminary and might either stabilize or change with more collected data sets.

One factor that might largely influence the current results is medication. All patients receive antipsychotic drugs, whereas the matched control participants do not. Some patients additionally receive anti-epileptic, anti-parkinsonian and other co-morbidity-related medication, which causes a variety of different combination of treatments within the patient group. Due to the low number of patients measured so far, correlational analyses between type and dosage of medication with the behavioural and neural measures applied in this paper are not conclusive. Once data acquisition is completed we will calculate those correlations in order to quantify the impact of medication on the findings.

Further, we only tested patients with SSD and matched controls. It is thus unclear whether the differences between the groups are specific for patients with SSD or whether they are generally present in mental disorders. Symptoms, as determined by SAPS and SANS, show no significant correlations with the results of Experiment 2, but given the low number of patients we cannot derive any conclusions from this finding. Stronger claims about the current findings can only be made after more participants have been tested and also sub-scores of SAPS and SANS are correlated. Strong claims, moreover, can only be made once the current results are replicated in one or more separate replication studies and they are shown to be specific to patients with SSD.

Different Uncertainty Effects in patients with SSD compared to matched controls

In the hypothesis-driven analysis we investigated possible amplitude modulations of the ERP Uncertainty Effects between patients with SSD and matched controls. Such modulations in amplitude, given the presence of the focused ERP signatures, would indicate similar processes but potentially different processing intensities related to (un)certainty in the two groups. We do, however, find no significant difference in the focused ERP Uncertainty Effects between the two groups. Due to the currently small sample size of this study it is not clear whether or not amplitude effects will become significant between patients and controls with more measurements. The grand mean data shown in Figure 8 seem as if amplitudes heights in response to low-visibility stimuli are similar between groups. Amplitude heights in response to high-visibility stimuli, however, seem to be smaller in patients compared to controls. If this difference would manifest in the statistical results with more data, then one could speculate that the differences between groups would not be related to the difficulty of the task, but that they are rather due to general differences in the processing of certainty. This would stand in line with the notion of Phillips et al. [41], who speculated that patients with SSD have a lower threshold for stimuli to being perceived as ambiguous.

We identified one control participant with unusually large amplitudes for both, the P200 and the P400 ERP component. This person may distort the grand means in the control group (see individual data in Fig. 8). Exclusion of this person, however, would further reduce the already low number of participants and would thus provide no real gain for the statistics.

Another interesting observation of the ERP Uncertainty Effects is that there seems to be a difference in inter-individual variability between the groups, with a tendency for smaller inter-individual variability in the patients group compared to the control group (see Fig 8 b). Again, more data sets will reveal whether this is actually a systematic effect or just a momentary impression due to the underpowered study.

Further, the grand mean display of the ERP Uncertainty Effects in patients reveals three peaks (210 ms, 305 ms, and 370 ms after stimulus onset) instead of two (at 200 ms and at 400 ms after stimulus onset), as found in previous studies [14–16]. We inspected the individual patients data in order to (dis)proof the three peaks assumption arising from the grand mean level on the individual level. We find no systematic differences in the number of peaks between patients and controls. We do, however, observe more variance in latency of the P400 in patients compared to controls. This might cause an averaging artefact resulting in three peaks in the grand mean ERP, even though only two peaks are present on the individual level. Systematically analysing the latency differences between patients and controls will be conducted when more data sets are collected. This analysis might provide valuable information about differences in processing speed between the two groups.

In the preliminary results, the amplitude modulations of the ERP Uncertainty Effects do not significantly differ between the groups. The amplitude analysis relies on the assumption that the same processes are present in different strengths between the groups. One could also hypothesise that different processes are present in the two groups. Different processes should be evoked by different brain structures, which should be reflected in different locations in the brain and which should thus evoke different topographic patterns. This idea is reflected in the microstates analysis. Microstates are short periods of stable brain states that are identified with EEG. Importantly, a microstate has a fixed topography, which might vary in strength and polarity [42]. In typical microstate analyses, four main microstates as initially defined within a resting state paradigm [43], are investigated. In the current study an onset paradigm is used, which evokes stimulus-specific processes. These processes might not be represented by the resting state microstates and therefore we performed a data-driven microstate analysis, similar to Bhatia [44]. Note that all of the results from this explorative analysis are reported without correction for multiple testing and should thus not be over interpreted.

We applied a hierarchical clustering algorithm and a data-bound decision criterion for the number of clusters. This analysis was conducted on the individual differences of neural responses to high-visibility minus low-visibility conditions. The idea behind this was to eliminate neural activity related to the processing of the low-level visual features of the smiley stimuli, like circles and lines, and therewith to isolate the EEG related to perceptual decision making under different certainty conditions. Importantly, a microstate analysis is only valid under the assumption that similar topographies generally represent similar neural processes and that particularly similar topographies between individuals also represent similar neural processes, despite of possible differences in brain anatomy. The same reasoning underlies a variety of analyses of EEG features across participants. We would thus expect a homogenous picture of the dominant microstates between participants.

Observation of Figure 9 (left and middle column), however, shows that the temporal sequence of microstates within the temporal ROI varies considerably between individuals both within groups but also between groups. One reason may be that some of the identified microstate topographies are very similar (e.g. meta-clusters C, F, G, and H all have a frontal positivity). The hierarchical clustering groups together those topographies with the least Euclidean distance, starting from the smallest distance where two topographies, e.g. at two time-points, are grouped together and calculates the distances iteratively up to the largest distance where all topographies, e.g. at all time-points, are grouped together. The criterion to decide for the number of microstates or to put it in other words the criterion to decide which similarity/Euclidean distance between the topographies should be set as the threshold is chosen by the experimenter. We used a modified elbow-method, which is based on the slope of the explained variance. It is important to notice that this choice of the threshold does not necessarily have an output in which the different microstates actually represent different states of the brain. Further, every microstate topography comprises several processes. If topographies are very similar between microstates then the majority of sub-processes may be the same and only few sub-processes may be different. In the current result we can see that microstates mainly show frontal or central positive spatial distributions, with only two exceptions (Microstate J, Microstate M). Having this in mind, the temporal sequences of microstate topographies between participants may be less heterogeneous than it seems.

We find that Microstate Uncertainty Effects differ between patients and controls. In particular, we find that three microstates occur more frequently in controls than in patients and only one microstate is more frequent in patients than in controls.

It is important to notice that in the occurrence frequency analysis a certain microstate can either be present in a participant or not. Therefore, not all of the participants within a group do necessarily have to show the microstate. The comparison between groups thus depends on probabilities of a microstates' occurrence frequency. The reason for a certain microstate only occurring in parts of the group can be (1) that the groups comprise sub-groups which do not share the same neural processes, (2) that individual anatomies do not allow to detect the same topographies even though the signals are the same, or (3) that the signal processing evokes different topographies even though the signals are the same. Importantly, the fact that the microstates are not present in all participants within a group limits the conclusions that can be drawn from the results. Given the current data, we cannot infer statements about the whole population and the Microstate Uncertainty Effects cannot be used as a physiological signal to differ between patients and controls.

It is, however, very interesting to investigate the functional role of the microstates that differ between groups. Brain regions evoking the microstates reported above might help to understand this functional role. Two of the identified microstates that differ between patients and controls show a central/centro-parietal distribution and the two others show a frontal distribution. Once data acquisition is completed, we will investigate the neural sources using source analysis methods such as eLORETA [45] and recently developed methods such as ConvDip [preprint: 46], which is based on convolutional neural networks. In future studies, advanced source analyses should be applied, optimally using a combined MRI measurement in order to individually determine the brain anatomy and thus have more precise source localisation.

Further, it is important to understand why the microstates only occur in some of the participants within a group. Three microstates are represented in 1/3 of the controls each and they do not occur at all in the patients. Another microstate was found more frequently in patients (in roughly 70% of the individuals) compared to controls (in roughly 30% of the individuals). The existence of sub-groups within the groups might be a possible explanation. We will try to identify those sub-groups and understand the common basis within one sub-group once data acquisition is completed. As mentioned previously, a correlational analysis at the current stage, i.e. with only 11 patients and 12 controls, is not conclusive. To rule out general differences between patients and controls, we tested for a difference in the amount of variability of the topographic patterns between the two groups. To this end, we computed the correlation coefficients of the topographic variability and do not find any significant differences, which is in favour of the sub-group interpretation.

Similar ocular fixation behaviour in patients with SSD and matched controls

In the current study we find no significant amplitude ERP Uncertainty Effects, but we find differing microstate patterns between the two groups, which indicates a difference in (un)certainty processing between the two groups. Differences in fixation behaviour might be the cause for differences in processing or they could constitute a confound. We investigated this possible influence and find no differences of fixation behaviour between patients with SSD and matched controls. There are controversial findings in the literature regarding ocular fixation behaviour. Some studies report differences between patients with SSD compared to control participants [e.g. 47,48] and others only a trend [e.g. 49]. However, there are also studies in line with the current finding, which report no differences of ocular fixations of patients with SSD compared to controls [e.g. 50,51]. Further, it has been proposed that patients with SSD exhibit differences in visual scanning of faces during passive viewing tasks, while they do not differ compared to controls during an active and instructed task [52], which is similar to the current paradigm. Differences between studies might be due to differences in medication status of the patients, different stimuli, different tasks and/or other methodological aspects, as pointed out by Gooding et al. [51]. Future research should focus on the ocular fixation behaviour and systematically account for medication status and methodology to get a clearer picture. For the purpose of this study, the current results stand in line with the findings of the emotion recognition ability, which reveals no significant difference between patients and controls. One has to keep in mind, however, that the current study is underpowered and more data has to be collected to make valid statements.

Differences in the number manual responses in patients with SSD compared to matched controls

We find differences in the number of manual responses in Experiment 1. Patients with SSD show less manual responses for four variants of the low-visibility stimuli compared to controls. Two of those stimulus variants contained rather sad emotional expressions, while the two other stimulus variants contained rather happy emotional expressions. In order to test for a dependency between the number of manual responses and the negative symptom scores, as indicated by [53], we will correlate the two variables once the data set is completed. Especially interesting is that before correction for multiple testing the number of manual responses for seven out of ten smiley variants was marginally significantly lower in patients compared to controls. The lack of statistical difference might thus be related to the underpowered data set and the results and possible interpretations might thus change with a complete data set.

In Experiment 2 participants had to perform an n-back comparison task. We find that the number of valid responses for highly visible stimuli was significantly lower in patients compared to controls. This might be related to memory impairments, as was already found extensively in patients with SSD [e.g. 54]. Another explanation might be that patients are less successful in correctly discriminating the different emotional facial expressions. In order to test this interpretation in a future study, one could present two smiley stimuli simultaneously and systematically vary same and different stimuli. The resulting number of correct responses would be compared between patients and controls. If the above-mentioned discrimination task is deficient in patients, the number of correct responses should be less compared to controls. Further, we will also correlate the number of manual responses in Experiment 2 with the negative symptom scores once data collection is completed.

Similar emotion recognition in patients with SSD and matched controls

It has been shown that patients with SSD have difficulties in interpreting emotional expressions [23–25]. We do not find any significant differences in emotion recognition/classification between patients with SSD and matched controls in Experiment 1. One has to keep in mind, however, that we did not use actual pictures of human beings, as was done in the previously mentioned studies, but we presented abstract representations of faces in the form of smileys. A study by Manalai et al. [55] shows that patients with psychotic disorders perform worse than controls when recognizing emotional expressions of actual face pictures, but interestingly outperform controls when recognizing emotional expressions of emoticons. One could conclude from this study that complex information about an emotional expression induces difficulties in their interpretation in patients in SSD. On the other hand, coarse information about a mouth bending upwards or downwards does not impair patients' ability to recognize emotions, as seen in the current study, or that they even outperform control participants, as seen in the study by Manalai et al. [55].

Reaction time patterns (Exp. 1) in patients with SSD and matched controls

The generality of the ERP Uncertainty Effects [14–16] along with their late latencies led to the hypothesis that they reflect higher-level/cognitive rather than lower-level sensory processing steps. We thus interpret them in the following way: Due to evolutionary reasons the perceptual system produces perceptual interpretations as fast as possible and in a highly automatic manner [see 56 for a more detailed discussion]. Certainty or uncertainty of these quickly generated perceptual interpretations is then rated in a second step, probably by a meta-perceptual evaluation instance [see also 57]. We hypothesise that the ERP Uncertainty Effects and possibly also the Microstate Uncertainty Effects reflect the differential meta-perceptual evaluation results given different degrees of stimulus visibility. In a third step, different levels of (un)certainty might influence the behaviour. In the current study, we indirectly measure (un)certainty by means of reaction times. It is known for a long time that uncertainty, as measured with rating scales, is correlated with long reaction times [e.g. 58]. The reaction time results from control participants from the behavioural Experiment 1 confirm this by showing longer reaction times in response to stimulus variants S6 and S5 (most low-visibility stimuli) compared to the other variants. It seems therefore reasonable that controls experience uncertainty when observing the most low-visibility stimuli, resulting in long reaction times, and that they experience certainty when observing higher-visibility stimuli, resulting in short reaction times. The reaction times of patients with SSD clearly differ in terms of duration and dynamics from those of controls. In detail, patients with SSD show longer reaction times compared to controls for all stimulus variants except for stimuli S7, S6, and S5, i.e. the most low-visibility stimulus variants. Further, the actual reaction time values do not differ between the stimulus variants in patients. Patients with SSD thus may experience the same amount of subjective uncertainty in response to all used stimulus variants, independent of the amount of visual cues. The finding that all reaction times of the patients are very similar to the reaction times of controls in response to the most low-visibility stimuli is in favour of this speculation. Like for the EEG results, this interpretation stands in line with the notion of Phillips et al. [41], suggesting that patients with SSD are more likely to perceive stimuli in general as ambiguous.

The relation between behavioural (reaction times) and electrophysiological measures (ERP/Microstate Uncertainty Effects) of (un)certainty is not entirely clear. One way to investigate this relation would be to introduce a certainty rating as a second task, which would allow assessing certainty on a behavioural level and to correlate this with reaction times and electrophysiological measures.

How can the conflicting patterns (Exp. 1 vs. Exp. 2) of reaction time results be explained?

One remaining problem for the above presented interpretation is that we should expect also significant reaction time differences between visibility levels in Experiment 2, but do not find them. Previous studies, using a highly similar experimental paradigm to investigating the ERP Uncertainty Effects [14–16] did also reveal no systematic differences between median reaction times in response to different levels of ambiguity/visibility.

In the following these discrepancies between the reaction time findings of the behavioural Experiment 1 and that of the electrophysiological Experiment 2 are discussed. It is important to emphasize the differences between the two experimental paradigms:

- Visibility of the stimuli: in Experiment 1 ten different happy and sad stimuli with differences in the visibility of the emotional expression were presented. In Experiment 2 only one happy and one sad low-visibility smiley and one happy and one sad high-visibility smiley were presented.

- Number of stimuli within one experimental condition: in Experiment 1 the ten stimulus variants were randomly presented within one experimental condition. Experiment 2 consisted of two conditions. In one condition only one happy and one sad low-visibility smiley, i.e. 2 different stimuli, were presented repeatedly in a randomised order. In the other condition the happy and sad high-visibility smiley were presented in the same way.
- Task: in Experiment 1 participants had to categorize the presented stimulus as either happy or as sad. In Experiment 2 an n-back task was introduced, following the typical paradigm used in previous studies about the ERP Uncertainty Effects [14–16]: Participants had to indicate same or different emotional expression of the current stimulus compared to the previous one.

It has been shown that in general task difficulty correlates positively with the duration of reaction times (the more difficult the slower) [59]. It is reasonable to assume that task difficulty also correlates positively with uncertainty, which in turn results in longer reaction times [58]. The n-back task (Experiment 2) explicitly involves the access to memory traces and may thus be regarded as more difficult compared to the identification task in Experiment 1, which does not involve memory. One would therefore expect longer reaction times in the n-back compared to the identification task. We do, however, find the opposite pattern for both controls and patients. The median reaction times are up to 100 ms longer in Experiment 1 compared to Experiment 2. A possible explanation of this unexpected finding will be described in the following: Both experiments have in common that two responses are possible (Experiment 1: happy and sad; Experiment 2: same and different). The number of stimuli within one experimental condition, however, is different. More stimulus variants in the behavioural Experiment 1 might explain long reaction times from a predictive processing perspective, because the probability of one stimulus to occur is only 10% and thus the identity of the upcoming stimulus is poorly predictable. In Experiment 2, in contrast, only two different stimuli are presented and thus the probability of one stimulus to occur is 50% and therefore the identity of the upcoming stimulus is easily predictable. Generally, more accurate predictions enable more accurate and faster responses and vice versa. In Exp. 2 stimuli are much more predictable and might thus lead to generally shorter reaction times than the ten stimuli in Exp. 1.

Furthermore, the finding that both groups exhibit similar reaction times for low- and high-visibility stimuli in Experiment 2 might be due to physiological restrictions: The high predictability of the stimuli (50% occurrence probability), which is irrespective of their visibility level, might make reaction times as short as physiologically possible. In Experiment 1, contrarily, no such limiting physiological effect is found, which might again be related to the low predictability of the stimuli (10% occurrence probability). Under normal, non-laboratory circumstances the predictability of the upcoming sensory information is usually lower than 50% occurrence probability, because we move in space, interact with other beings that act independently and stimuli are not presented with numerous repetitions as in typical lab experiments. Experiment 1 might thus come a bit closer to non-laboratory situations than the high predictability situation in Experiment 2.

We observe a tendency of reaction time differences between the two groups. Patients with SSD are 25 ms slower than controls in the low-visibility condition and over 100 ms slower than controls in the high-visibility condition. These differences in reaction times are, however, not statistically significant. Earlier studies repeatedly found slower reaction times in patients with SSD compared to matched controls [60–62]. The reaction time differences between groups are around 50 ms in the literature [63]. Thus, the observed non-significant tendency is in directionality and quantity roughly in confirmation with these studies. The lack of statistical significance of the group difference in the current study might be due to the low sample size. More participants have to be measured in order to see whether the observed tendency transforms into a statistically significant effect. Hereafter this reaction time difference between groups is neglected due to its statistical insignificance.

Predictive coding and (un)certainty

Predictive processes are described in more detail by the frameworks of Bayesian probability [64] and predictive coding [65,66]. According to these theories, the brain forms a model about the external world. Whenever new sensory information enters the brain, this information is compared with the previously formed model and the error between sensory information and the model is calculated (the "prediction error"). The model then becomes updated in a recursive manner until the prediction error is minimized. In typical EEG paradigms aiming to investigate predictive processes, the predictions are based on frequent repetitions of the same stimulus. Sudden presentations of rare stimuli violate these predictions and thus maximize the prediction error. EEG differences between frequent and rare stimuli are then interpreted as correlates of the prediction error [e.g. the mismatch negativity (MMN) 67]. The stimuli used in such paradigms were typically unambiguous and clearly visible. In a recent study by our group [40], we investigated predictive processes in response to different ambiguity levels of a stimulus rather than its occurrence frequency. It was shown that the ERP Uncertainty Effects varied as a function of the predicted stimulus ambiguity level. Further, we found that predictive processes always modulate processing of the perceptual present, even if those predictions are irrelevant for the present percept and task. In the following we will speculate about predictive processes evoked by high and low quality of the sensory information as used in the current study. Importantly, in this study the occurrence probability of the sensory information is high due to the block-design paradigm, irrespective of the quality of the sensory information.

In the case of highly visible stimuli, the low-level differences between a picture of a clearly happy and a clearly sad expression are relatively large, because the mouth curvatures within those pictures strongly differ. If the brain has predicted, for example, an upcoming clearly happy smiley picture at a time-point t = -1, but the actual sensory input at t = 0 is a picture of a clearly sad smiley, one would expect a large prediction error due to the large low-level differences between what has been expected and what is seen. In the condition with low-visibility smileys, the low-level differences between a slightly happy and a slightly sad expression are small, because the mouth curvatures within those pictures only slightly differ. If the brain has predicted, for example, an upcoming slightly happy smiley picture at t = -1 and the actual sensory input at t = 0 is a picture of a slightly sad smiley, one would expect a small prediction error due to the small low-level differences between predicted and seen stimuli. We thus hypothesise generally smaller prediction errors in the case of less visible compared to highly visible sensory information (under the assumption of equal occurrence probabilities).

Following this argumentation, we can speculate that beyond a postulated prediction error signal the brain also produces a signal reflecting prediction success. A prediction success would be if the predicted stimulus (at t = -1) equals the sensory information (at t = 0). In this case the match between predicted and actual sensory information should be larger in the case of highly visible compared to less visible stimuli, because more low-level details are present in the highly compared to the less visible stimuli. Accordingly, the postulated prediction success should thus be high in the case of highly visible and low in the case of less visible stimuli. The amplitudes of the ERP Uncertainty Effects might reflect such a prediction success with large amplitudes in the case of a high prediction success and small amplitudes in the case of a low prediction success.

We previously postulated that the prediction is formed at a time-point t = -1 and that the sensory information is perceived at t = 0. Afterwards the predictive model is updated, using the prediction error, until the prediction error is close to zero at time-point t = 1 and a new prediction is formed. Further, it is known for a long time that perception results from a weighting of the exogenous sensory information with the endogenous, e.g. memorized, information [6].

In the case of highly visible stimuli, one sensory input allows for one highly probable perceptual interpretation. This might evoke a high perceptual certainty about the sensory information. Consequently, the sensory information might be strongly weighted during perceptual processing. The strong weighting of the sensory information might result in a large contribution of the highly visible input during minimization of the prediction error, because the sensory input is judged as being reliable enough to update the model accordingly. In a very simplified way, one could say that the prediction error will be minimized until it reaches a value close to zero in the case of highly visible stimuli.

In the case of less visible stimuli, one sensory input allows for two or more equally likely perceptual interpretations (see the most low-visibility stimuli in the behavioural Experiment 1). This might evoke perceptual uncertainty about the sensory information. Consequently, the sensory information might be weighted weakly during perceptual processing, resulting in a small contribution of the less visible input during minimization of the prediction error. In a very simplified way, one could say that the prediction error will always be larger than zero in less visible stimuli, because the sensory information might not be regarded as reliable enough to update the model accordingly.

Importantly, it is proposed that updating of the model is disturbed in patients with SSD, resulting in an erroneous interpretation of the sensory information [8,10,68–70]. One consequence of these aberrant updating mechanisms might be that the prediction error can never come close to zero in patients with SSD. In the case of less visible stimuli, which are proposed to always having a prediction error larger than 0, the aberrant processing in patients with SSD might not have a strong influence. In the case of highly visible stimuli, however, which are proposed to produce a prediction error close to zero after the updating process, a possibly general increase of the prediction error in patients with SSD might have severe consequences. This reasoning might explain the tendency for smaller ERP amplitudes in response to highly visible stimuli in patients compared to controls in Experiment 2 (see results "ERP Uncertainty Effects"). Further, this reasoning might explain differences in the Microstate Uncertainty Effects between the groups and ultimately might explain the reaction time differences found between groups in Experiment 1.

Earliest differences between groups

Most studies investigating face-processing in patients with SSD focus on the N170 as the earliest time-point to differ between patients and controls [71,72]. The current study, however, shows that the EEG traces differ between groups already at about 115 ms after stimulus onset, indicating a remarkable early, lower-level difference in perceptual processing for patients with SSD compared to controls. These results stand in line with recent findings of sensory deficits in psychiatric diseases, which is highly interesting because psychiatric diseases are typically regarded as diseases of the higher-level cognitive system [26,27,73–75]. Further, the above-raised hypothesis that the meta-perceptual certainty rating is altered in patients with SSD, resulting in aberrant predictive processes, might be related to these early differences in processing of (un)certainty in patients compared to controls. The framework of predictive coding assumes that the prediction error is integrated on all hierarchy levels during the perceptual process [65]. The different time-points in which patients with SSD show altered results compared to controls, i.e. the early occipital differences, the ERP/Microstate Uncertainty Effects, and the deviating reaction times, could reflect those different hierarchy levels of the prediction error integration.

Future studies should systematically investigate whether this early peak reliably differs between patients with SSD and matched controls. If this early effect will be replicated in follow-up studies it will be necessary to investigate whether it is specific to the current stimuli or whether it represents a general feature of deviant visual processing in patients with SSD.

Conclusion and Outlook

The current study compared the neural and behavioural correlates of (un)certainty between patients with SSD and matched controls using happy and sad smiley face stimuli differing in visibility of their emotional face expressions. We focused on the differential processing of stimuli with high- versus low-visibility and compared the EEG and behavioural correlates of the resulting high versus low certainty about the respective perceptual outcomes in the two groups. Our analysis followed two parallel approaches:

In one approach, we postulated same processes in patients with SSD as in healthy controls but different intensities. We thereby focused on the previously reported ERP Uncertainty Effects [14–16] and replicated previous findings of larger ERP amplitudes with high-visibility compared to low-visibility smiley stimuli in healthy controls and found the same pattern in SSD patients. This finding is in line with similar ocular fixation behaviour and reaction times between groups in Experiment 2. Some non-significant tendency towards overall smaller amplitudes in patients than in controls is observable in the grand mean ERP traces. However, the present results are based on an underpowered data set and additional data sets will probably provide more clarification in one or the other direction.

In our first data analysis approach, we postulated differences in quantity/intensity of otherwise equal processing steps. In our second approach, we postulated qualitative differences in perceptual processing between patients and controls. In order to test this hypothesis, we calculated ERP microstates of the difference traces (high- minus low-visibility smileys) and compared their temporal evolution between patients with SSD and matched controls. We found evidence for deviating microstate patterns of sub-groups within patients and controls. In summary we found certain microstate patterns that were present in a number of member of one group but completely absent in the other group. This pattern of results indicates qualitative differences in (un)certainty processing between groups but also some indications for the existence of sub-groups within groups.

Recent predictive coding approaches postulate deviant integration of bottom-up sensory with top-down endogenous conceptual information during the perceptual process in patients with SSD. As a consequence, patients may create deviating models about the external world. The deviating microstate (Exp. 2) and reaction time patterns (Exp. 1) in patients with SSD, as is present in the current data, might reflect certain steps during such a deviant model formation. In a recent study in our lab with only healthy controls, we varied the current experimental paradigm such that influences from the immediate perceptual past and predictions about the immediate perceptual future on the perception of the present could be systematically investigated [40]. With this paradigm we tested whether the here reported ERP Uncertainty Effects stand in line with the predictive coding approach. In yet unpublished results we found that the ERP Uncertainty Effects are in perfect agreement with the predictive coding models. Important next steps on our agenda are (1) to increase the number of participants in order to see whether the currant findings stabilize statistically. (2) In a follow-up study with patients with SSD we plan to adopt the above-mentioned variant of the experimental paradigm [40], which allows quantification of predictive processes. With this we may be able to test more specifically the hypothesis of deviant predictive coding model formation in patients compared to controls. (3) Further, adding a certainty rating as a secondary task will allow to investigate the relation between electrophysiological and behavioural correlates of (un)certainty.

One important finding in our exploratory analysis is the very early occipital amplitude differences (at 115 ms after stimulus onset) between groups, which indicates that also low-level processes related to the sensory information are altered in patients with SSD. Future studies, of course, have to replicate the current findings and importantly investigate whether this difference is specific to patients with SSD or generally occurs in mental disorders. Overall, we are optimistic that the experimental paradigm used in this study is a promising tool to identify strongly demanded physiological markers of Schizophrenia Spectrum Disorder.

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4. PhD article No. 3: Using the perceptual past to predict the perceptual future influences the perceived present

4.1 Summary

The perceptual inference problem is solved with the help of information from the immediate perceptual history, experiences over lifetime and the predictions about upcoming sensory information formed thereof. Previous studies regarding this temporal aspect of perception primarily focused on either the influence of past experiences on the perceptual processes in the present (e.g. priming, hysteresis: Long et al., 1992; Liaci et al., 2018) or primarily focused on the influence of predictions about future stimuli on present perceptual processes (e.g. predictive coding: Näätänen et al., 2007). The current study builds a bridge between those different lines of research by acknowledging the interplay between previous experiences and predictions and its combined influence on the perceptual present. In the following this interplay will be labelled as *temporal context*. The stimuli used in previous studies investigating aspects of temporal context integration were typically unambiguous, highly visible, and mainly differed in their occurrence frequency (e.g. Näätänen et al., 2007). However, solving the perceptual inference problem might be most difficult when the stimulus is of low quality, e.g. when it is ambiguous. Further, ambiguous stimuli in the immediate past might evoke less reliable predictions about the immediate perceptual future compared to previous unambiguous stimuli. In the current study, ambiguous and unambiguous lattice variants were presented (similar to Kornmeier and Bach, 2009; Kornmeier et al., 2016), with ambiguity being the independent stimulus variable to study temporal context effects during perception. The ERP Uncertainty Paradigm (Kornmeier and Bach, 2009; Kornmeier et al., 2016; Joos et al., 2020b), however, was not suited for systematic analyses of temporal context effects, because the level of ambiguity was kept constant within conditions (block design). The paradigm was thus modified such that the stimuli were presented in pairs, where stimulus S1 was followed by stimulus S2. Four different experimental conditions were created with a paired design (2x2) with differing ambiguity levels of S1 and S2 (ambiguous vs. unambiguous). This allowed for the investigation of neural responses elicited by the same S1 stimuli over different levels of ambiguity in its temporal context, i.e. preceding S2 of the previous

pair and predicted S2 of the current pair.
It is hypothesised that information from the temporal context is automatically integrated into the processing of the sensory present and into the execution of a present task. In the first experiment of this study, reaction times and ERP Uncertainty Effects (P200 and P400) were compared between two conditions: condition 1 had a temporal context consisting of unambiguous stimuli and condition 2 had a temporal context consisting of ambiguous stimuli. ERP amplitudes were larger with an unambiguous temporal context compared to an ambiguous temporal context, i.e. *ERP Temporal Context Effects*. Reaction times were also affected by the temporal context stimuli. Specifically, reaction times were short when the ambiguity level was the same in S1 and S2 while reaction times were long when the ambiguity level was different in S1 and S2.
In the second experiment, it was investigated whether the same results from Experiment 1 could be found when information to predict the perceptual future is provided as an abstract symbol, and not based on the direct perceptual experience of sensory regularities in the past. To this end, preceding S2 stimuli were replaced with a symbolic representation of the upcoming stimuli that was presented at the beginning of each block. Block length was dramatically shortened from 9 minutes to 9 seconds (i.e. three pair presentations) and concurrently block repetitions were increased. This enabled the separate analysis of the first, second, and third stimulus presentation. The results showed that exposure to the sensory information indeed is a necessary precondition for the ERP Temporal Context Effects. Only in the third stimulus presentation a significant effect was observable for an ERP difference between disambiguated and ambiguous stimuli in the temporal context. Reaction time differences, on the other hand, were present already in the second stimulus presentation, i.e. after exposure to one sensory experience.
The paper "Using the perceptual past to predict the perceptual future influences the perceived present - a novel ERP paradigm" (Joos et al., 2020a) indicates that previous and predicted sensory information have a strong influence on the processing of the present and can be measured both behaviourally and electrophysiologically. Importantly, this is the case even though the task was not dependent on information from the temporal context. This indicates an automatic integration of previous and predicted information about the certainty of perceptual outcomes. The brain always estimates the reliability of previous and predicted sensory information and integrates them into the current one, despite actual relevance. Experiencing the sensory information directly, however, is necessary to form those predictions about the perceptual future, whereas a symbolic information about the future is not sufficient.
In psychiatric diseases such as Schizophrenia Spectrum Disorder, predictive processes are proposed to being altered compared to controls (Shergill et al., 2005; Fletcher and Frith, 2009; Notredame et al., 2014; Schmack et al., 2015; Sterzer et al., 2019). The current findings might help to investigate aberrant predictive processes in psychiatric patients by means of the ERP Temporal Context Effects.

Contribution to the paper I was part of the funding acquisition, as well as the conceptualisation and administration of the project. I was responsible for data curation, formal analysis, investigation, methodology, software, validation, visualisation, writing the original draft and reviewing and editing the manuscript.

4.2 Main Manuscript

PLOS ONE

RESEARCH ARTICLE

Using the perceptual past to predict the perceptual future influences the perceived present – A novel ERP paradigm

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Abstract

The information available through our senses is noisy, incomplete, and to varying degrees ambiguous. The perceptual system must create stable and reliable percepts out of this restricted information. It solves this perceptual inference problem by integrating memories of previous percepts and making predictions about the perceptual future.

Using ambiguous figures and a new experimental approach, we studied whether generating predictions based on regularities in the past affects processing of the present and how this is done. Event-related potentials (ERPs) were measured to investigate whether a highly regular temporal context of either ambiguous or unambiguous stimulus variants differently affects processing of a current stimulus and/or task execution. Further, we tested whether symbolic announcements about the immediate perceptual future can replace the past experience of regularities as a source for making predictions. Both ERP and reaction time varied as a function of stimulus ambiguity in the temporal context of a present stimulus. No such effects were found with symbolic announcements.

Our results indicate that predictions about the future automatically alter processing of the present, even if the predictions are irrelevant for the present percept and task. However, direct experiences of past regularities are necessary for predicting the future whereas symbolic information about the future is not sufficient.

OPEN ACCESS

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Introduction

The information entering our senses is inherently noisy, incomplete, and to varying degrees ambiguous. In order to disambiguate and interpret the strongly limited sensory information, our perceptual system must include non-sensory (top-down) information from spatial and temporal contexts. This enables the brain to construct stable and reliable percepts that allow for a successful interaction with our environment. Perception has already been described as an

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unconscious inference process by Hermann von Helmholtz [1], where perception results from a combination of bottom-up sensory evidence with top-down contextual information. A more detailed historical overview of the roots of von Helmholtz's "perception as unconscious inference" account can be found in the introduction of Brascamp et al. [2]. One prominent example of the perceptual inference problem is three-dimensional (3D) perception. We live in a three-dimensional world but in the first step of vision, the observed three-dimensional environment is projected onto two-dimensional retinae [e.g. 3]. Therefore, only two of the three dimensions can be accessed directly from this projection. The third dimension, however, has to be reconstructed out of secondary information like occlusion, binocular vision etc. [e.g. 4]. The Necker cube [5] is a famous ambiguous figure consisting of a two-dimensional representation of a three-dimensional cube grid, which can be perceived as two mutually exclusive cube variants with different spatial orientations. Fig 1 presents a so-called Necker lattice, a combination of 9 assembled Necker cubes, together with the two unambiguous lattice variants with 3D cues [6,7]. During prolonged observation, our perception of the Necker cube becomes unstable and alternates between these two interpretations. The reason behind this perceptual instability is that the retinal projection is equally compatible with the two alternative three dimensional cube variants. In fact, the retinal image of the Necker cube is also compatible with other geometric object interpretations with no 90˚ angles, as nicely demonstrated in Kersten & Yuille (2003) [8]. Nevertheless, our perception typically alternates exclusively between the 90˚ alternatives. This perceptual bias is already evidence that our perceptual history influences our current percept, since we live in a world where 90˚ objects are much more common, and thus, more probable than objects that do not contain 90˚ angles [e.g. 9].

Different lines of research have investigated the influence of the perceptual history, at different time scales, on the current percept. Typical experimental paradigms presented stimuli with different degrees of similarity in sequence and compared the influence of preceding stimuli on the perceptual interpretation of the current stimulus. Several studies reported positive effects (positive priming [10–12], positive hysteresis [9,13], serial dependence [14–16]) of the

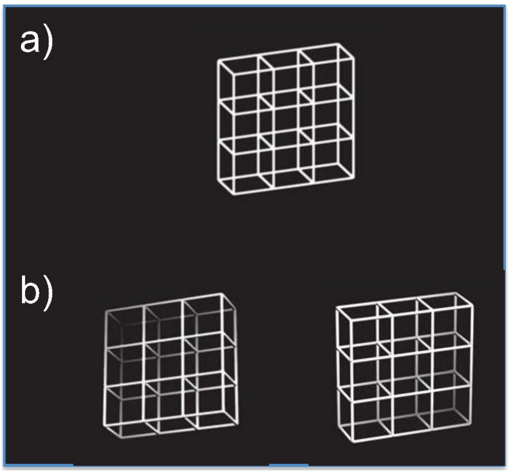

Fig 1. Stimuli. (a) depicts the ambiguous Necker lattice, a variant of the Necker cube [5]. The unambiguous variants are displayed in (b) with the front side facing towards the top (front-top = FT) on the left and the front side facing towards the bottom (front-bottom = FB). Stimuli were created in the laboratory of Dr. Kornmeier.

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perceptual history on current percept (e.g. current stimuli are likely to be perceived in the same way as previous ones). In contrast, other studies reported negative effects (e.g. adaptation, negative hysteresis [9,17–19]) of perceptual history on current stimuli (e.g. current stimuli are likely to be perceived as opposite of the previous one).

Taking information of the perceptual past into account is an efficient strategy of the perceptual system to handle the perceptual inference problem. Typically, our environment only slightly changes from one moment to another. Predicting the future using regularities from the immediate past can thus substantially help to overcome the inherent sensory limitations. Concurrently, both speed and efficacy of perceptual processes are increased.

Recent Bayesian probability [8] and predictive coding [20,21] approaches provide a general theoretical framework that may be able to integrate the above mentioned findings. The basic idea is that the perceptual history is used to generate a model of the external world and to make predictions about the upcoming sensory future. A measure of the error between generated predictions and the actual sensory evidence (prediction error) is minimized during a variable number of recurrent loops of feed-forward (bottom-up) and feedback (top-down) neural activity [e.g. 22].

The electroencephalogram (EEG) monitors the activity of the brain non-invasively. Its high temporal resolution allows for observation of neural processing on a millisecond scale. The influence of the immediate perceptual history on the current percept can thus be analysed in terms of EEG correlates. The event-related potential (ERP) is the averaged EEG response over many stimulus repetitions, which isolates processing steps time-locked to the stimulus. Several studies have used ERPs to test predictive coding approaches. In typical paradigms, the predictions are based upon frequent repetitions of the same stimulus in the immediate past. These predictions are then infrequently violated by sudden presentation of a deviant stimulus. Differences between predicted (frequently presented) and unpredicted (rare deviant) stimuli are then interpreted as correlates of the prediction error. The ERP correlate of this postulated prediction error is the so-called Mismatch Negativity (MMN), a negative ERP component between 100 and 250 ms after onset of the deviant stimulus, with maximal amplitude at temporal and frontal electrode locations [MMN, 23–25]. The MMN is regarded as an important physiological correlate within the predictive coding account and is interpreted as reflecting the prediction error, i.e. the outcome of the comparison between prediction and actual sensory input.

The current study differs in two aspects from the previously described MMN studies:

(1) Stimulus quality instead of stimulus frequency

The stimuli used in the MMN studies introduced above were typically unambiguous, highly visible, and mainly differed in their occurrence frequency. However, in our natural environment, exploiting the perceptual past and relying on a predicted future may become increasingly important in perceptual situations with low quality of the sensory input, e.g. when the stimulus is ambiguous. In this situation, the occurrence frequency of a certain stimulus in a short period of time is less important. Furthermore, stimuli from the immediate past, that are ambiguous or low in visibility, may make predictions about the immediate perceptual future less reliable than unambiguous previous stimuli. Therefore, we presented ambiguous and unambiguous lattice variants [26,27], with ambiguity as the independent stimulus variable to study temporal context effects during perception. The term 'temporal context' can refer to differences in temporal aspects of the stimuli such as presentation duration of the stimuli [28,29]. Further, the term is used in memory studies and can refer to features and/or objects that occur simultaneously with an object of interest, which are thus linked together in the perceptual memory [30]. In the current study we present certain sequences of stimuli repeatedly within experimental blocks. This makes an actual stimulus sequence within an experimental block highly memorable and predictable. In the following, the 'temporal context' of a certain stimulus thus implied both, the immediately preceding stimulus and the highly predictable subsequent stimulus.

We hypothesize that predictions based on previous experience with an ambiguous stimulus (temporal context = ambiguous) are less reliable than predictions based on previous experience with clear and unambiguous stimuli (temporal context = unambiguous).

(2) Ambiguity-sensitive ERPs as dependent variables

Kornmeier et al., in a series of ERP studies, presented either ambiguous or unambiguous stimulus variants in separate experimental conditions and compared the resulting ERPs. They found prominent P200 and P400 amplitude effects (Cohen's d between 0.6 and 1.2). The unambiguous stimulus variants resulted in large amplitudes and the ambiguous stimuli in small amplitudes [26,27]. These prominent ERP effects were found across different categories of stimulus ambiguity (geometry, motion, Gestalt perception) and recently also for smiley stimuli with low and high visibility of their emotional expression [31]. The authors interpreted the P200 and P400 amplitude effects as correlates of certainty about perceptual outcomes [see also 32] or–in other words–as a measure of success in solving the perceptual inference problem. In their recent study they labelled these effects "ERP Uncertainty Effects" [31].

Assuming that this interpretation is valid and that perceptual outcomes are always the result of integrating bottom-up sensory information with top-down temporal context information, it would be reasonable to expect that the sizes of these effects not only depend on the quality of the current stimulus, but also on the quality of the stimuli within the temporal context. The experimental design of our previous studies [26,27,31] did not allow for systematic analyses of sensory quality within the temporal context because the level of ambiguity/visibility was kept constant within conditions (block design).

In contrast to this, in the current study, we presented stimuli in pairs, where stimulus S1 was followed by stimulus S2. Furthermore, we created four different experimental conditions with a paired design (2x2) with differing ambiguity levels of S1 and S2 (ambiguous vs. unambiguous). Designing the experiment in this way allowed us to investigate neural responses elicited by the same S1 stimuli over different levels of ambiguity in its temporal context, i.e. preceding S2 of the previous pair and subsequent S2 of the current pair. We were thus able to investigate neural responses to an ambiguous S1 stimulus and compare an ambiguous temporal context with an unambiguous temporal context. Similarly, neural responses to unambiguous S1 stimuli were compared between ambiguous and unambiguous temporal contexts. We postulate that responses to stimuli S1 should reveal higher ERP amplitudes when the temporal context consists of unambiguous stimuli compared to ambiguous stimuli, meaning that ERP responses should be higher in amplitudes when the temporal context is certain as opposed to uncertain. This effect is expected to be independent of the ambiguity level (ambiguous, unambiguous) of S1 itself. Furthermore, an ambiguous context (i.e. an uncertain temporal context) may drive the observer into an uncertain, and thus, less stable current perceptual state, making them react more hesitantly. As a result of this, we expect longer reaction times.

In short, we hypothesize that the automatic integration of the stimulus information from the temporal context affects processing of the sensory present and the execution of a present task.

The current study consists of two experiments. In Experiment 1, we compared both the reaction times to a stimulus-related task as well as the P200 and P400 ERP components (ERP Uncertainty Effects [26,27,31]) evoked by two factors: ambiguity level of the current stimuli (ambiguous vs. unambiguous) and ambiguity level of the stimuli within the temporal context (ambiguous vs. unambiguous).

In Experiment 1, the temporal context consisted of either ambiguous or unambiguous lattice stimuli. In Experiment 2, we replaced the preceding S2 stimuli with abstract symbolic information about the future stimulus and studied whether this replacement alters the ERP and reaction time results, which were obtained in Experiment 1.

Material and methods—Experiment 1

Participants

Thirteen participants (seven females) took part in this study. The median age was 24 with participants ranging from 21 to 34 years old. Twelve participants were right-handed and one was ambidextrous. All participants had normal or corrected-to-normal visual acuity [33] and gave their written informed consent. The study was approved by the ethics committee of the University of Freiburg and was performed in accordance with the ethical standards laid down in the Declaration of Helsinki [34].

Stimuli. We used the ambiguous Necker lattice, a combination of nine Necker cubes [5,6] and two unambiguous lattice variants corresponding to the two perceptual interpretations of the ambiguous lattice, see Fig 1. The unambiguous lattice variants included depth cues, like shading, central projection, and aerial perspective based on OpenGL lighting model [35]. The lattice stimuli had a size of 7.5˚ x 7.5˚ visual angle. Both ambiguous Necker lattices and unambiguous lattice variants had a mean luminance of 40 cd/m^2 (the unambiguous stimuli luminance being calculated by averaging the four outer corners of the lattice). All lattices were presented on a black background (0.01 cd/m^2).

Procedure. Participants were tested in a dimly lit room in the Eye Center, in the Medical Center of the University of Freiburg, Germany. They were seated at a distance of 114 cm in front of a Philips GD 402 monochrome CRT screen (refresh rate = 85 Hz, screen resolution = 800×600 pixels), which was operated by an Apple Mac mini computer. During the experiment, participants were instructed to focus their gaze on a fixation point in the middle of the screen.

One observation sequence (OS) consisted of the successive presentation of two lattice stimuli (S1 and S2). Each stimulus was presented for 800 ms. S1 and S2 were temporally separated by an inter-stimulus interval (ISI) of 400 ms. During presentation of the lattice S1, participants were instructed to identify its 3D orientation (front side perceived either right/downwards or left/upwards) and to indicate their percept by key press. During the subsequent presentation of the second lattice (S2), participants compared their perceived 3D orientation of S2 with that of the previously perceived and memorized S1. By pressing separate keys, participants indicated perceived orientation reversal or stability (i.e. percepts of identical 3D orientations of S1 and S2). Key presses were performed on a keyboard with four keys, and key assignment (two scenarios) was counterbalanced between participants.

Key assignment scenario 1: keys 1 and 2 were associated with the orientation task and pressed with the left thumb, with key 1 indicating the left/upwards orientation and key 2 the right/downwards orientation. Keys 3 and 4 were associated with the memory task and pressed with the right thumb, with key 3 indicating perceptual stability and key 4 perceptual reversal trials.

Key assignment scenario 2: keys 1 and 2 were associated with the memory task and pressed with the left thumb, with key 1 indicating perceptual stability and key 2 perceptual reversal trials. Keys 3 and 4 were associated with the orientation task and pressed with the right thumb, with key 3 indicating the left/upwards orientation and key 4 the right/downwards orientation.

Successive observation sequences (OS) were separated by an inter-observation sequence interval (IOSI) of 1000 ms (see Fig 2).

Experiment 1 consisted of four different experimental conditions (see Fig 3). The ambiguity levels of both S1 and S2 varied between but stayed constant within experimental conditions. The analysis only focused on EEG and behavioural responses to stimulus S1 (the currently observed stimulus) as a function of the ambiguity levels of preceding and upcoming stimuli S2 (see details below). S1 stimuli, denoted as "S", occurred in different experimental conditions with two different ambiguity levels with the following coding: S_A = ambiguous lattice; S_U = unambiguous lattice variant. The stimulus S2 from the preceding pair and the upcoming S2 from the current pair had always the same ambiguity level within an experimental condition. We will label these preceding and upcoming S2 stimuli as the temporal context "C" of S1. The

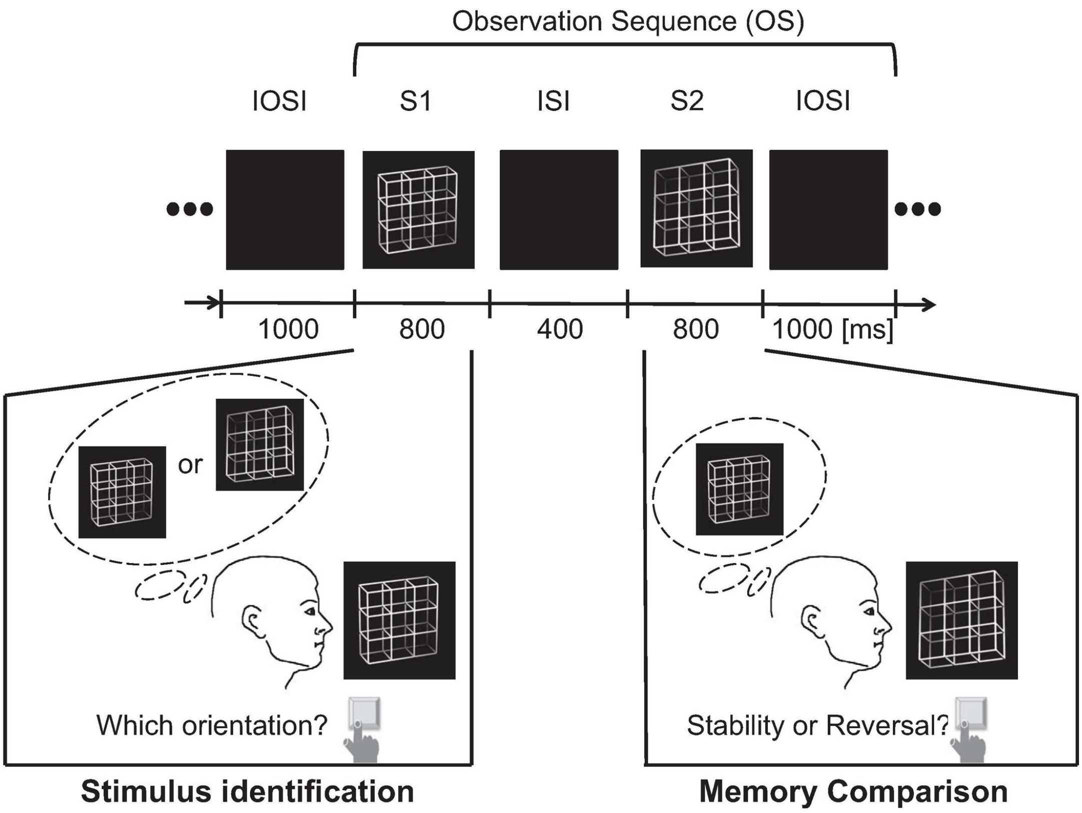

Fig 2. Paradigm of Experiment 1. Stimuli were presented in pairs one after the other and formed one Observation Sequence (OS). Each stimulus was presented for 800 ms. Stimulus 1 (S1) and Stimulus 2 (S2) were presented in succession and temporally separated by an inter-stimulus interval with a dark screen for 400 ms. Presentation of a dark screen for 1000 ms separated subsequent OS from each other. The experimental paradigm consisted of two tasks: during the presentation of the lattice stimulus S1 participants indicated the perceived orientation of S1 (Task 1). During the subsequent presentation of the lattice S2, they compared their perceived S2 orientation with the previously perceived and memorized orientation of lattice S1 and indicated either percepts of identical or reversed orientation (Task 2). Notice that the Task 1 was only related to stimulus S1. Neither the information about the preceding and subsequent stimuli nor information about their ambiguity levels was necessary for the execution of this task.

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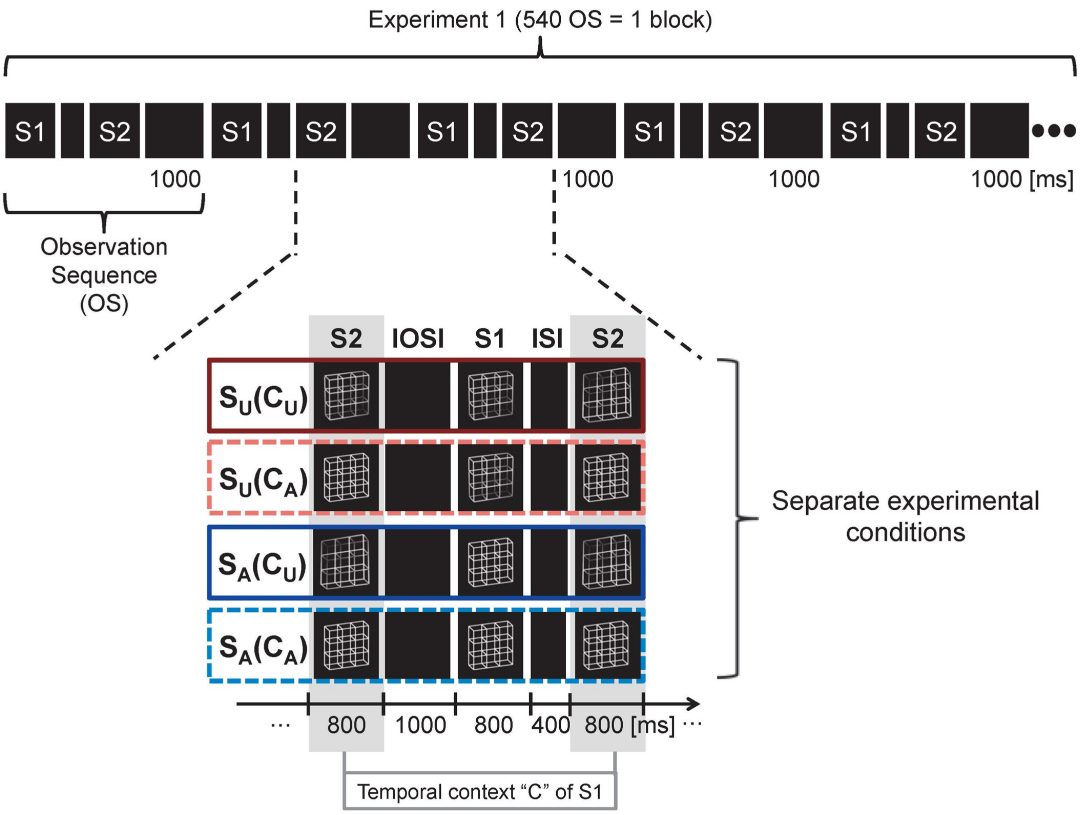

Fig 3. Conditions of Experiment 1. The current experiment consisted of four separate experimental conditions with a 2 x 2 design. $S_U(C_U)$: Both lattices S1 and temporal context stimuli (preceding and upcoming S2) were unambiguous; $S_U(C_A)$: S1 unambiguous and temporal context ambiguous; $S_A(C_U)$: S1 ambiguous and temporal context unambiguous; $S_A(C_A)$: both S1 and temporal context ambiguous. Ambiguity levels of S1 and the temporal context were kept constant and were thus highly predictable within conditions but differed between conditions. In Experiment 1, each experimental block consisted of 180 observation sequences (OS) with the same stimulus pairs. Each block was repeated 3 times across the experiment. (U = Unambiguous, A = Ambiguous).

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ambiguity level of the temporal context stimuli will be coded as follows: C_A = temporal context consists of ambiguous lattices; C_U = temporal context consists of unambiguous lattice variants.

The ERP and reaction times to a currently observed stimulus S1 will be described as a function of the ambiguity level of the currently seen stimulus S1 and of its temporal context with the following labels:

$S_A(C_A)$: response (i.e. ERPs and reaction times) to an ambiguous S_A (S1 from a stimulus pair) as a function of an ambiguous temporal context C_A (i.e. ambiguous S2 from the preceding stimulus pair and ambiguous upcoming S2 from the current pair)

$S_A(C_U)$: response to an ambiguous S_A as a function of an unambiguous temporal context C_U

$S_U(C_A)$: response to an unambiguous S_U as a function of an ambiguous temporal context C_A

$S_U(C_U)$: response to an unambiguous S_U as a function of an unambiguous temporal context C_U

In conditions with ambiguous lattice stimuli S_A, the perceived 3D orientation could reverse endogenously from one stimulus presentation to the next, while the stimulus itself stayed unchanged. The short presentation time of 800 ms prevented perceptual reversals during stimulus presentations. Therefore, perceptual reversals only took place from one presented stimulus to the next.

In conditions with unambiguous stimuli S_U, the two lattices variants corresponding to the two perceptual alternatives of the ambiguous lattice were presented with a 50% occurrence probability.

Each of the four experimental conditions was subdivided into three shorter experimental blocks that alternated in a pseudo-random order across the experiment. Experimental blocks lasted for about 9 minutes. It is important to note, that the blocked design with multiple repetitions of identical stimulus pairs introduced a sensory regularity within blocks and conditions and made upcoming ambiguity levels of stimuli highly predictable. For example, in the experimental condition $S_A(C_U)$, a currently presented S_A was always followed by a highly predictable unambiguous S2 and preceded by an unambiguous S2 from the previous stimulus pair, forming an unambiguous temporal context C_U of this S_A.

Participants learned the tasks with the $S_U(C_U)$ condition before the EEG experiment in training blocks of four minutes. The training blocks were repeated as many times as needed to reach an error rate of maximal 5% within one block. As a result, the number of repetitions varied slightly between participants.

Behavioural analysis

Lattice orientation. The Necker lattice stimuli used in this experiment can be described in terms of their ambiguity level, as well as in their perceived orientations. Ambiguous and unambiguous variants of the Necker lattice stimuli could be perceived with their front side facing towards the bottom (front-bottom = FB) or towards the top (front-top = FT). We report the ratio between the two perceived orientations of stimulus S1 separately for the four experimental conditions.

Reversal rates. We analysed the reversal rates from S2 of the preceding pair to the currently seen S1, i.e. those responses that indicate differently perceived orientation of S2 compared to S1. We separately calculated reversal rates towards percept FB ($RR_{FT=>FB}$) and reversal rates towards percept FT ($RR_{FB=>FT}$) as follows:

$$RR_{FT=>FB} = \frac{\#(S2 = FT, S1 = FB)}{\#(S2 = FT, S1 = FB) + \#(S2 = FB, S1 = FB)}$$

$$RR_{FB=>FT} = \frac{\#(S2 = FB, S1 = FT)}{\#(S2 = FB, S1 = FT) + \#(S2 = FT, S1 = FT)}$$

Wilcoxon signed-rank tests were used to test for difference of reversal rates between the different directions ($RR_{FT=>FB}$ and $RR_{FB=>FT}$) of reversals. This was done separately for each experimental condition ($S_A(C_A)$, $S_A(C_U)$, $S_U(C_A)$, $S_U(C_U)$). Furthermore, Wilcoxon signed-rank tests were used to compare differences of reversal rates between experimental conditions.

Effects of sensory quality within the temporal context

Reaction time. Reaction times from Task 1 (indicating perceived 3D orientation of lattice S1) were measured from the onset of lattice S1 to the participant's response. Responses were regarded as physiologically plausible if their earliest occurrence was 150 ms after stimulus onset. Reaction times were valid until the end of the inter-stimulus interval, i.e. 1200 ms after stimulus onset.

Electrophysiological recordings. *EEG recordings and pre-processing*. EEG was recorded with 32 active silver/silver chloride electrodes (Brain Products GmbH, 82205 Gilching, Germany) according to the extended 10–20 system [36]. Impedance was kept below 10 kΩ across all electrodes. EEG data were digitized with a sampling rate of 500 Hz, offline digitally filtered with a low-pass at 25 Hz and re-referenced to linked-ears. Data analysis was executed in Igor Pro 6.3 (WaveMetrics, Inc. 10200 SW Nimbus, G-7 Portland, OR 97223, USA).

Blinks and eye movements were detected and trials were excluded from analysis when reaching an artefact threshold of ±100 μV. Amplitudes were measured relative to the baseline, which was defined as the average from 60 ms before stimulus onset to 40 ms after. This baseline was determined following our lab's previous studies [26,27,31]. The present analysis focused on ERPs evoked by stimulus S1. EEG data from S1 were sorted with respect to the ambiguity levels of the S1 stimuli as well as the ambiguity level of the temporal context stimuli S2. The data were averaged separately for each participant and for each EEG electrode using the onset of S1 as time reference.

ERP analysis. Based on results from previous studies, we focused our analysis on two positive ERP components, a P200 with a latency of about 200 ms and fronto-central scalp distribution, and a P400 about 200 ms later with a centro-parietal scalp distribution from the so-called "ERP Uncertainty Effects" [26,27,31]. We selected electrode Cz as the spatial region of interest (ROI). Corresponding temporal ROIs ranged from 100 to 300 ms, covering the latency of the P200 ERP component and from 300 to 600 ms, covering the latency of the P400. We identified the individual peak amplitudes in the temporal and spatial ROIs and measured the average voltage in a ±30 ms time window around the individual peak [37].

We tested for the assumption of normality using the Shapiro-Wilk test. Significant departures from normality were found for the P200 in condition $S_A(C_A)$ ($W(13) = 0.81$, $p = 0.008$) and for the P400 in condition $S_U(C_A)$ ($W(13) = 0.84$, $p = 0.02$). Therefore, we based our statistical analysis of the ERP components on the non-parametric Wilcoxon signed rank test. The Wilcoxon tests were conducted for the P200 and the P400 amplitudes with a predefined alpha of 0.05.

Statistical analysis of reaction time and ERP data. The median reaction times and the P200 and P400 data were sorted with respect to the ambiguity levels of S1 and to the ambiguity level of its temporal context.

We tested for the influence of sensory quality within the temporal context on those variables (reaction time, P200, P400) in the case of an ambiguous current stimulus S1 (main effect 1), by comparing responses to condition $S_A(C_A)$ with responses to condition $S_A(C_U)$. Similarly, we tested this in the case of an unambiguous current stimulus S1 (main effect 2), by comparing condition $S_U(C_A)$ with condition $S_U(C_U)$. To test for possible differences in effects of sensory quality within the temporal context between ambiguous (S_A) and unambiguous (S_U) currently observed stimuli, we calculated the individual differences between conditions $S_A(C_U)$ minus $S_A(C_A)$ and between conditions $S_U(C_U)$ minus $S_U(C_A)$ and compared them.

It is important to note that we analysed the amplitudes of P200 and P400 ERP components evoked by lattice stimulus S1. The ERP amplitudes evoked by one and the same stimulus S1, as well as the reaction times of the task, was compared between the two conditions. In one of the conditions, the temporal context stimuli were ambiguous and in the other, the temporal context stimuli were unambiguous.

All Wilcoxon tests reported until now (reversal rates, reaction times, ERP data) were corrected for multiple testing according to the Holm procedure [38]. The effect size $r_{effect\ size}$ (r_{es}) was calculated by dividing the Z-score by the square root of the total number of observations [39].

Correlation between EEG data, reaction time data, and reversal rates

We calculated Pearson correlation coefficients $r_{Pearson}$ between the EEG data (P200 and P400 amplitudes), the reaction time data, and the reversal rates. We calculated these correlations on non-normalized and on normalized values. Normalization was done to account for individual differences regarding EEG data (anatomical differences) but also for individual response strategies, which could possibly influence reversal rates and reaction times. Normalization was accomplished within participants by dividing the individual value (e.g. participant 1, P200 peak amplitude, condition $S_A(C_A)$) by the sum of all experimental conditions (e.g. participant 1, P200 peak amplitude of $S_A(C_A)$+ $S_A(C_U)$+ $S_U(C_A)$+ $S_U(C_U)$). We did not correct the resulting p-values of this exploratory analysis for multiple testing.

Results from Experiment 1

In the present study, we focused on the P200 and P400 components of the ERP Uncertainty Effects [26,27,31] to test whether processing of a currently observed stimulus is affected by the ambiguity levels (ambiguous vs. unambiguous) of stimuli in its temporal context "C" (immediately preceding and upcoming stimuli) and how this is done.

Behavioural analysis

Trial numbers. In Task 1 related to stimulus S1, participants were instructed to indicate the orientation of the currently perceived Necker lattice stimulus. When presented with the currently seen unambiguous stimuli (conditions $S_U(C_U)$ and $S_U(C_A)$), participants, on average, responded correctly more than 90% of the time (96.5% ±0.04 SD and 90.9% ±0.12 SD, respectively). When presented with currently seen ambiguous stimuli (conditions $S_A(C_U)$ and $S_A(C_A)$), only one stimulus variant was presented so correctness of the response could not be determined.

We restricted the time window for valid responses for all experimental conditions from 150 to 1200 ms after stimulus onset. Participants reacted to this time window almost perfectly and we only had to exclude 0.018% of all trials (0.04% SD) per participant and condition due to invalid response times. Invalid trials are defined as trials containing incorrect responses, responses outside of the predefined time-window and trials containing EEG artefacts. All other trials are defined as valid trials. The average number of valid trials can be found in Table 1 (middle column) and the average number of all stimulus presentations (including EEG artefacts, incorrect responses and responses outside of the predefined time-window) can be found in the right column of Table 1.

Lattice orientation. For the unambiguous stimuli S1 (= S_U), the ratio of perceived orientations (front-bottom (FB) vs. front-top (FT) view) was averaged across participants. In condition $S_U(C_U)$, the ratio was 193:210 and in the condition $S_U(C_A)$, the ratio was 176:182. The two

Table 1. Number of trials of Experiment 1.

	Average number of valid trials (±SD)	Average number of all stimulus presentations (±SD)
$S_U(C_U)$	404 (±71)	537 (±12)
$S_U(C_A)$	358 (±75)	539 (±9)
$S_A(C_U)$	390 (±99)	520 (±53)
$S_A(C_A)$	341 (±100)	492 (±39)

Table 1 displays the average number of valid trials (±SD) across participants in the middle column and the average number of all stimulus presentations (±SD) in the right column, separately for the experimental conditions (rows: U = Unambiguous, A = Ambiguous).

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stimulus variants were presented with equal frequency by the stimulus program. The deviations of the perceived lattice orientation from exactly equal presentation frequencies are due to some trials being categorised as invalid trials (incorrect responses, responses outside of the predefined time-window, trials containing EEG artefacts). The ambiguous Necker lattices can be perceived in two different orientations. It is known from the literature (e.g. [40]) that observers show a perceptual bias in favour of the front-bottom view (which is a from-above perspective). This a priori bias can also be seen in the results of the current study, in conditions where an ambiguous Necker lattice is the stimulus S1 (S_A). For the condition $S_A(C_U)$, a front-bottom to front-top ratio of 247:142 was observed and for the condition $S_A(C_A)$, the front-bottom to front-top ratio was 233:108. The ratios reported are averages across participants.

Reversal rates. Numbers of perceptual reversals from S2 of the preceding pair to the currently seen S1 are listed in Fig 4C separately for the four different conditions. Comparing the different directions of reversal (FB = >FT vs. FT = >FB) within conditions, we only found significantly more reversals from FB = >FT compared to FT = >FB in condition $S_U(C_A)$ (Z = -2.41, r_{es} = -0.47, p = 0.03).

For ambiguous S1 stimuli (S_A) we did not find differences between the directions of reversals. When comparing reversal rates between conditions $S_A(C_A)$ and $S_A(C_U)$, we calculated cumulative reversal rates across reversal directions and found significant differences between the conditions (Z = -3.18, r_{es} = -0.62, p = 2e-07). We found no significant difference of reversal rates between conditions $S_U(C_A)$ and $S_U(C_U)$, which were separately analysed for both reversal directions.

We do not see a consistent pattern in the reversal rate results and therefore, FB and FT percepts will not be separately analysed from now on. The EEG and the reaction time data will not be separated depending on their perceptual reversals or stability from a preceding S2 to the currently seen S1. Correlation coefficients between reversal rates, reaction time data and ERP data will be provided after presentation of the main results.

Effects of sensory quality within the temporal context

In this results section, we will present the analysis of the influence of sensory quality within the temporal context, i.e. ambiguity level of preceding and subsequent S2 stimuli, on a currently seen S1 stimulus. The temporal context was either ambiguous (= C_A) or unambiguous (= C_U), see methods section for more detail. Effects of sensory quality within the temporal context were analysed separately for ambiguous S1 stimuli (= S_A) and for unambiguous S1 stimuli (= S_U). Further, the interactions between effects of sensory quality within the temporal context of S_A and S_U conditions were tested. This procedure is adopted for both the reaction time and the ERP data.

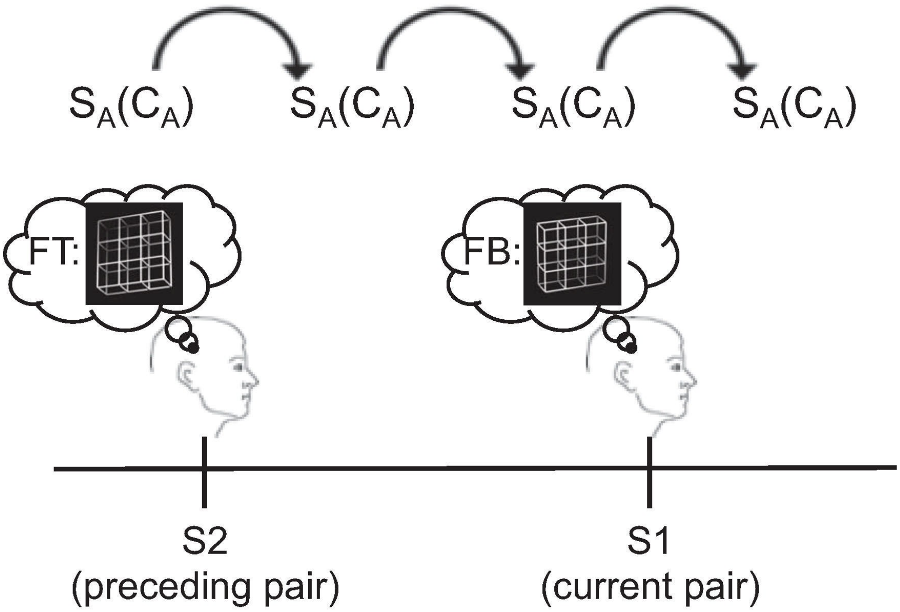
Note that all main effects reported hereinafter represent differences in processing of one and the same stimulus information but varying stimulus information in the temporal contexts. We want to particularly emphasize that the information about the temporal context was completely irrelevant for the execution of Task 1 related to S1.

Reaction times. Reaction times of Task 1 related to an ambiguous stimulus S_A were longer if the temporal context was unambiguous compared to an ambiguous temporal context ($S_A(C_U)$ vs. $S_A(C_A)$: Z = -3.11, r_{es} = -0.61, p = 0.00024). This reaction time effect can be seen in the scatter plots in Fig 5A (12 out of 13 data points are above the diagonal).

We found the opposite effect if the observed stimulus was unambiguous. Reaction times of Task 1 related to an unambiguous stimulus S_U were shorter if the temporal context was unambiguous compared to an ambiguous temporal context ($S_U(C_U)$ vs. $S_U(C_A)$: Z = -3.18, r_{es} = -0.62, p = 0.00012). This effect can be seen in the scatter plots in Fig 5B (all data points are below the diagonal). Median values and interquartile ranges of reaction times for all experimental conditions can be found in Fig 5C.

(a)

(b)



(c)

	Reversal rate towards FB	Reversal rate towards FT
$S_A(C_A)$	0.09 (±0.09)	0.1 (±0.09)
$S_A(C_U)$	0.58 (±0.12)	0.61 (±0.13)
$S_U(C_A)$	0.39 (±0.18)	0.63 (±0.22)
$S_U(C_U)$	0.52 (±0.06)	0.51 (±0.09)

Fig 4. Reversal rate Necker lattices. We calculated the reversal rate towards front-bottom (FB) and the reversal rate towards front-top (FT) views of the Necker lattice from the preceding S2 of the previous pair towards the currently seen S1. A schematic overview of condition $S_A(C_A)$ can be seen in a) and an example with stimuli in b). In c) the average (±SD) values are displayed for both view orientations and for each condition.

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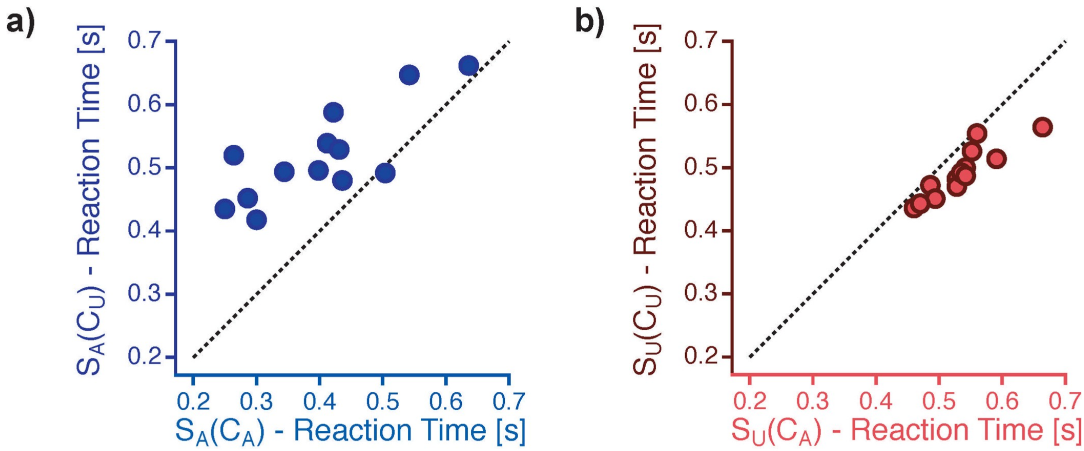
The differences in reaction time context effects is statistically indicated by an interaction: Comparing the reaction time differences ($S_A(C_A)$–$S_A(C_U)$) with ($S_U(C_A)$–$S_U(C_U)$) reveals a significant effect (Z = -3.18, r_{es} = -0.62, p = 0.00012).

ERP data

Fig 6A displays the ERP traces at electrode Cz evoked by an ambiguous currently observed stimulus, separately for condition $S_A(C_A)$, in a block in which the temporal context was ambiguous (light blue dotted trace) and for condition $S_A(C_U)$, in a block in which the temporal



c)

Condition	Median	Interquartile Range
$S_A(C_A)$	0.41	0.3-0.44
$S_A(C_U)$	0.5	0.48-0.54
$S_U(C_A)$	0.54	0.49-0.55
$S_U(C_U)$	0.49	0.47-0.51

Fig 5. Reaction time data for task 1. Blue colours indicate reaction times to ambiguous stimuli S_A (a) and red colours to unambiguous stimuli S_U (b). Reaction times show opposite effects of stimulus ambiguity within the temporal context for ambiguous compared to unambiguous currently observed stimuli: reaction times were generally shorter when the stimuli S2 from the temporal context were of the same ambiguity level as the currently perceived stimulus compared to those conditions with differing ambiguity levels of temporal context stimuli S2 compared to the perceived S1. (c) List of median reaction time [s] values with the interquartile ranges [s], separately for each experimental condition.

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context was unambiguous (dark blue traces). The amplitudes of both the P200 and the P400 were significantly larger in the case of an unambiguous temporal context compared to an ambiguous temporal context ($S_A(C_U)$ vs. $S_A(C_A)$: P200: $Z = -2.3$, $r_{es} = -0.46$, $p = 0.02$; P400: $Z = -3.18$, $r_{es} = -0.62$, $p = 0.0007$). Fig 6A shows this effect in the grand mean ERP traces (electrode Cz) and Fig 6B left shows the individual data in scatter plots. In the left scatter plot, each point represents the P200 amplitudes evoked by the ambiguous currently observed stimulus S_A from one individual participant when the temporal context is also ambiguous ($S_A(C_A)$: abscissa), versus an unambiguous temporal context ($S_A(C_U)$: ordinate). The data points for the most participants (only three exceptions) are located above the diagonal, confirming the above-described temporal context effect on the P200 amplitude. The corresponding context effect for the P400 amplitude moves in the same direction and is even larger than the P200. This is visible in all participants, as indicated in the corresponding scatter plot (Fig 6B right).

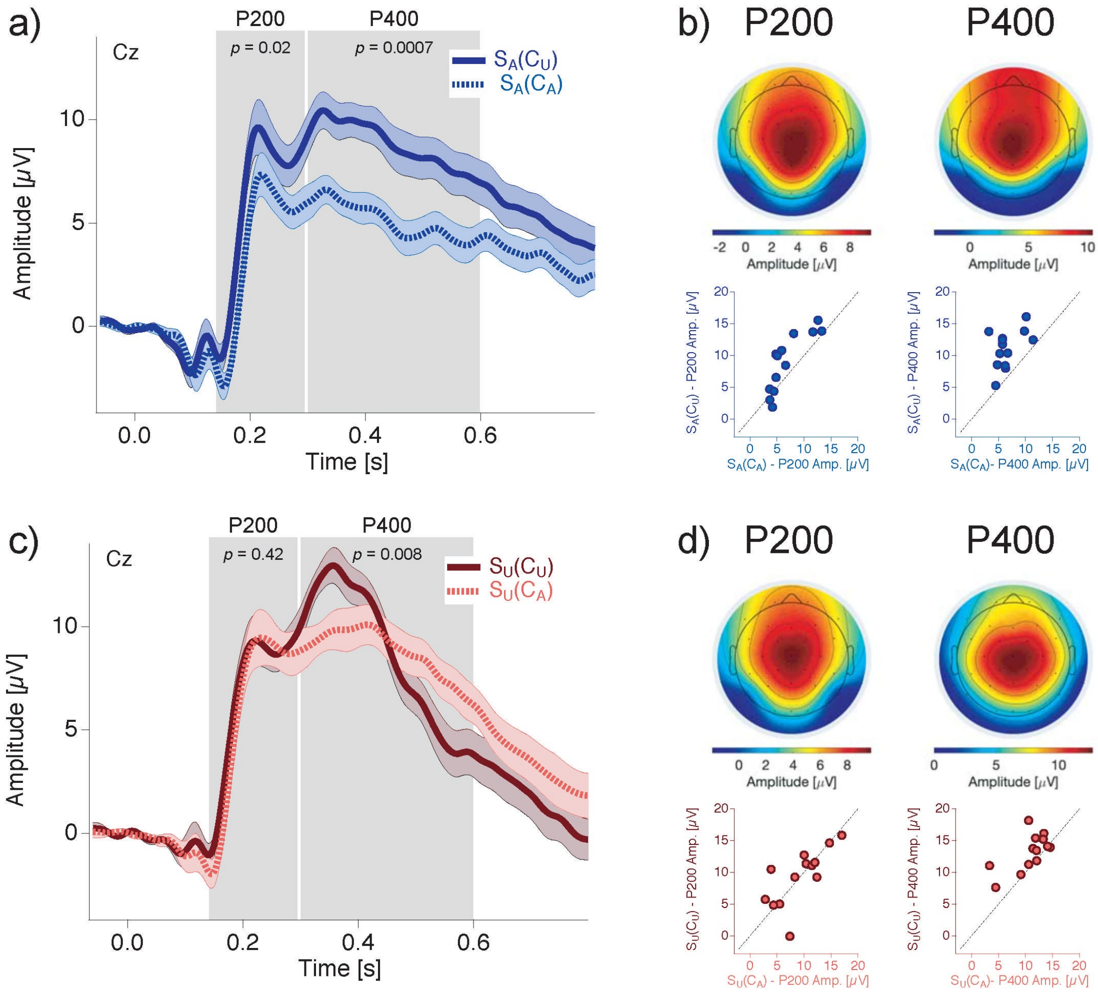

Fig 6. ERP effects of sensory quality within the temporal context. (a) ERP traces at electrode Cz during perception of an ambiguous lattice S_A, when the stimuli in the temporal context (i.e. S2 from the preceding pair and the predicted S2 from the current pair) were unambiguous ("$S_A(C_U)$", dark blue continuous trace) and when the stimuli from the temporal context were ambiguous ("$S_A(C_A)$", light blue dashed trace). Notice that the same ambiguous current S_A lattice stimulus evoked larger P200 and P400 amplitudes with an unambiguous temporal context compared to an ambiguous temporal context. (b) Voltage maps (top) showing the spatial distribution of P200 (left, t = 214 ms) and P400 (right, t = 326 ms) and scatter plots (bottom) showing individual mean amplitude data for the P200 (left) and the P400 (right), which correspond to (a). Notice that for almost all participants the P200 and P400 ERP components evoked by S_A show larger amplitudes when the temporal context stimuli were unambiguous (data points are above the diagonal). (c) ERP traces during perception of an unambiguous lattice S_U, when the temporal context stimuli were unambiguous ("$S_U(C_U)$", dark red continuous trace) and when the temporal context stimuli were ambiguous ("$S_U(C_A)$", light red dashed trace). Notice that the amplitude of the P400 evoked by the one and the same unambiguous present S_U lattice stimulus varied as a function of the ambiguity level within the temporal context. No such effect is visible for the P200. (d) Same logic as in (c) but with an unambiguous present stimulus S_U (data related to c; Voltage maps: P200—t = 222 ms, P400—t = 358 ms). U = unambiguous, A = Ambiguous, S = stimulus S1, C = temporal context (preceding and subsequent S2).

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Fig 6C displays the ERP traces at electrode Cz for an unambiguous current lattice S_U, separating the ambiguous temporal context C_A (light red dotted trace) from the unambiguous temporal context C_U (dark red traces).

In contrast with the findings from an ambiguous current stimulus S_A, the P200 did not show an effect of stimulus ambiguity within the temporal context when the current stimulus was unambiguous S_U ($S_U(C_U)$ vs. $S_U(C_A)$: P200: $Z = -0.25$, $r_{es} = -0.05$, $p = 0.42$). The corresponding scatter plot (Fig 6D left) shows that six out of 13 points are above the diagonal but seven points are below.

Consistent with the findings from an ambiguous current stimulus S_A, the amplitude of the P400 evoked by an unambiguous current stimulus S_U was significantly larger when the temporal context was unambiguous than when it was ambiguous ($S_U(C_U)$ vs. $S_U(C_A)$: P400: $Z = -2.76$, $r_{es} = -0.54$, $p = 0.0085$). This grand mean effect (Fig 6C) can be seen in more detail in the scatter plot in Fig 6D right, where 11 out of 13 points are located above the diagonal, confirming the above-described amplitude difference between conditions.

The P200 results indicate a significant interaction between effects of stimulus ambiguity within the temporal context of an ambiguous stimulus S_A and an unambiguous stimulus S_U ($S_A(C_U)$-$S_A(C_A)$ vs. $S_U(C_U)$-$S_U(C_A)$: P200: $Z = -2.41$, $r_{es} = -0.47$, $p = 0.02$). The P400 was similarly modulated by the stimulus ambiguity within the temporal context and thus no such interaction was found for the P400 ($Z = -1.71$, $r_{es} = -0.34$, $p = 0.09$).

Correlation between EEG data, reaction time data, and reversal rates

We calculated correlations between the EEG data (P200 and P400 amplitudes) and the median reaction times (see Table A in S1 File), between the EEG data and the reversal rates (see Table B in S1 File), as well as between the median reaction times and the reversal rates (see Table C in S1 File). These correlations were calculated separately for each experimental condition. This exploratory post-hoc analysis was not systematically corrected for multiple testing. However, since we calculated 20 independent correlation coefficients in total (not counting the additional tests with the non-normalized data), we pre-defined an alpha threshold of 0.01.

There are no significant results when correlating the EEG data (P200, P400) with the median reaction time, the EEG data (P200, P400) with the reversal rates, and the reversal rates with the reaction time.

Summary and discussion of Experiment 1

We compared the amplitudes of two ERP components evoked by the same current stimulus and the reaction times of a stimulus-related task in a condition with ambiguous stimuli in the temporal context C_A (i.e. an ambiguous preceding and an ambiguous subsequent stimulus) with a condition with unambiguous stimuli in the temporal context C_U (i.e. an unambiguous preceding and an unambiguous subsequent stimulus). Each condition consisted of several experimental blocks. Within the blocks, the condition-specific ambiguity levels of the presented stimuli were kept constant, which made the stimulus sequence highly predictable (see Fig 3).

ERP results

We found that the P400, evoked by the same stimulus, was generally larger, with an unambiguous temporal context compared to an ambiguous temporal context. This effect was observed irrespective of the ambiguity level of the currently observed stimulus.

We found a similar effect for the P200, when the currently observed stimulus was ambiguous. In contrast, we found no such P200-effects when the currently observed stimulus was unambiguous.

Reaction time results

The ambiguity level of the temporal context stimuli also affected reaction times related to the execution of Task 1. More specifically, reaction times from Task 1 related to the same unambiguous stimulus S_U were longer, if the temporal context contained ambiguous compared to unambiguous stimuli. This finding is striking, because Task 1 was exclusively related to the currently observed stimulus, whereas the ambiguity levels of the stimuli in the temporal context were irrelevant for its execution.

We expected a similar reaction time effect of the temporal context when an ambiguous stimulus S_A was observed. However, we found an opposite effect with shorter (rather than longer) Task 1-related reaction times with ambiguous context stimuli compared to than unambiguous temporal context stimuli.

The role of perceptual reversals for the reported ERP and reaction time effects

Our experimental paradigm contained conditions where the level of ambiguity changed between S1 and S2 stimuli ($S_A(C_U)$ and $S_U(C_A)$) and conditions where the ambiguity level stayed the same between stimulus presentations ($S_A(C_A)$ and $S_U(C_U)$). Our analysis so far suggests that the ERP amplitude and the reaction time effects reflect differences in the ambiguity level of the stimuli in the temporal context (S2) of a currently perceived stimulus (S1).

However, another aspect that changed (or stayed stable) between stimulus presentations is the perceived 3D orientation of the presented lattice stimuli. In the case of the unambiguous lattice stimuli, we presented the stimulus variants with depth cues corresponding to the two most probable perceptual interpretations of the ambiguous lattice variant (see Fig 1) with a predefined rate (of 0.5) of 3D orientation reversals (by the stimulation program) from one stimulus to the next. The perceptual interpretations of the unambiguous stimulus variants, as indicated by the participants, almost fully corresponded to what was presented on the screen (see section "Lattice orientation" in the behavioural results section).

During observation of the ambiguous Necker lattice, the perceptual interpretation is endogenously driven (see [41] for more information about perceptual endogenous reversals during observation of ambiguous figures). As a result, the rate of perceptual reversals could not be controlled by the computer program when the condition included ambiguous lattices ($S_A(C_A)$, $S_A(C_U)$, $S_U(C_A)$). Consequently, reversal rates between stimuli could vary between the four experimental conditions and such variations could also have contributed to the ERP amplitude and reaction time effects reported above.

We compared reversal rates between the experimental conditions and found significantly reduced reversal rates in condition $S_A(C_A)$, i.e. when an ambiguous stimulus S1 was combined with an ambiguous temporal context, compared to the other conditions. In order to study how much the reversal rates influenced the ERP amplitude and reaction time modulations, we calculated post-hoc correlation coefficients between reversal rates, amplitude effects and reaction times, respectively, but found no significant correlation. We thus conclude that differences in reversal rates cannot explain the observed amplitude and the reaction time effects.

P200 vs. P400 ERP components

The ambiguity level of the stimuli in the temporal context of a currently observed stimulus affects the P400 amplitude, regardless of the currently observed stimulus being ambiguous or unambiguous. The pattern of results is slightly different for the P200 ERP component, where we only see effects of sensory quality within the temporal context if the currently observed stimulus is ambiguous. Those effects cannot be observed when the currently presented stimulus is unambiguous. Potential explanations for this observation will be outlined in the General Discussion.

Are the effects of sensory quality within the temporal context low-level or high-level/cognitive effects?

A possible explanation for the ERP effects described above could be that unambiguous lattice stimuli are processed differently. The unambiguous lattice stimuli have brighter and darker edges that are cues for the third dimension and result in different local retinotopic adaptation during their observation. The ambiguous lattice stimuli have exclusively isoluminant edges with an intermediate brightness and so, homogeneous adaptation across the retinotopic visual maps could be expected in this case. Thus, a visual stimulus presented to a perceptual system in a differently adapted state may thus be differently processed. Therefore, the ERP components evoked by this stimulus may differ in amplitude as a function of the difference in adaptation levels. Temporal context stimuli differing in their degree of ambiguity may drive the perceptual system into differently adapted states and thus account for the previously reported ERP effects. This low-level interpretation of the results is related to the findings from Cicchini et al [15], where the authors found low-level influences of the immediate past on perception in an uncertain but not in a certain situation.

On the other hand, several results indicate an involvement of high-level cognitive processes. The late latencies of the affected ERP components, 200 ms and 400 ms after stimulus onset, the reaction time modulations, as well as the lack of correlations between ERP data, reversal rates, and reaction times all indicate this.

We suggest that the effects of the ERP amplitude and reaction time are related to differences in the ambiguity level of the temporal context. Several studies have shown that the perceptual system continuously evaluates the sensory regularities from the past to make predictions about the future [e.g. 23,24]. Therefore, we postulate that the previously presented effects may be related to such evaluation and prediction processes.

In a next experimental step, we aimed to estimate at which level a potential evaluation of regularities within the temporal context takes place. It could be that the direct perceptual experience of regularities in the immediate perceptual past is a necessary condition for such predictions about the future. Alternatively, this effect could be located at such a high level that informing the observer about the identity of a future stimulus with an abstract symbol, making the future stimuli 100% predictable, could be sufficient.

The previously found effects should disappear when the information about the perceptual future is only provided in an abstract symbol, if they reflect the predictability of the perceptual future based on the direct perceptual experience of regularities in the temporal context. However, if the abstract information is sufficient, the ERP effects should still be observable.

In Experiment 2, we were unable to measure all four conditions from Experiment 1 due to limited time. Therefore, we focused on the two conditions with an ambiguous current stimulus S1 and ambiguous vs. unambiguous temporal context stimuli S2. The reason behind this being that Experiment 1 revealed amplitude effects for both ERP components, the P200 and the P400. We were interested in how the specific experimental manipulation of Experiment 2 may affect the amplitude effects of both ERP components.

Experiment 2

In Experiment 2, we investigated whether the same results of Experiment 1 can be found when information to predict the perceptual future is provided in an abstract symbol, and not based on the direct perceptual experience of sensory regularities in the past.

Therefore, we changed the paradigm from Experiment 1 in the following way:

(I) Before presenting the stimulus pairs of a specific condition ($S_A(C_A)$ or $S_A(C_U)$), we displayed a symbolic representation of the experimental condition that followed. We did not present the actual stimuli that were shown during the experimental condition to avoid low-level effects like adaptation. Instead, two symbols were presented on a screen with one symbol being on the left and the other being on the right. A symbol could be either a question mark, coding for an ambiguous stimulus, or an exclamation mark, coding for an unambiguous stimulus. The position of the symbols on the screen coded for the two stimuli presented in one observation sequence. The left symbol coded for the first stimulus (S1) and the right symbol for the second stimulus (S2; see Fig 7).

(II) We shortened the experimental block durations dramatically from around 9 minutes to 9 seconds. Consequently, each experimental block consisted of only three observation sequences resulting in three repetitions of a specific stimulus pair S1S2 (see Fig 8). This shortening of block duration allowed us to strongly increase the number of blocks. Note that in Experiment 2, the term experimental "block" refers to a presentation of an experimental condition lasting 9 seconds. This includes three repetitions of an observation sequence. Such a short experimental block is immediately followed by the next 9 seconds presentation of an experimental condition (block). The conceptual meaning of an experimental block is identical between Experiment 1 and 2. Only the duration and therefore, the number of repetitions of observation sequences differ between blocks of Experiment 1 and 2.

(III) We aimed to extinguish short-term memory effects from one block of Experiment 2 to the next one by a 'nesting technique'. The blocks of Experiment 2 were interlaced with blocks from a second experiment lasting for about 10 seconds. This second experiment used completely different stimuli and was not related to the lattice stimuli. Therefore, each block of Experiment 2 was followed by a block from this additional experiment with different stimuli.

(IV) Due to limitations in the total experimental time, we only varied the ambiguity levels of the temporal context stimuli (S2) but not of the currently observed stimuli (S1). Meaning

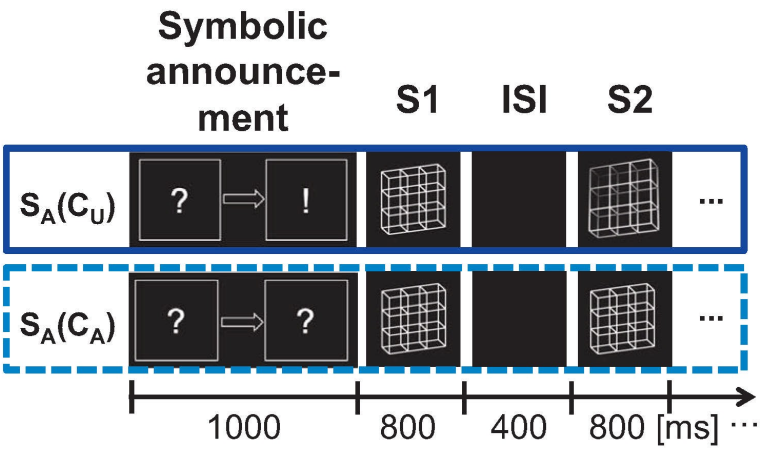

Fig 7. The symbolic announcement in Experiment 2. Ambiguous stimuli are announced by question marks, while unambiguous stimuli are announced by exclamation marks. Before each block of condition $S_A(C_U)$ a picture was presented with a question mark symbol (left) pointed towards an exclamation mark symbol (right). Before each block of condition $S_A(C_A)$ a picture with two question marks was presented.

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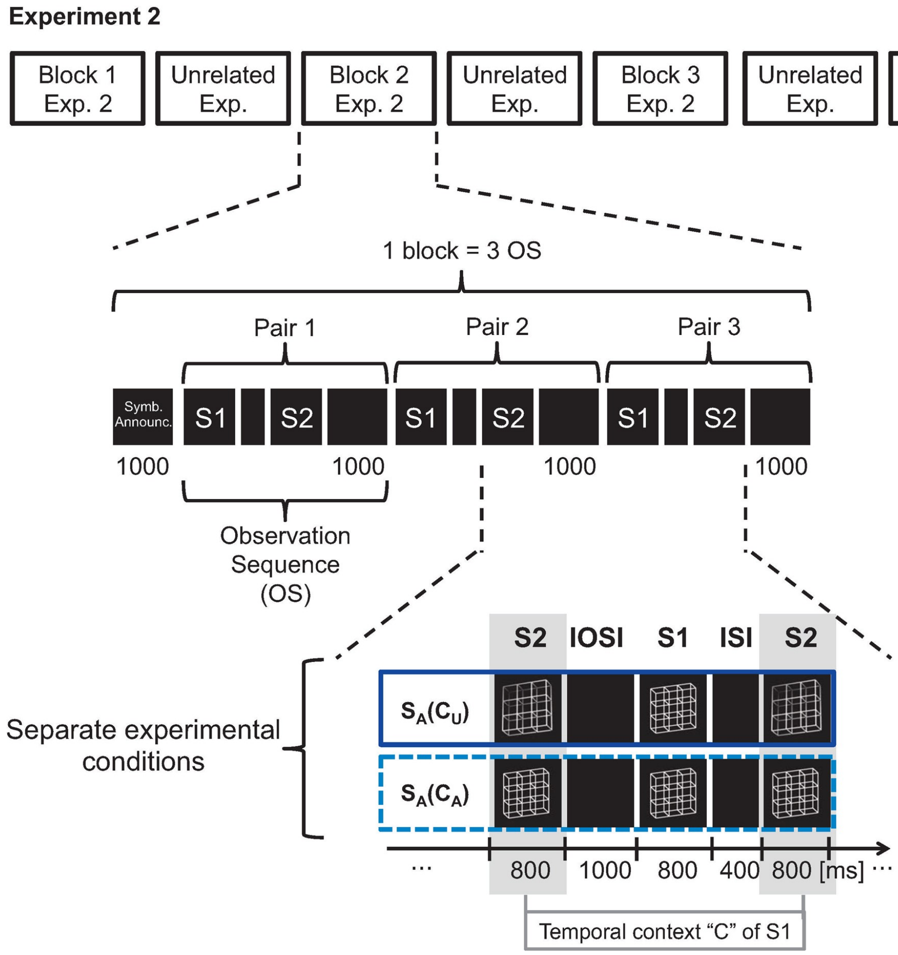

Fig 8. Conditions of Experiment 2. Experiment 2 consisted of two separate experimental conditions (bottom part). Within experimental conditions, ambiguity levels of currently observed S1 stimuli and ambiguity levels of their temporal context (preceding and subsequent S2) were kept constant and were highly predictable within conditions. The ambiguity level of the temporal context differed between conditions. $S_A(C_U)$: current ambiguous stimulus S_A and unambiguous temporal context; $S_A(C_A)$: both S_A and temporal context ambiguous. One observation sequence (OS) consisted of an S1 stimulus (800 ms), an inter-stimulus interval (400 ms), a S2 stimulus (800 ms), and an inter-observation sequence interval (1000 ms). One experimental block consisted of a symbolic announcement and three repetitions of the observation sequence. Each block of Exp. 2 was followed by an experimental block from another unrelated experiment with completely different stimuli to increase the temporal distance between blocks of Exp. 2 and thus to minimize low-level memory effects (e.g. priming, adaptation, etc.) from one block to the other. (U = Unambiguous, A = Ambiguous).

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that in Experiment 2, only conditions $S_A(C_A)$ and $S_A(C_U)$ were presented. The sequence of blocks was pseudo-randomized.

The rationale behind these changes in the experimental design from Experiment 1 to Experiment 2 was the following:

The announcement (I) at the beginning of each experimental block contained only abstract symbolic information about the ambiguity levels of the upcoming series of three stimulus pairs. The stimuli themselves were not experienced during this announcement. Additionally, the announcement mostly avoided a surprise-P3b [42–44] ERP response to the very first stimulus (or stimulus pair) within one experimental block. The reduction of block length (II) allowed us to increase the number of experimental blocks for each condition from 3 (Exp. 1) to 120 (Exp. 2). This enabled separate analyses of the effects of sensory quality within the temporal context, reported in Exp. 1, for each of the three stimulus pairs within a block. The interlacing of the unrelated experimental blocks, resulting in an alternation of stimulus types between blocks (III), was intended to allow for the recovery of the perceptual system from possible lower-level conditioning effects (types of serial dependence or adaptation) or recency effects, potentially resulting from the repetitions of one and the same stimulus pair per block.

As a result of this experimental manipulation, the first pair of each experimental block should be unaffected by lower-level footprints from the immediate past. It can only be influenced by the symbolic announcement, assuming that the recovery period introduced by the interspersed unrelated experimental blocks was long enough. However, the second pair was preceded by one presentation of a stimulus pair and the third pair was preceded by two presentations of a stimulus pair. The influence of memory on the three separately analysed stimulus pairs allowed us to study the different effects of cognitive (pair 1) and sensory (pair 2 and pair 3) temporal context information on the processing of a currently observed stimulus. We were also able to study the different effects on related reaction times.

Material and methods—Experiment 2

Participants

Twenty-three participants (16 female) took part in Experiment 2. The median age was 24, with participants ranging from 19 to 31 years old. All participants had normal or corrected-to-normal visual acuity [33] and gave their written informed consent. The study was approved by the ethics committee of the University of Freiburg and in accordance with the ethical standards laid down in the Declaration of Helsinki [34]. We had to exclude two participants from the analysis due to low number of trials that survived the artefact rejection ($<$30 in at least one condition). Eighteen participants were right-handed, two participants were left-handed, and one participant was ambidextrous.

Procedure

Experiment 2 was very similar to Experiment 1 with three exceptions:

1. At the beginning of each experimental block, we announced the experimental condition ($S_A(C_A)$ or $S_A(C_U)$) that the block belonged to abstract symbols (see Fig 7)
2. Experiment 2 was restricted to conditions $S_A(C_A)$ and $S_A(C_U)$ (see Fig 8). As a result, only the ambiguity level of the stimuli S2 in the temporal context varied, whereas the currently perceived stimulus S1 in the analysis window stayed ambiguous.
3. In this Experiment 2 one experimental block consisted of the symbolic announcement and only three stimulus pairs. With this we decreased the block duration from 9 minutes (Exp. 1) to 9 seconds (Exp. 2) and concurrently increased the number of experimental blocks per condition from 3 (Exp. 1) to 120 (Exp. 2).
4. In this Experiment 2 it was important to extinguish short-term perceptual memory between experimental blocks as much as possible. Thus, we separated the blocks from Experiment 2 by blocks from a separate and unrelated experiment with completely different stimuli (smiley stimuli with different emotional expressions).

Before the start of the main experiment, participants learned the tasks in training blocks of three minutes. In the training blocks, we presented the paradigm with only unambiguous stimuli, which allowed us to distinguish between correct and false responses. The training blocks were repeated as many times as needed to reach a maximal error rate of 10% within one block. Thus, the number of repetitions varied slightly between participants.

Analyses

Like in Experiment 1, we analysed the ERPs evoked by stimulus S1 from a pair S1S2. In Experiment 2, this S1 stimulus was always ambiguous and is thus labelled accordingly as S_A (see Fig 8 for details). The EEG data from this stimulus S_A were sorted with respect to participant, to the ambiguity level of the temporal context stimuli S2, to the order of S_A in the experimental block (S_A-pair 1, S_A-pair 2, S_A-pair 3), and to electrode. The onset of S_A served as a time reference.

As in Experiment 1, we selected electrode Cz as the spatial region of interest (ROI) in Experiment 2. Corresponding temporal ROIs ranged from 100 to 300 ms, covering the latency of the P200 ERP component, and from 300 to 600 ms, covering the latency of the P400. We identified the individual peak amplitudes in the temporal and spatial ROIs and measured the average voltage in a ±30 ms time window around the peak [37].

We tested for the assumption of normality using the Shapiro-Wilk test. Significant departures from normality were found for the P200 in condition $S_A(C_U)$-pair 1 (W(21) = 0.9, $p = 0.04$) and for the P400 in condition $S_A(C_A)$-pair 1 (W(21) = 0.87, $p = 0.008$). Therefore, we based our statistical analysis on the non-parametric Wilcoxon signed rank test.

Reaction times were regarded as physiologically plausible if their earliest occurrence was at least 150 ms after stimulus onset. Reaction times were treated as valid until the end of the inter-stimulus interval, i.e. 1200 ms after stimulus onset. We calculated the median reaction times and conducted Wilcoxon signed-rank tests.

The Wilcoxon tests were conducted for the P200 and the P400 amplitudes and for the median reaction time data with a predefined alpha of 0.05. The resulting *p*-values were corrected for multiple testing with the Holm procedure [38]. The effect size r_{es} was calculated by dividing the *Z*-score by the square root of the total number of observations [39].

We tested for the influence of the ambiguity level of the temporal context (preceding and subsequent stimuli) on the amplitudes of the S_A-evoked P200 and P400 ERP components. This was done by comparing conditions $S_A(C_U)$ with $S_A(C_A)$. The related tests were calculated separately for the S_A-evoked ERPs and reaction times to the related task from pair one, pair two, and pair three within experimental blocks. This allowed us to investigate the influence of the accumulating perceptual memory, as well as the increasing evidence about stimulus regularity in the temporal context of S_A on the reaction times and ERP amplitudes.

Results from Experiment 2

In Experiment 2, we investigated whether abstract symbolic knowledge about the perceptual future, without sensory history, is sufficient to evoke the effects of sensory quality within the temporal context (P200 and P400) from Exp. 1, or whether the direct perceptual experience of stimulus regularity is necessary. We presented a symbolic announcement of the upcoming conditions $S_A(C_A)$ and $S_A(C_U)$ at the beginning of each block. Each block consisted of only three stimulus pairs and we analysed S_A-evoked ERPs from S_A–pair 1, S_A–pair 2, and S_A–pair 3 separately. If the ERP effects found in Experiment 1 are related to processes of predicting the immediate perceptual future, and if the abstract symbolic knowledge about the immediate perceptual future is sufficient to evoke these predictions, we should find effects of sensory quality within the temporal context in the ERPs and in reaction times already in the first stimulus of the first pair. If, however, direct perceptual experience of stimulus regularity is necessary for these effects, we should see earliest evidence for these effects with the first stimulus of the second pair and perhaps a slow build-up of the effect with the third stimulus pair.

Behavioural data

Trial numbers. The average number of valid trials can be found in Table 2. Based on the restriction of a valid response time window from 150 to 1200 ms after stimulus onset, we only had to exclude 0.0006% of all trials (0.003% SD) per participant and condition due to invalid response times. The remaining difference between the average number of all stimulus presentations (Table 2, right column) and the average number of valid trials (Table 2, middle column) between participants and conditions is due to EEG artefacts.

Reaction times. We found no significant effects of stimulus ambiguity within the temporal context on S_A-related reaction time in the first pair ($S_A(C_A)$–pair 1 vs. $S_A(C_U)$–pair 1: Z = -0.64, r_{es} = -0.095, p = 0.27, see Fig 9). Note that the temporal context of S_A from the first pair differs substantially from the temporal contexts of S_A in the second and third pair. S_A from the first pair was only preceded by a symbolic announcement about the current condition, i.e. the ambiguity levels of the upcoming stimuli. The S_A stimuli from the second and the third pair were preceded by lattice stimuli instead of abstract information.

We found significantly longer reaction times for an unambiguous temporal context compared to an ambiguous temporal context in the second ($S_A(C_A)$–pair 2 vs. $S_A(C_U)$–pair 2: Z = -3.91, r_{es} = -0.58, p = 2.38e-06) and the third stimulus pair ($S_A(C_A)$–pair 3 vs. $S_A(C_U)$–pair 3: Z = -3.95, r_{es} = -0.58, p = 2.86e-06). Note that the reaction times were related to an identification task of the currently seen stimulus S_A. The temporal context stimuli were completely irrelevant for the execution of this task.

ERP data

The amplitudes of the S_A-evoked P200 and P400 show no significant effects of stimulus ambiguity within the temporal context in the first pair ($S_A(C_A)$–pair 1 vs. $S_A(C_U)$–pair 1: P200: Z = -0.16, r_{es} = -0.02, p = 0.45; P400: Z = -1.16, r_{es} = -0.17, p = 0.42) or in the second pair ($S_A(C_A)$–pair 2 vs. $S_A(C_U)$–pair 2: P200: Z = -0.82, r_{es} = -0.12, p = 0.52; P400: Z = -0.19, r_{es} = -0.03, p = 0.68). Further, there was no significant effect of stimulus ambiguity within the temporal context for the S_A-evoked P200 in the third pair ($S_A(C_A)$–pair 3 vs. $S_A(C_U)$–pair 3: P200: Z = -1.62, r_{es} = -0.24, p = 0.25;). Interestingly, there was a significant effect of stimulus ambiguity within the temporal context for the S_A-evoked P400 amplitudes in the third pair ($S_A(C_A)$–pair 3 vs. $S_A(C_U)$–pair 3: P400: Z = -2.69, r_{es} = -0.4, p = 0.016).

Table 2. Number of trials of Experiment 2.

	Average number of valid trials (±SD)	Average number of all stimulus presentations (±SD)
$S_A(C_U)$–pair 1	83 (±17)	109 (±11)
$S_A(C_A)$–pair 1	83 (±17)	110 (±9)
$S_A(C_U)$–pair 2	82 (±19)	108 (±12)
$S_A(C_A)$–pair 2	84 (±20)	109 (±9)
$S_A(C_U)$–pair 3	81 (±19)	105 (±13)
$S_A(C_A)$–pair 3	81 (±20)	107 (±9)

Table 2 displays the average number of valid trials (±SD) in the middle column and the average number of all stimulus presentations (±SD) in the right column, both separately for the experimental conditions.
(U = Unambiguous, A = Ambiguous).

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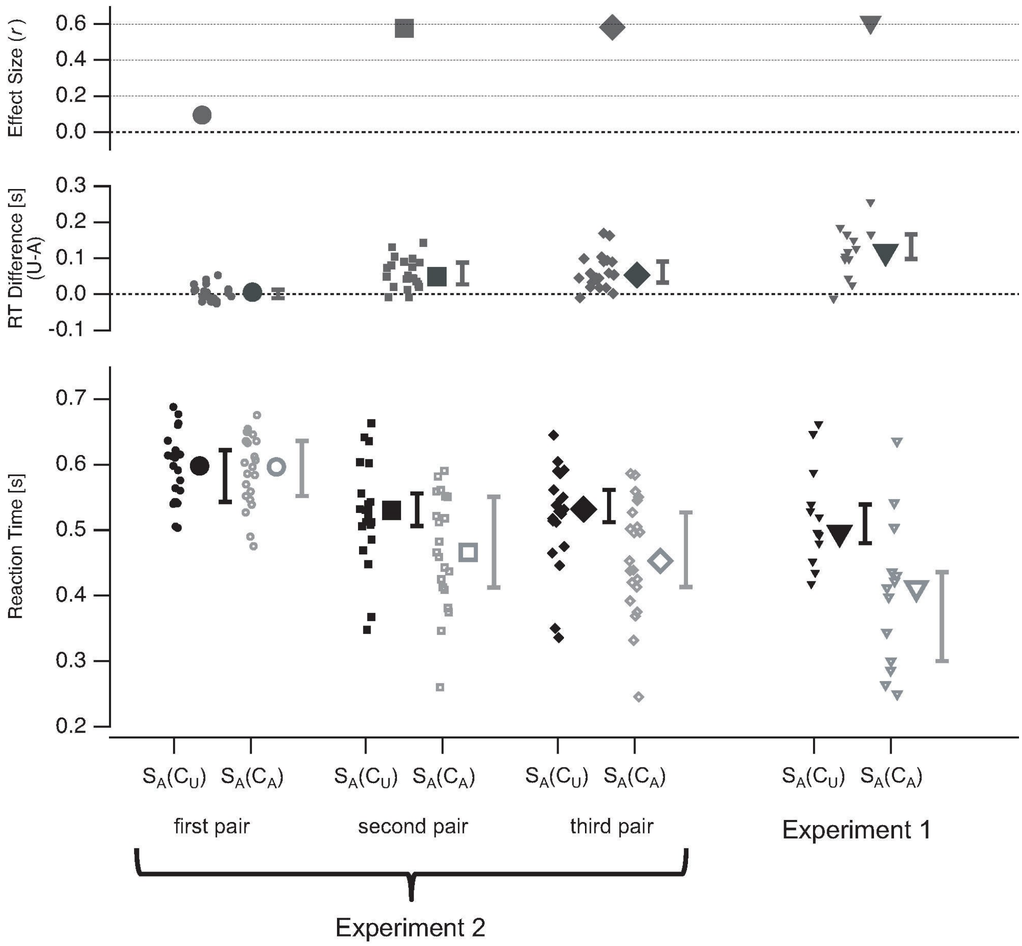

Fig 9. Reaction time results from Experiment 2. Bottom row depicts the median reaction times evoked by a currently observed stimulus separately for the two experimental conditions with unambiguous (black) and ambiguous (grey) stimuli in the temporal context of S_A. Reaction times are separately shown for the first (circles, first column), second (squares, second column), and third pair (diamond, third column). For comparison, the results from Exp. 1 (triangles) are plotted on the right (fourth column). The data from individual participants are represented with small icons, while the large icons represent the median reaction time data with interquartile ranges (whiskers). In the middle row the median reaction time differences (large icons ± interquartile ranges) between the two conditions (unambiguous temporal context minus ambiguous temporal context) are depicted together with data from the individual participants (small icons). The top row shows the sizes of the reaction time effects (r_{es}). U = Unambiguous, A = Ambiguous.

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Fig 10 displays the grand mean ERPs at electrode Cz for the three stimulus pairs separately. Fig 11 shows the summarized results for the three stimulus pairs from Exp. 2 together with the results from Exp. 1 for the P200 and Fig 12 for the P400.

Summary and discussion of Experiment 2

In Experiment 2, we presented an abstract symbolic announcement before each experimental block and only three stimulus pairs within experimental blocks. We separately analysed ERPs and reaction times from the first, second and third stimulus pair presentations within the blocks. This allowed the comparison between stimulus processing without an immediate perceptual history (first pair) and the slow build-up of a perceptual memory trace across the second and third stimulus pair. The aim of Experiment 2 was to study whether the ERP and reaction times effects of sensory quality within the temporal context are also present when only symbolic knowledge about upcoming temporal context regularities is available (first stimulus pair) and/or whether they build up over accumulating perceptual memory (second and third stimulus pair within experimental blocks). We found no such ERP effects for stimulus S_A from the first and second stimulus pair and only a P400 amplitude effect for stimulus S_A from the third stimulus pair.

Further, there was no reaction time effect for Task 1 of the first stimulus pair, but similarly strong reaction time effects in the second and the third pair as in Experiment 1.

The results from Experiment 2 indicate that providing only abstract symbolic information about the upcoming stimuli and their ambiguity levels is not sufficient to evoke effects of sensory quality within the temporal context as found in Experiment 1. These effects start to be visible only in the third stimulus pair, i.e. after two exposures to the sensory information and only for the P400 ERP component. Therefore, it can be concluded that the direct sensory experience of regularities is a necessary precondition to evoke the effects of sensory quality within the temporal context found in Experiment 1. This indicates that the abstract symbolic information did not evoke a proper expectation in the participants. Rather, the direct perceptual experience of the stimuli and their regularities must be in the perceptual memory. Although effects of sensory quality within the temporal context for Task 1 reaction times are already present in the second stimulus pair, they are absent for the first pair, again indicating that the direct sensory stimulus experience is a necessary precondition.

Summary and general discussion

In the present study, we investigated whether the automatic integration of observed regularities across previous percepts and the generation of predictions based on these observed and memorized regularities, affect processing of the sensory present and the execution of a present task. To study this question, we applied a novel experimental paradigm with ambiguous and

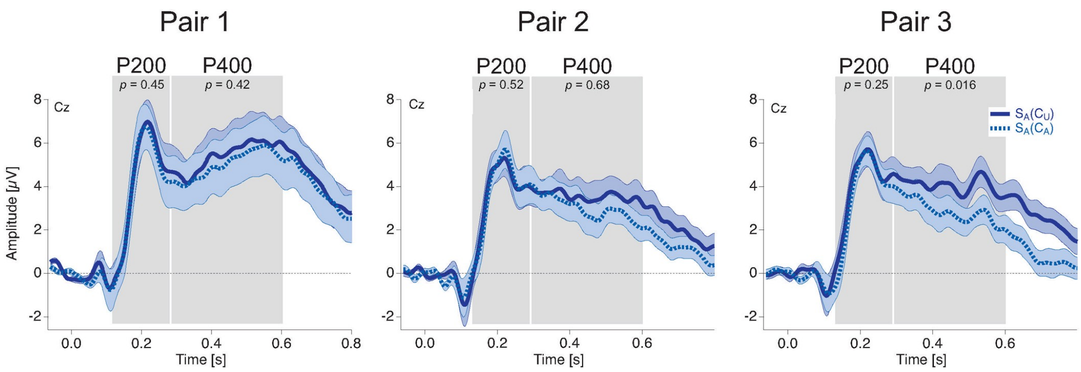

Fig 10. Grand mean ERP results from Experiment 2. Grand means (±SEM) in response to a currently observed stimulus are separately shown for conditions $S_A(C_U)$ (dark blue solid lines) and $S_A(C_A)$ (light blue dotted lines). S_A-evoked ERP traces from stimulus pair 1 (left), 2 (middle), and 3 (right) are depicted separately. All traces are displayed for electrode Cz.

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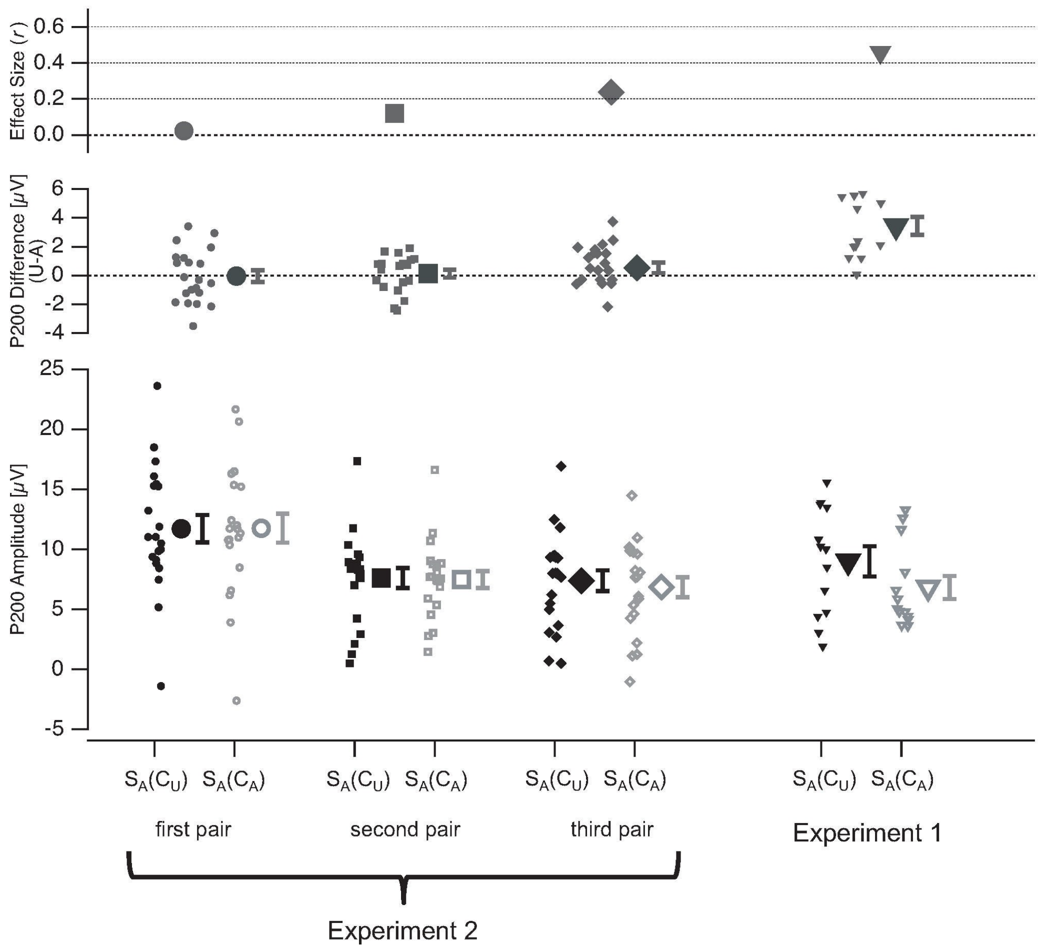

Fig 11. P200 ERP results from Experiment 2. Bottom row depicts the mean amplitudes of the P200 evoked by a currently observed stimulus S_A separately for conditions with unambiguous (C_U, black) and ambiguous (C_A, grey) stimuli in the temporal context of S_A. P200 amplitudes are separately shown for S_A from the first (circles, first column), second (squares, second column), and third pair (diamond, third column). For comparison, the results from Exp. 1 (triangles) are plotted on the right (fourth column). The data from individual participants are represented with small icons, while the large icons represent the mean amplitudes with SEM (whiskers). In the middle row, the mean ERP differences (large icons ±SEM) between the two conditions (unambiguous temporal context minus ambiguous temporal context) are depicted together with data from the individual participants (small icons). The top row shows the effect size (r_{es}) of the temporal context effects. U = Unambiguous, A = Ambiguous.

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unambiguous stimulus variants and investigated two ambiguity-sensitive ERP components (P200 and P400). We used stimulus ambiguity to manipulate the reliability of the perceptual history and the predictions about the perceptual future.

We found that the amplitudes of P200 and P400 ERPs evoked by identical lattice stimuli differ as a function of the temporal context, i.e. the ambiguity level of a preceding stimulus (S2 from the previous pair) and the expected ambiguity level of a subsequent stimulus (S2 from the current pair). Similarly, reaction times from a stimulus-related Task 1 differ as a function

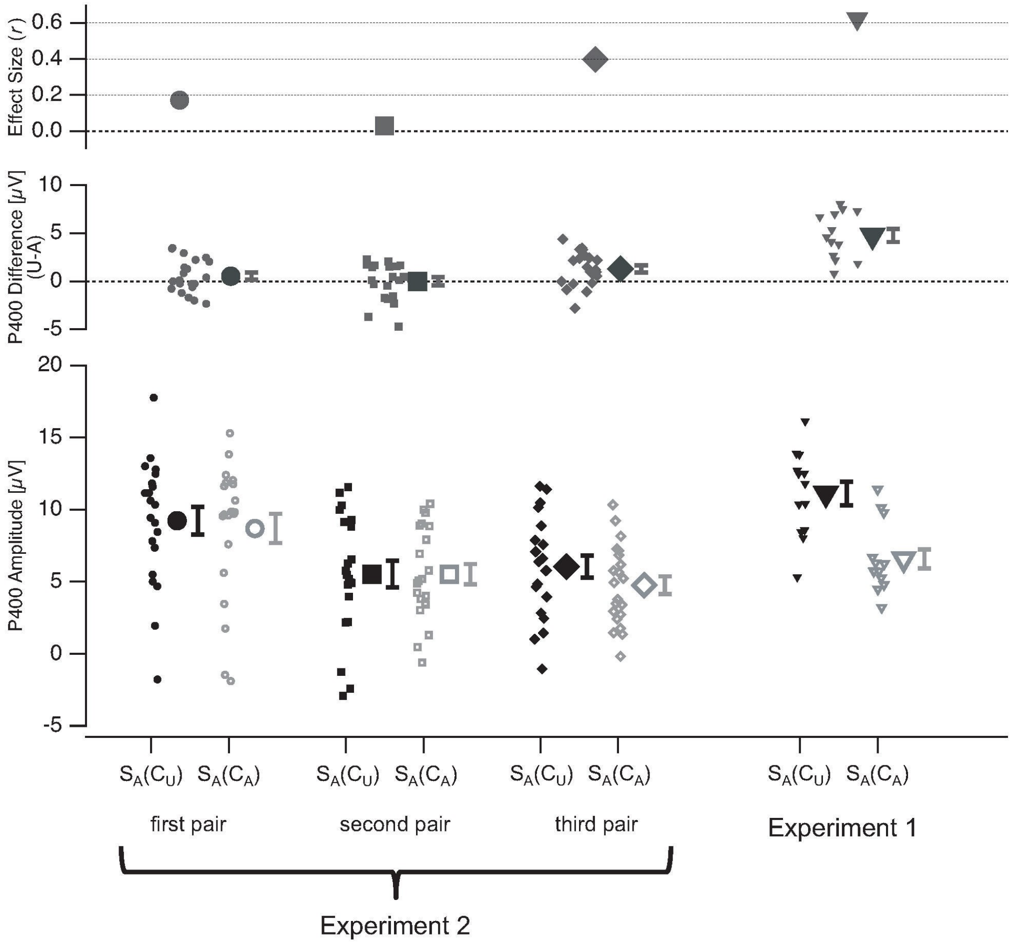

Fig 12. P400 ERP results from Experiment 2. Bottom row depicts the mean amplitudes of the P400 evoked by a currently observed ambiguous stimulus S_A, separately for conditions with unambiguous (C_U, black) and ambiguous (C_A, grey) stimuli in the temporal context. P400 amplitudes are separately shown for the first (circles, first column), second (squares, second column), and third pair (diamond, third column). For comparison, the results from Exp. 1 (triangles) are plotted on the right (fourth column). The data from individual participants are represented with small icons, while the large icons represent the mean amplitudes with SEM (whiskers). In the middle row the mean ERP differences (large icons ±SEM) between the two conditions (unambiguous temporal context minus ambiguous temporal context) are depicted together with data from the individual participants (small icons). The top row shows the effect size (r_{es}) of the temporal context effects. U = Unambiguous, A = Ambiguous.

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of the ambiguity level of the stimuli within the temporal context, even though they were irrelevant for the execution of this task.

In the following, we will first discuss general limitations of the current study. We will then describe previous findings of P200 and P400 ERP components, similar to the ones found in the present study. Next, we discuss whether our results reflect "footprints" from the perceptual past or rather mechanisms underlying predictions of the perceptual future, or both. Finally, we will speculate about the specific functional roles of the identified ERP effects and provide a possible explanation for the differing pattern of reaction time effects.

Limitations of the current study

In Experiment 1, thirteen participants were measured. We conducted a power analysis [45] on the basis of previous results [26,27], which indicated 12 participants as sufficient. Even though the previously found exceptionally large P200 and P400 amplitude effects related to stimulus ambiguity [26,27,31] suggested this small number of participants, a larger number of participants in a follow-up replication of the present study may confirm the present findings and even reveal more subtle effects.

Our current EEG setup contains only 32 electrode channels. For future attempts to determine the brain sources underlying the reported effects, one should use a setting with 64 or even 128 electrodes, combined with anatomical MRI scans. These two extensions would decrease the well-known inverse problem in EEG, when trying to identify sources [46,47].

P200 and P400 in the literature

Only a few studies report a positive deflection with a fronto-central distribution 200 ms after stimulus onset, as shown in the current study. Similar P200 ERP components were found during feature detection across visual dimensions [48], modality-independent emotional salience [49], and the match of sensory input with memory contents [11]. The latter finding is in line with our current finding of a P200 amplitude modulation, which is dependent on information from the temporal context. Perri et al. [50] found frontal components (pP1, pP2) in the P200 time-range related to decision-making. These ERP components originate from the anterior insula and reveal larger amplitudes in response to complex compared to simple stimuli. The present P200 findings show an opposite pattern, i.e. larger ERP amplitudes in response to easy perceptual decisions (unambiguous stimuli) and smaller ERP amplitudes in response to difficult/uncertain perceptual decisions (ambiguous stimuli). It may be very interesting to systematically compare similarities and differences in the paradigms and results of the study by Perri et al. and the current experiments in a follow-up study, which then may include source analysis, in a way suggested above.

The positivity 400 ms after stimulus onset with its central distribution resembles the well-known P300 ERP component (specifically P3b [42]). The P300 is typically reported in "oddball paradigms" evoked by infrequent and task-relevant stimuli. The P300 latency is found to be negatively correlated with reaction times (for reviews see [43,44]). In the current study, we aimed at excluding typical oddball situations as much as possible in order to avoid P300 contributions to our results. The present P400 may still share some neural mechanisms with the P300 but cannot be completely reduced to it, at least because of the obvious differences in the respective characteristics. This issue has been discussed in more detail in a recent publication of Kornmeier et al. [27].

Do the present findings reflect "footprints" from the past or predicting the future—or both?

Our findings indicate that the amplitude modulations of the P200 and P400 ERP components evoked by one and the same stimulus are based on different sensory qualities within the temporal contexts. One interesting question is now, whether these amplitude effects result from predictions about the future or whether they are "footprints" from the perceptual past–or whether both factors play a role?

Effects of the perceptual history on early perceptual processing of a current stimulus are well known from the literature. The immediate perceptual history can have both facilitating (serial dependence) and inhibitory (adaptation) effects on the perceptual outcome during observation of ambiguous figures [9,10,13–15,51]. Further examples are motion aftereffects [52], contrast aftereffects [18], or repetition suppression [53]. Moreover, both serial dependence and adaptation effects can be found at different levels along the perceptual processing chain, up to the processing of emotional contents of faces and even beyond [9,54,55].

The amplitude differences of the P200 and P400, as found in the present study, may be simply caused by low-level influences from the immediate past rather than reflecting predictions about stimuli in the immediate future. In particular, the results from Experiment 2 point in this direction: Given our experimental design, stimulus S1 from the first of three stimulus pairs and the related Task 1 have no influential immediate perceptual history (see Methods above). Accordingly, the amplitudes of the P200 (Fig 11) and P400 (Fig 12) evoked by the first stimulus of the first stimulus pair and the corresponding task-related reaction times (Fig 9) do not differ between conditions. The influence from the past seems to build up over time: we found reaction time effects as early as the second stimulus pair and also for the third pair. We found P400 amplitude effects for the third pair, which has a perceptual history of two preceding stimulus pairs, but no significant effects for the P200.

On the other hand, it is also possible that the current amplitude and reaction time modulations reflect processes underlying the generation of predictions about the future rather than footprints from the past. A necessary precondition for reliable predictions about the future is the identification of reliable statistics in the past. Having this in mind, the results from Experiment 2 are also compatible with the predicting approach: if there is no history of regularities, there will also be no reliable source for the generation of a prediction and thus, neither a difference in ERP amplitudes nor in reaction times, as found for the first stimulus pair in Experiment 2. Further, with an accumulating perceptual history (second and third stimulus pair) including mounting evidence for regularities, predictions can be generated and become increasingly reliable, resulting in ERP amplitude and reaction time differences between conditions. We found P400 amplitude effects for the third stimulus pair and observed in Fig 11 a weak but not yet significant tendency for a P200 amplitude difference with this third stimulus pair. Interesting in this context is a study by Jazayeri and Shadlen [56]. They demonstrated that if stimuli are drawn from a certain distribution, perception of a current stimulus is biased towards the mean of the distribution that the stimulus originates from, and that response behaviour is best explained by a Bayesian observer model. Of course, this is only possible if the observer relies on a certain type of statistics across a certain time window of repeated presentations of stimuli from this specific distribution. One interesting question is, how many stimuli from such a distribution need to be presented in order to get a reliable estimate of the distribution's mean. Correspondingly, it would be interesting to extend our Experiment 2 by adding more stimulus pairs to one experimental block and see at which point effect sizes as found in Experiment 1 are reached. Such a follow-up study is on our agenda.

Jazayeri and Shadlen [56] investigated perceptual un/certainty by varying temporal aspects of the stimuli, i.e. presenting stimuli for different durations. The current study might add to this line of research in that it also investigates perceptual un/certainty but here this is introduced through the sensory quality of the stimulus instead of its temporal extend.

The considerations above raise the fundamental question whether memory and prediction effects are at all experimentally separable or whether they are inextricably entangled. Current predictive coding approaches [24] assume numerous cycles of generating and evaluating predictions along the (hierarchical) chain from early sensory to cognitive processing [57]. Effects of adaptation and/or serial dependence, typically labelled as low-level sensory effects [58], may thus be exploited during the prediction process and have been discussed to involve predictive properties [59]. One can therefore inversely ask the question whether low-level memory effects, as mentioned above, can occur without influencing the prediction of future sensory input.

Effects of sensory quality within the temporal context on reaction times

The reasoning above may also explain longer reaction times related to a currently observed stimulus if an ambiguous future stimulus is expected, compared to the expectation of an unambiguous future stimulus. The problem with this, initially intuitive, explanation of the reaction time effects is that it only fits to those conditions with an *unambiguous* currently observed stimulus S1. For an *ambiguous* current stimulus, we found the opposite pattern, i.e. longer reaction times with an unambiguous temporal context.

This finding seems counter-intuitive at first sight, but makes much more sense if we look at it from a different point of view: There is *perceptual continuity over time* in the case of $S_A(C_A)$, i.e. if both the currently observed stimulus and its temporal context are ambiguous. Similarly, there is perceptual continuity over time in the case of $S_U(C_U)$, i.e. if both the currently observed stimulus and its temporal context are unambiguous. In contrast, there is *perceptual discontinuity over time* in the case of $S_A(C_U)$, i.e. if the currently observed stimulus is ambiguous and its temporal context is unambiguous. There is also perceptual discontinuity over time in the case of $S_U(C_A)$. Reaction times were consistently shorter in the perceptual continuity case compared to a perceptual discontinuity case. The reaction time effect thus may not reflect the expected quality of a stimulus but, in contrast, the expected perceptual continuity or discontinuity–concerning ambiguity levels–between the currently observed stimulus and its temporal context. This interpretation stands in line with behavioural findings from task-switching paradigms [60]. They show slower reaction times when the task switches from one stimulus to the next, and faster reaction times when the tasks stay the same. However, the ERP effects found in task-switching paradigms [60] are different from our findings. This indicates that the ERP effects reflect a different processing step in the current study than in studies only dealing with task switching and not ambiguity level switching.

To sum up, our results indicate that the perceptual system exploits regularities from the immediate perceptual past in order to generate predictions about the expected sensory quality of a future stimulus in at least two steps, reflected by the P200 and P400 ERP components. Separately, automatic predictions are generated about perceptual continuity, i.e. whether the given sensory quality of a stimulus at time point t_1 is expected to continue to another stimulus at time point t_2. An expected change of sensory quality may require the pre-activation of additional neural resources in order to be prepared for an expected larger environmental change. This pre-activation may increase reaction times related to the execution of a current task by about 100 ms, even though this task is restricted to the sensory evidence from the current stimulus, while perceptual past and expected perceptual future are irrelevant. Of course, this interpretation is speculative and needs to be further confirmed or even disproved in future studies.

What do the present findings tell us about the integration of information from the temporal context?

The available sensory information is noisy, incomplete and, to varying degrees, ambiguous. Thus, finding the most appropriate perceptual interpretation as quickly and as efficiently as possible was, most probably, a critical factor during the evolution of perception. This is known as the perceptual inference problem [1] and has the consequences that we exploit even tiniest bits of stimulus [40] and contextual information [61] in order to resolve it. Adaptation [62,63] and serial dependence [14–16] are examples of how past temporal regularities in the sensory environment influence current percepts. Predictions about the immediate future based on current percepts and identified regularities in the past, can facilitate and optimize the perceptual process, because typically our environment does not change fundamentally from one moment to the next. Thus, several of the previous arduously created perceptual concepts can simply be kept for the next perceptual moment [64].

Interestingly, even though predictions obviously influence conscious experience, they seem to be generated automatically and neither awareness nor task-relevance of, or attention to the predicted stimulus seem to be necessary preconditions [e.g. 65,66].

Most studies on predictive coding focused on how predictions facilitate perception [20–22]. Only a few studies focused on neural correlates of *generating predictions* at a time point t_1 concerning the expected sensory information at a time point t_2 (few examples are fMRI measurements in humans [65] and voltage sensitive dye measurements in ferrets [67]). The current results can be interpreted as evidence for EEG and behavioural measures of how making predictions about the future, based on regularities in the past, affects perceptual processing of a present stimulus and execution of a present task. We found larger amplitudes of two ERP components evoked by the same stimuli when an unambiguous future stimulus can be predicted from the temporal context than when an ambiguous future stimulus can be predicted (effect sizes between 0.24 and 0.62).

Also noteworthy is the observation that the sensory quality within the temporal context also modulates reaction times of the present Task 1, even though the sensory quality within the temporal context is completely irrelevant for the execution of this task. This is further evidence for the inevitability and automaticity of integration of information from the temporal context.

The present results are threefold and may reflect three processing steps. The first step is indicated by the modulation of the fronto-central P200. The second step follows 200 ms later, as indicated by the modulation of the centro-parietal P400 and the deviating pattern of reaction time results indicate a different third step. Both ERP effects point in the same direction (larger amplitudes if stimuli in the temporal context were unambiguous compared to ambiguous), but the results indicate small differences between the P200 and the P400 amplitude effects. Particularly, the results from Experiment 1 show that the ambiguity level of the temporal context of a currently observed stimulus affects the P400 amplitude, irrespective of the ambiguity level of the observed stimulus itself. However, we only see P200 effects of sensory quality within the temporal context if the currently observed stimulus is ambiguous. Further, although the functional difference between processes underlying the two ERP components is currently not entirely clear, recent evidence from our lab indicates that the fronto-central P200 component reflects—at least partly—the reactivation of memory traces during comparison of present with previous perceptual interpretations [68,69]. The absence of the P200 effects of sensory quality within the temporal context during observation of an unambiguous current stimulus may be a simple ceiling effect: The amplitude of the P200 evoked by an unambiguous currently observed stimulus S1 is larger than the amplitude of the P200 evoked by an ambiguous stimulus S1 (compare dashed traces in Fig 6A and 6C). The amplitude of the P200 evoked by an unambiguous S1 may already be at such a high level that it cannot further increase due to physiological and/or brain anatomy reasons. On the other hand, it may also be possible that in a situation when an unambiguous stimulus S1 is currently observed, i.e. when high quality sensory evidence is present, a possible contribution of the working memory may be reduced and a potentially smaller P200 effect of sensory quality within the temporal context may become insignificant.

With the simplified explanation of the effects of sensory quality within the temporal context on the processing of a current stimulus reported in this study, one could assume that–based on reactivated information from perceptual memory–large amplitudes reflect the expectation of an unambiguous and thus, easy-to-process future stimulus. This may therefore serve as a kind of go-signal, affecting both the current task (i.e. faster reaction times), and the future perceptual process. Expecting an ambiguous, thus unclear future, in contrast, may cause an inhibition of the go-signal (resulting in smaller ERP amplitudes). Furthermore, expecting a discontinuity in the visual flow over time may result in a more careful execution of actions in the present. All of this is currently a very speculative explanation of our results and far away from a well-founded theoretical framework. Of course, further experimental steps are necessary to get a clearer picture and to confirm or disconfirm these speculative interpretations.

Conclusion and outlook

One strategy to make perception metabolically more efficient, more reliable and faster may include accounting for stimulus regularities in the past to anticipate the immediate future. Predictive strategies are thus powerful contributions to the resolution of the perceptual inference problem [1]. The current findings show that information from the temporal context strongly modulate perceptual processes in a highly automatic manner, even if those temporal context stimuli are outside the focus of attention and irrelevant for a given task. It seems as if the information from the temporal context is always integrated into the current percept and we cannot avoid doing so. Further evidence for such automaticity comes from the observation that the direct experiences of perceptual regularities in the past are necessary preconditions for the current effects to occur. Symbolic announcements at a higher cognitive level alone are not sufficient, as found in Experiment 2.

Previous studies about influences of past events and prediction mechanisms during perception used unambiguous and clearly visible stimuli. Typical studies on prediction mechanisms compared frequently presented and thus highly predictive stimuli with rare unpredictable stimuli. Stimulus frequency, not stimulus quality, was the critical factor. The current study used stimulus quality, namely stimulus ambiguity, as the critical factor. In our study, the compared perceptual situations were identical concerning stimulus frequency but different concerning perceptual reliability. The different paradigms may have lead to differing results. An interesting next step may be to bridge the gap between the different approaches and to extend the given theoretical framework in a follow-up step by incorporating the differing results.

The current findings indicate that the sensory quality within the temporal context can influence the present and slow down a current task. Importantly, this is the case even when the immediate past and the immediate future are irrelevant for the execution of this current task. Therefore, integrating information from the temporal context may, in certain situations, have impeding effects on how we see the present and how (fast) we act at a present moment. Everyone is familiar with situations where the anticipation of an unpleasant future inhibits us mentally or makes us less motivated during an unrelated current task. Depression may be an extreme case of such a scenario. The current results highlight lower-level perceptual states and mechanisms whose characteristics potentially parallel those of such higher-level mental states and mechanisms. Depression is typically regarded as a higher-level psychiatric disorder. Interestingly, recent evidence indicates that also lower-level visual processing steps are affected [e.g. 70]. It may be interesting to apply the current paradigm to patients with depression and see whether they show an altered pattern of effects of sensory quality within the temporal context. This is one of our next steps on the agenda.

A better understanding of the mechanisms underlying the automatic integration of the temporal context for the generation of predictions may thus help to understand basic principles of perception. At the same time, it may also help to better understand basic principles of higher-level mental states and mental disorders.

Supporting information

S1 File. Result tables of correlations between EEG data, reaction time data, and reversal rates.
(DOCX)

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4.3 Supplementary Material 1

S1 File. Result Tables of correlations between EEG data, reaction time data, and reversal rates.

Table A. Correlation between EEG data (P200, P400) and reaction time data.

	Condition	Pearson correlation coefficient	*p*-value
P200	$S_A(C_A)$	-0.346 (-0.07)	0.25 (0.59)
	$S_U(C_U)$	0.33 (0.1)	0.14 (0.37)
	$S_U(C_A)$	-0.29 (-0.35)	0.32 (0.24)
	$S_U(C_U)$	0.17 (-0.27)	0.29 (0.36)
P400	$S_A(C_A)$	-0.36 (-0.16)	0.23 (0.61)
	$S_U(C_U)$	0.18 (0.14)	0.28 (0.32)
	$S_U(C_A)$	-0.002 (-0.29)	0.5 (0.35)
	$S_U(C_U)$	0.03 (-0.39)	0.46 (0.19)

Table A displays the Pearson correlation coefficients and corresponding *p*-values for normalized (and non-normalized) data between the EEG data (P200 and P400 amplitudes) and the median reaction time data. No significant correlations were found.

Table B. Correlation between EEG data (P200, P400) and reversal rates.

	Condition	Pearson correlation coefficient	*p*-value
P200	$S_A(C_A)$	-0.03 (0.27)	0.54 (0.19)
	$S_U(C_U)$	0.34 (0.25)	0.13 (0.21)
	$S_U(C_A)$	0.12 (0.03)	0.35 (0.46)
	$S_U(C_U)$	0.41 (0.09)	0.08 (0.38)
P400	$S_A(C_A)$	-0.12 (0.04)	0.66 (0.45)
	$S_U(C_U)$	0.19 (0.19)	0.26 (0.26)
	$S_U(C_A)$	-0.19 (-0.49)	0.53 (0.08)
	$S_U(C_U)$	-0.16 (-0.24)	0.6 (0.43)

Table B displays the Pearson correlation coefficients and corresponding *p*-values for normalized (and non-normalized) data between the EEG data (P200 and P400 amplitudes) and the reversal rates. No significant correlations were found.

Table C. Correlation between reversal rates and reaction time data.

Condition	Pearson correlation coefficient	*p*-value
$S_A(C_A)$	0.61 (0.61)	0.01 (0.01)
$S_U(C_U)$	0.3 (0.39)	0.15 (0.1)
$S_U(C_A)$	0.04 (0.51)	0.45 (0.04)
$S_U(C_U)$	0.46 (-0.18)	0.06 (0.56)

Table C displays the Pearson correlation coefficients and corresponding *p*-values for normalized (and non-normalized) data between the reversal rates and the median reaction time data. Only in condition $S_A(C_A)$ a significant correlation was found.

5. Discussion

In this dissertation, different aspects of the brain's resolution of the perceptual inference problem are investigated. In chapter 2, I showed that ambiguity and also low-visibility evoke very similar ERP components 200 ms and 400 ms after stimulus onset (*ERP Ambiguity Effects* Kornmeier and Bach, 2009; Kornmeier et al., 2016), which show small ERP amplitudes in response to ambiguous/low-visibility stimuli and large ERP amplitudes in response to disambiguated/high-visibility stimuli. The ERP effects are related to brain states of perceptual (un)certainty and accordingly relabelled to *ERP Uncertainty Effects*. In chapter 3, I showed that patients with Schizophrenia Spectrum Disorder (SSD) reveal similar but also different steps during the (un)certainty processing compared to matched control participants, both behaviourally and electrophysiologically. This suggests that solving the perceptual inference problem is partially altered in patients with SSD, which is hypothesised to be based on aberrant predictive processes. In chapter 4, I modified the previously used ERP Ambiguity Paradigm (Kornmeier and Bach, 2009; Kornmeier et al., 2016) such that predictive processes can be investigated. I showed that the brain uses information from the temporal context, i.e. information from the perceptual past that evoke predictions about the perceptual future, in order to solve the perceptual inference problem of a given sensory information in a highly automatic manner. This confirms previous theories (based on von Helmholtz, 1867) using electrophysiological measures of neural responses and allows for the investigation of the underpinnings of perceptual processing alterations in terms of predictive coding mechanisms related to low quality of the sensory information.

5.1 Probability estimations

As described in the introduction (chapter 1), perception is of a probabilistic nature. Sometimes, a large number of possible perceptual interpretations of a given sensory information have to be reduced to one highly probable interpretation to provide a stable and reliable representation of the external world. This is done by probability estimations, which are based on information from endogenous factors such as memory. The time scales on which this reduction of probable interpretations is allocated seems to vary between different types of stimuli.

The dynamic field of human interaction (Jack et al., 2014) is strongly influenced by updating mechanisms. Even though the core features of emotional facial expressions are learnt very early during development, the association between a certain configuration of face muscle contractions and an emotional expression is individual to each person. Thus the learnt associations have to be updated with every new individual that we get to know. It might be speculated that continuous

updating might result in various different possible interpretations of emotional expressions that ultimately result in a continuous scale of possible perceptual interpretations.
In the case of classical ambiguous figures such as the Necker cube, one sensory input allows for exactly two possible interpretations, even though there are, in principle, infinitely many possible interpretations (Kersten and Yuille, 2003). The two cube interpretations that can be perceived both contain 90° angles. This is most probably due to the fact that we live in a world with many 90° angles and all other angles are less common. The two 90° angle interpretations of the Necker cube are thus the most probable ones to occur in our environment. The finding that only two out of the infinitely many possible interpretations are typically perceived, therefore shows how well the perceptual system adjusts to the external world and the regularities detected within. The reduction of possible interpretations due to those regularities might be learnt once and is then confirmed over one's lifetime. It might be speculated that this learnt regularity should not be affected by updating mechanisms, because perceptual knowledge, such as the high probability of 90° angles in our environment, is valid over time and will not change during one's lifetime. In the case of the Necker cube, this might result in exactly two possible interpretations and thus might explain the special case of binarity in classical ambiguous figures.

5.2 Perceptual (un)certainty

In the current dissertation I showed that, despite the difference mentioned above, very similar EEG effects in response to classical ambiguous figures and low-visibility of emotional facial expressions were found. The common factor between them might be that they both result in a low reliability of the perceptual outcome. Contrarily, disambiguated figures and high-visibility of a certain feature might result in high reliability of the perceptual outcome. Assuming that this is the source of the ERP Effects, it can be hypothesised that low reliability of the perceptual outcome leads to a brain state of perceptual uncertainty, while high reliability of the perceptual outcome leads to a brain state of perceptual certainty. The similar modulation of two ERP components that are 200 ms apart from each other suggests that not only one event in time but rather a longer-lasting brain state of (un)certainty arises through sensory information of low quality (ambiguity and low visibility). Further, the behavioural findings in chapter 2 strongly support the idea of perceptual (un)certainty. Ultimately, evidence for this interpretation is provided by the Master thesis of Kriti Bhatia (Bhatia et al., 2019; Bhatia, 2020), which was supervised by Jürgen Kornmeier and I during the time of my PhD. In this work, ERP Effects (P200 and P400) were found for poorly visible stimuli, which were embedded in a high amount of noise compared to clearly visible stimuli embedded in a low amount of noise.
The previously labelled *ERP Ambiguity Effects* have been shown to occur for classical ambiguous figures and also for different levels and types of visibility. Perceptual uncertainty might be the common factor between the ERP Effects and it is thus proposed to relabel the ERP Effects to *ERP Uncertainty Effects*.
One important next step in order to test whether the ERP Effects really represent (un)certainty is to introduce a certainty rating after the perceptual decision. This would allow to study whether the ERP Effects vary as a function of (un)certainty and would also allow the comparison of the current neural responses to other previously shown meta-cognitive processes (Mamassian, 2016).

5.3 Predictive mechanisms and Schizophrenia Spectrum Disorder

In chapter 3, I investigated processing of perceptual (un)certainty in controls and in patients with Schizophrenia Spectrum Disorder (SSD). A possible cause for the behavioural and electrophysiological alterations between (1) low-visibility and high-visibility stimuli, as well as between (2) patient with SSD and controls, can be found using Bayesian probability (Kersten and Yuille, 2003) and predictive coding mechanisms (Friston, 2012; Kok and de Lange, 2015). According to these theories, the brain forms a model about the external world and compares the actual sensory information with the previously formed model. The difference between model and sensory information is then computed by means of a *prediction error*. Updating the model according to the sensory information minimises this prediction error. In the case of high-visibility smiley stimuli, low-level differences are large between happy and sad expressions, i.e. strong upwards vs. strong downwards bending of the mouth curvature. The comparison of a predicted happy smiley and an actually presented sad smiley should thus evoke large prediction errors. In the case of low-visibility stimuli, the low-level differences between emotions are small and thus the prediction error should also be small. The amplitudes of the ERP Uncertainty Effects might reflect this with large ERP amplitudes in the case of a small prediction error and small ERP amplitudes in the case of a large prediction error.

During the process of model formation, the prediction error is minimised in order to update the model most efficiently. In the case of high-visibility, the sensory information might be regarded as reliable enough to integrate all sensory information into the formation of predictions. In the case of low-visibility, on the other hand, the sensory information might be regarded as unreliable and not all of the information is integrated into the formation of predictions. The underlying idea that the prediction error is weighted with its estimated precision was proposed by Friston (2010). Importantly, it is proposed that the formation of predictions is disturbed in patients with SSD (Notredame et al., 2014; Fletcher and Frith, 2009; Sterzer et al., 2019; Schmack et al., 2015; Shergill et al., 2005). One consequence might be that the sensory information is never regarded as being fully reliable in the patients. This might explain the alterations in patients with SSD compared to neurotypicals as found and discussed in chapter 3.

The ERP Uncertainty Paradigm, as was used in chapter 2 and in chapter 3, does not allow for a systematic investigation of predictive processes in the ERP Uncertainty Effects. In those studies, it was only possible to analyse the neural processing related to a currently perceived stimulus, while the influences of predicted upcoming sensory information was not measurable. Therefore, the experimental paradigm was modified in chapter 4 such that the influences from the immediate past and the resulting predictions about the immediate perceptual future on the perceptual processing of the present could be investigated. It was found that the temporal context (memorised immediate perceptual past and predicted immediate perceptual future) alters the processing of the perceptual present according to the quality of the sensory information in the temporal context, i.e. ERP Temporal Context Effects. Interestingly, this was found to occur irrespective of the relevance of this temporal context information for a present task. The integration of information from the temporal context is thus proposed to act in a highly automatic manner. How long this influence lasts was not in the focus of this study. Systematic investigation of the influence of temporal distance between the stimuli of interest on the temporal context integration would be a very interesting next step. In predictive coding theories there is only one factor, the prior, covering the previous perceptual information. Perceptual memories on different time scales might be integrated with different weightings, e.g. dependent on their temporal distance and/or importance. Further, it was found that the direct experience of past regularities are necessary in order to predict the perceptual future, whereas a symbolic representation did not evoke such predictions. The findings from chapter 4 highlight the importance of information in the temporal context of a given stimulus for its perceptual processing. Importantly, the ERP effects are strongly modulated by this integration of temporal context integration, shedding more light on their functional roles.

These findings should be considered when using the ERP Uncertainty Effects to investigate alterations in patients with psychiatric diseases. The proposed aberrant predictive processes in patients with SSD (Notredame et al., 2014; Fletcher and Frith, 2009; Sterzer et al., 2019; Schmack et al., 2015; Shergill et al., 2005) should thus be investigated using the ERP Temporal Context Effects as found in chapter 4. With this experimental manipulation it would be possible to investigate the temporal aspects of the alterations in predictive mechanisms in patients with SSD in more detail. Furthermore, the current dissertation shows that perceptual (un)certainty is reflected in the ERP Uncertainty Effects not only by classical ambiguous figures, but also by socially relevant stimuli, like emotional facial expressions. These are found to be especially difficult to process for patients with SSD. Combining the ERP Temporal Context Paradigm with the smiley stimuli would yield a very promising next step to study the proposed aberrant predictive processes in patients with SSD. This might be especially important when dealing with uncertainty in social interactions.

Van de Cruys et al. (2014) argue that patients with Autism Spectrum Disorder (ASD) reveal impairments in the prediction error integration. In particular, it is hypothesised that patients with ASD fail to assign the appropriate level of relevance to the prediction error signal, which is dependent on its level of reliability. This is exactly what is proposed to be studied with the ERP Temporal Context Paradigm. In a future study, patients with ASD should also be presented with the ERP Temporal Context Paradigm in order to (dis)prove and possibly quantify alterations in predictive mechanisms related to the reliability of the sensory information.

5.4 Electrophysiological correlates of psychiatric diseases

The entire concept of schizophrenia is currently challenged (Van Elst, 2017). Guloksuz and Van Os (2018) argue that the current concept of schizophrenia only represents one third of a multidimensional psychotic syndrome, supposedly resulting in a neglect of diagnoses other than schizophrenia within the psychotic spectrum. Diagnostics are based on behavioural measures that rely on an estimation of the related symptom severity. Scientists try to find reliable physiological markers of psychiatric diseases, but this goal is not accomplished to date. In typical studies such as the one presented in chapter 3, patients are diagnosed according to current standards and data from one patient group is compared to data from neurotypical control participants, in order to find physiological markers for the disease. This approach relies on the assumption that the combination of symptoms that form a disease are based on a certain aberrant neural mechanism, which has to be coherent within the selected group. Since it was not possible for scientists to find a reliable physiological marker so far, it can be speculated that this assumption is not valid. Another possibility, for example, could be that one symptom might be traced back to exactly one aberrant neural mechanism. Symptom severity, however, usually varies between patients of a studied group. Consequently, a certain neural mechanism related to a certain symptom might be altered to different degrees, depending on symptom severity. Due to this heterogeneity within the patients group, the so-far used experimental approach might not be able to reliably differ between groups. Another possibility would be that one aberrant neural mechanism only causes partial aspects of one or several symptoms, which again might not yield enough difference to reliably separate the groups. This would especially be the case if the symptoms would not be classified within one disease.

A paradigm-shift might yield interesting new approaches for the investigation of altered neural mechanisms in patients compared to controls. The main idea would be to shift the focus of the experimental studies from a currently used symptom-based distinction between two groups of participants (patients vs. controls) towards a neural correlate-based distinction between participants. This might be achieved by ignoring the diagnostics and then using e.g. clustering algorithms and recent innovative machine learning methods (e.g. Banville et al., 2020) to group the data only regarding the neural correlates. As a result, new categorisations of participant groups dependent on their neural responses, not on their symptomatology, might yield interesting new insights about the underlying structure of neural responses between participants. These results might then be related to the previously defined structure of symptoms, thus helping to unravel the relation between neural responses and behavioural symptoms. This approach might ultimately help to further improve treatment of the altered neural mechanisms in patients.

Neural correlates of predictive coding mechanisms might be a promising candidate for such an approach. Patients with SSD and patients with ASD vary considerably in their symptomology. It is, however, proposed that both show very similar alterations in predictive coding mechanisms, i.e. aberrant updating of the predictive coding model, as already discussed above. The idea that one aberrant neural mechanism might cause very different symptoms in different diseases is thus already indicated in the case of predictive coding mechanisms. A promising candidate for such a reflection of an aberrant neural mechanism might be the altered Microstate Uncertainty Effects as found in chapter 3, which indicate sub-groups within the patients' sample. Increasing the sample size and a replication of these findings in an independent study will reveal whether this pattern of results stabilises.

Importantly, the ERP Temporal Context Paradigm in combination with the emotional smiley stimuli, as introduced in the current dissertation, yield a very interesting experimental setup that resembles uncertainty in social interactions. This can be used to study predictive coding mechanisms that might form groups beyond currently existing disease classifications. Further, studying the exceptionally large ERP Uncertainty/Temporal Context Effects with respect to predictive processes might help unravel fundamental processing steps and mechanisms during the process of solving the perceptual inference problem.

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A. Zusammenfassung

Die Wahrnehmung der uns umgebenden Welt erscheint stabil und verlässlich. Der Zugang über unsere Sinne ist jedoch limitiert und unser Gehirn muss die exogene Information mit Hilfe von erinnerten Konzepten und gelernten Regelmässigkeiten rekonstruieren (von Helmholtz, 1867). Durch diesen Rekonstruktionsprozess gibt es immer verschiedene Möglichkeiten wie die aktuelle sensorische Information interpretiert werden kann. Dies wird als das Wahrnehmungsinferenzproblem (*perceptual inference problem*) bezeichnet und es wird offensichtlich in der Verarbeitung von mehrdeutigen Figuren, z.B. des Necker-Würfels (Necker, 1832, s. auch Figure 1.1). Bei diesen Figuren kann eine sensorische Information auf zwei oder mehr Arten interpretiert werden, wobei die Wahrnehmung spontan zwischen diesen wechselt.

In diesem Kontext sind die Befunde von Kornmeier et al. interessant (Kornmeier and Bach, 2009; Kornmeier et al., 2016). Die Autoren präsentierten mehrdeutige Necker-Würfel (zwei mögliche Interpretationen) in einer experimentellen Bedingung und eindeutige gemachte Reizvarianten davon (eine mögliche Interpretation) in einer anderen experimentellen Bedingung. Der Kontrast der beiden Bedingungen zeigt zwei ereigniskorrelierte Potentiale (EKPs) 200 ms und 400 ms nach Reizbeginn auf, welche große Amplituden bei eindeutigen und kleine Amplituden bei mehrdeutigen Reizen haben. Diese Effekte werden deshalb als die *EKP Ambiguitäts Effekte* bezeichnet. Die Effekte wurden für unterschiedliche Manifestationen von Mehrdeutigkeit in den Reizkategorien Geometrie (Necker-Würfel), Bewegung (SAM/Bewegungsquartett) und Gestaltwahrnehmung (Borings Alte/Junge Frau) gefunden und sind auf Einzelpersonenniveau sichtbar (s. auch Figure 1.1 Kornmeier and Bach, 2009; Kornmeier et al., 2016). Die Generalität in Verbindung mit dem späten Auftreten der Effekte (200 ms und 400 ms nach Reizbeginn) lassen vermuten, dass die Effekte eher spätere, kognitive Prozesse abbilden statt frühe Prozesse, welche an die sensorischen Reizeigenschaften gebunden sind. Laut der aktuellen Interpretation (Kornmeier et al., 2016) spiegeln die Effekte eine Evaluation der Wahrnehmungsverlässlichkeit wider, welche niedriger ist im Falle von zwei möglichen verglichen mit einer möglichen Interpretation.

Falls diese Hypothese zutrifft, sollten die Effekte auch durch Reize hervorgerufen werden, welche eine andere Quelle für unterschiedliche Wahrnehmungsverlässlichkeiten haben als Mehrdeutigkeit. Im ersten Teil meiner Doktorarbeit (chapter 2) habe ich deshalb Reize mit unterschiedlichen Sichtbarkeitsstufen präsentiert. Ich habe Smiley-Gesichter mit entweder klar sichtbarem traurigem oder fröhlichem oder schlecht sichtbarem traurig oder fröhlichem Gesichtsausdruck gezeigt, sowie eindeutigen und mehrdeutigen Necker-Würfeln als Kontrollbedingung. Die Ergebnisse zeigen, dass sowohl die Necker-Würfel als auch die Smiley-Gesichter die gleichen EKP Effekte hervorrufen und liefern somit mehr Evidenz dafür, dass die Effekte eine reizunabhängige Verlässlichkeitsabschätzung des perzeptuellen Konstrukts darstellt. Diese Verlässlichkeitsabschätzung wiederum könnte in einer (Un)Sicherheit der Wahrnehmungsinterpretation resultieren. Die Effekte werden deshalb im Folgenden als *EKP Unsicherheitseffekte* bezeichnet.

Patienten mit einer Schizophrenie-Spektrums-Störung (SSD) zeigen fundamentale Unterschiede in der Wahrnehmungsprozessierung (Silverstein et al., 2015) und in der Integration von sensorischen Informationen mit endogenen Informationen (Notredame et al., 2014; van Assche and Giersch, 2011) verglichen mit Kontrollpersonen. Des Weiteren wurde gezeigt, dass die Patienten Probleme mit der Verarbeitung von mehrdeutigen Reizen im Allgemeinen (Notredame et al., 2014; King et al., 2017; McBain et al., 2011) und im Speziellen mit mehrdeutigen emotionalen Gesichtsausdrücken haben (Dlabac-de Lange et al., 2018; Turetsky et al., 2007; Kohler et al., 2003, 2000). Die EKP-Unsicherheitseffekte, wie im ersten Teil dieser Doktorarbeit beschrieben, sollten deshalb in Patienten mit SSD verändert sein und könnten aufgrund ihrer großen Effektstärke und Sichtbarkeit in den Einzelpersonen ein bereits seit langem gesuchtes physiologisches Korrelat der Erkrankung darstellen. Die entsprechende Untersuchung im zweiten Teil meiner Doktorarbeit (chapter 3) konnte leider noch nicht abgeschlossen werden, weshalb die Ergebnisse sowie die Diskussion vorläufig sind. Die EKP-Unsicherheitseffekte wurden bei den Smiley-Gesichtern repliziert. Diese Effekte waren tendenziell kleiner bei den Patienten verglichen mit den Kontrollen, jedoch erreichte der Unterschied zwischen den beiden Gruppen keine statistische Signifikanz. Explorative Analysen von Verhaltens- sowie elektrophysiologischen Daten zeigen allerdings signifikante Unterschiede zwischen den Gruppen. Laut der aktuellen Interpretation könnten diese Befunde im Zusammenhang mit abweichenden predictive coding-Prozessen bei Patienten mit SSD stehen. Das Konzept von predictive coding geht davon aus, dass das Gehirn ein Modell über die exogene Welt erstellt, welches mit jedem neuen sensorischen Reiz auf allen Hierachieebenen der Wahrnehmungsverarbeitung aktualisiert wird (Friston, 2012; Kok and de Lange, 2015). Der Aktualisierungsprozess des Predictive-Coding-Modells scheint in Patienten mit SSD verändert zu sein (Notredame et al., 2014; Fletcher and Frith, 2009; Shergill et al., 2005). Es wird spekuliert, dass diese Veränderung im Zusammenhang mit der Evaluation der Wahrnehmungsqualität und somit auch mit veränderten ERP Uncertainty Effects steht.

Das bisher benutzte EKP-Unsicherheits-Paradigma erlaubt die Untersuchung einer aktuellen sensorischen Information, wohingegen der Einfluss von vorangegangenen und erwarteten Reizen auf die Verarbeitung einer aktuellen sensorischen Information nicht systematisch untersucht werden können. Dieser Einfluss ist jedoch essentiell für Wahrnehmungsprozesse, wie bereits von von Helmholtz (1867) hervorgehoben. Im dritten Teil meiner Doktorarbeit (chapter 4) wurde das Paradigma dahingehend verändert, dass der Einfluss des Grades der Mehrdeutigkeit eines vorangegangenen und eines erwarteten Reizes auf die Verarbeitung eines aktuellen Reizes untersucht werden konnte. Es zeigte sich, dass diese zeitlichen Aspekte einen starken Einfluss auf Verhaltens- und elektrophysiologische Daten während der Verarbeitung eines aktuellen Reizes haben. Dies ist der Fall obwohl diese zeitlichen Aspekte irrelevant für die Lösung der aktuellen Aufgabe sind. Dies impliziert, dass das Gehirn zu jedem Zeitpunkt die Informationen aus vergangenen und erwarteten Reizinformationen in die Verarbeitung eines jetzigen Reizes

mit einbezieht.
Diese Befunde sollten in die Untersuchung von physiologischen Korrelaten psychiatrischer Erkrankungen mit einbezogen werden. Im Speziellen sollten die veränderten prädiktiven Prozesse in Patienten mit SSD mit Hilfe des experimentellen Paradigmas aus chapter 4 untersucht werden. Des Weiteren sollten, wie in chapter 2 und chapter 3 gezeigt, Smiley-Gesichter mit unterschiedlicher Erkennbarkeit emotionaler Ausdrücke als Stimulationsreize verwendet werden. Dieser Ansatz erlaubt in zukünftigen Untersuchungen die Messung und Quantifizierung von prädiktiven Prozessen in Patienten mit psychiatrischen Erkrankungen und in neurotypischen Personen in einer sehr alltagsnahen Situation von Unsicherheit in sozialen Interaktionen.

B. Résumé

Introduction

Les informations dont disposent nos sens sont limitées, bruitées et plus ou moins ambiguës. La perception humaine, cependant, est stable et fiable. Pour fournir une représentation stable et fiable du monde extérieur, le système perceptif complète l'information exogène incomplète (bottom-up sensoriell) par une information endogène (top-down, par exemple des concepts mémorisés Kersten and Yuille, 2003). La qualité de l'information exogène et la précision de l'information endogène déterminent la contribution des deux types d'information au résultat perceptuel. En outre, le processus d'intégration en lui-même entraîne le problème de l'inférence perceptuelle, c'est-à-dire qu'une information sensorielle permet des interprétations multiples.

Des figures ambiguës, comme le fameux cube de Necker (Necker, 1832, voir Figure B.1) sont paradigmatiques pour étudier l'intégration des informations exogènes top-down avec les informations endogènes bottom-up. Dans ces figures, une seule information sensorielle permet deux ou plusieurs interprétations possibles. Lors d'une inspection prolongée d'une figure ambiguë, la perception devient instable et alterne de manière répétée entre différentes interprétations. Les figures ambiguës permettent donc de démêler le traitement lié à l'entrée sensorielle constante du traitement lié à l'interprétation perceptive alternée.

Dans ce contexte, il est intéressant de noter deux études de Kornmeier et al. (Kornmeier and Bach, 2009; Kornmeier et al., 2016) dans lesquelles le traitement de stimuli ambigus (une entrée sensorielle évoque deux interprétations perceptuelles) a été comparé au traitement de variantes de stimuli désambiguïsées (une entrée sensorielle n'évoque qu'une seule interprétation perceptuelle). Ils ont mesuré des potentiels évoqué (PE, données électroencéphalographie (EEG) moyennées) et ont trouvé de grandes amplitudes en réponse à des variantes de stimuli désambiguïsées et de petites amplitudes en réponse à des variantes de stimuli ambigus. Deux composantes PE, 200 ms et 400 ms après le début du stimulus, ont été identifiées (*effets d'ambiguïté de PE* Kornmeier and Bach, 2009; Kornmeier et al., 2016, voir Figure B.2). Ces effets sont remarquablement forts (Cohen's d = 0,8-2,1) et ont été trouvés dans des catégories visuelles très différentes (géométrie, mouvement, perception de la Gestalt).

La généralité de ces effets PE ainsi que les occurrences tardives (en termes de temps de traitement visuel) des PE correspondantes indiquent des étapes de traitement au-delà des

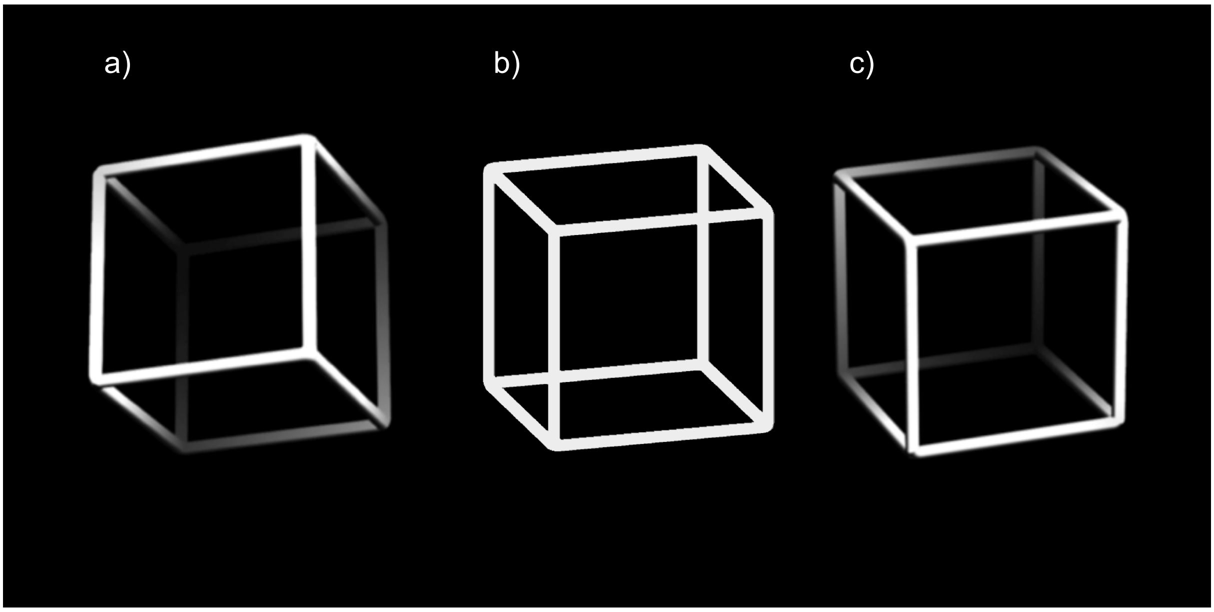

Figure B.1: (a) variante désambiguïsé du cube de Necker orienté à gauche/en haut. (b) cube de Necker ambigu (Necker, 1832) - lors d'une observation prolongée, la perception alterne spontanément entre les deux interprétations possibles comme on le voit en (a) et (c). (c) variante désambiguïsé du cube de Necker orienté vers la droite/vers le bas. Des variantes de stimulus désambiguïsées avec des indices de profondeur ont été créées dans le laboratoire du Dr Kornmeier.

étapes de traitement visuel de bas niveau. Selon l'interprétation actuelle, les résultats perceptifs (pondération des informations exogènes et endogènes) sont générés automatiquement et la fiabilité du résultat perceptif est évaluée par une instance d'évaluation méta-perceptive. Les effets ERP peuvent refléter cette évaluation avec de grandes amplitudes dans le cas d'une grande fiabilité du résultat perceptuel (stimuli désambiguïsés) et avec de petites amplitudes dans le cas d'une faible fiabilité du résultat perceptuel (stimuli ambigus).

Projet 1: *Généralisation des effets d'ambiguïté de PE*
Jusqu'à présent, les effets d'ambiguïté de PE ont été constatés pour des exemples très différents de figures ambiguës classiques (voir Figure B.2). La fiabilité des résultats perceptifs peut également varier pour les objets visuels autres que les figures ambiguës classiques, par exemple lorsque l'information transmise à nos sens est de mauvaise qualité, comme dans le cas de la pluie et du brouillard. Dans ce cas, la faible fiabilité des résultats perceptifs s'explique par la mauvaise visibilité. Une situation pertinente dans laquelle une mauvaise visibilité pourrait entraîner une interaction sociale altérée est celle où les expressions émotionnelles sont interprétées. Si l'interprétation susmentionnée selon laquelle les effets de PE reflètent une estimation de la fiabilité du résultat perceptuel, alors la source de cette (non) fiabilité ne devrait pas importer. Dans la première partie de cette thèse, je cherche donc à savoir si les effets d'amplitude de PE, appelés effets d'ambiguïté de PE par Kornmeier et al. (Kornmeier and Bach, 2009; Kornmeier et al., 2016) peuvent également être évoqués par la haute et la basse visibilité des expressions faciales émotionnelles.

Projet 2 : *Effets de l'incertitude PE chez les patients atteints de troubles du spectre de la*

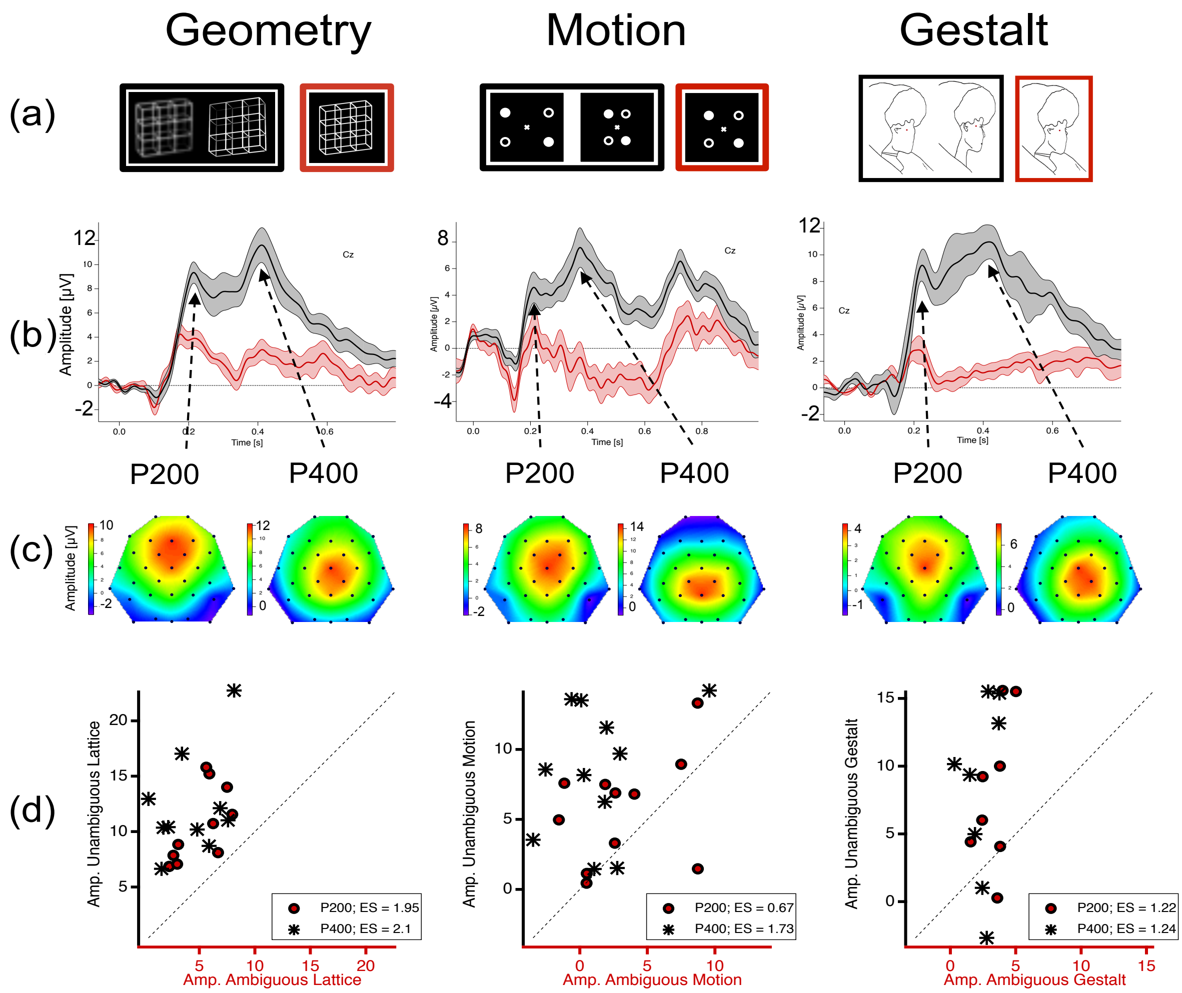

Figure B.2: Résultats précédents des effets d'ambiguïté de PE de Kornmeier et al.(Kornmeier and Bach, 2009; Kornmeier et al., 2016). (a) Trois figures ambiguës classiques différentes, la grille de Necker (géométrie Necker, 1832), le mouvement alternatif stroboscopique/SAM (mouvement, https://michaelbach.de/ot/mot-sam/ Schiller, 1933), et la vieille/jeune femme (Gestalt Boring, 1930) ont été présentées (cadres de figures rouges), ainsi que les variantes de stimulus désambiguïsées respectives (cadres de figures noires). (b) Les grands moyens PE entre les participants à l'électrode Cz. Les effets d'ambiguïté PE consistent en des amplitudes P200 et P400 plus importantes avec des variantes de stimulus désambiguïsés (traces et cadres de figures noirs) par rapport aux figures ambiguës (traces et cadres de figures rouges ; Cohen's d entre 0,8 et 2,1). (c) Cartes de tension (scalp schématique avec distribution interpolée et codée par couleurs des tensions entre les électrodes EEG à un moment donné) aux heures de pointe P200 et P400 (stimuli désambiguïsés). Les résultats sont très similaires pour les stimuli géométriques (grille de Necker), le mouvement (SAM) et la perception de la Gestalt (Borings Vieille/Jeunesse). (d) Dans les diagrammes de dispersion, les données individuelles sont présentées. Un cercle représente le P200 et une étoile les amplitudes ERP du P400 pour un participant. Presque tous les points de données se trouvent au-dessus de la diagonale, ce qui indique que les effets d'ambiguïté de PE sont clairement visibles dans les données individuelles. Ces graphiques ont été créées dans le laboratoire du Dr Kornmeiers.

schizophrénie :

Les troubles du spectre de la schizophrénie (SSD) sont un ensemble de troubles du développement neurologique dont la prévalence dans la population est d'environ 1 % (Jardri and Deneve, 2013).

Ces troubles ont de graves conséquences sur la vie sociale des patients et de leurs familles, ainsi qu'un fardeau socio-économique considérable. Les diagnostics sont basés sur des paramètres comportementaux (DSM-V), alors qu'il n'existe pas encore de marqueurs physiologiques fiables.

Les effets d'ambiguïté de PE pourraient représenter une solution efficace au problème de l'inférence perceptuelle, car une interprétation perceptuelle hautement probable qui entraîne une grande fiabilité de la construction perceptuelle (stimuli désambiguïsés) évoque des amplitudes PE plus importantes que deux interprétations perceptuelles également probables qui entraînent une faible fiabilité (stimuli ambigus). Il a été proposé que les patients atteints de SSD présentent des déficits fondamentaux dans le processus de perception (Silverstein et al., 2015). En outre, les patients atteints de SSD révèlent des déficiences dans l'intégration des informations sensorielles avec les concepts mémorisés (Notredame et al., 2014) et les contextes spatiaux et temporels (van Assche and Giersch, 2011). L'étude de la résolution de l'ambiguïté chez les patients atteints de SSD a été proposée afin de fournir un outil prometteur pour étudier les fondements de ce trouble (Jardri and Deneve, 2013; Notredame et al., 2014; Bortolon et al., 2016; Fujino et al., 2016). Il a déjà été constaté que les patients atteints de SSD présentent un traitement différent des chiffres ambigus par rapport aux contrôles (Notredame et al., 2014; King et al., 2017; McBain et al., 2011). En particulier, les patients atteints de SSD présentent des déficiences dans la désambiguïsation des stimuli au contenu émotionnellement ambigu (Dlabac-de Lange et al., 2018) et dans l'estimation des états émotionnels à partir des expressions faciales (Turetsky et al., 2007; Kohler et al., 2003, 2000). J'ai donc adopté le paradigme du projet 1 et introduit la (non) fiabilité de la construction perceptive par la faible et la forte visibilité des expressions émotionnelles dans les visages souriants. J'ai mesuré les réponses neurales correspondantes chez des patients atteints de SSD et chez des participants contrôles appariés. La deuxième question de recherche de ce projet de doctorat est la suivante : Les patients atteints de SSD traitent-ils la (non) fiabilité différemment des contrôles ? Si oui, alors on devrait trouver un schéma modifié des effets d'ambiguïté de PE.

Projet 3 : *Effets du contexte temporel sur le traitement perceptuel:*
Nous ne savons pas si les facteurs endogènes contribuant aux effets d'ambiguïté de PE sont uniquement constitués par la mémoire à long terme, comme les régularités générales apprises sur le monde dans lequel nous vivons, ou s'ils incluent également l'histoire perceptive immédiate. Si, par exemple, le stimulus vu précédemment était très fiable, le stimulus actuel l'est-il également ? Cela pourrait bien être possible, car dans des circonstances normales, notre environnement ne change pas de façon spectaculaire d'un moment à l'autre. Le concept sous-jacent selon lequel l'intégration des expériences antérieures est cruciale pour résoudre le problème de l'inférence perceptuelle a déjà été mis en évidence par von Helmholtz (1867). Les approches actuelles de la probabilité bayésienne (Kersten and Yuille, 2003) et du codage prédictif (Friston, 2012; Kok and de Lange, 2015) formalisent cette notion. Selon la théorie du codage prédictif, le cerveau crée un modèle sur le monde extérieur. À chaque nouvelle entrée sensorielle, l'erreur de prédiction entre le modèle et l'entrée est calculée et le modèle est mis à jour en conséquence (p. ex. Friston, 2012). Dans les études typiques, les stimuli fréquemment présentés sont

rarement perturbés par des stimuli déviants. L'hypothèse est que les stimuli fréquemment présentés optimisent le modèle de telle sorte que les informations sensorielles à venir soient prédites de manière fiable. Les stimuli déviants, en revanche, devraient provoquer de grandes erreurs de prédiction, que les auteurs mesurent ensuite à la fois sur le plan comportemental et électrophysiologique (Näätänen et al., 2007; Stefanics et al., 2014). Les stimuli utilisés dans ces études étaient généralement non ambigus, très visibles et différaient principalement par leur fréquence d'apparition. Toutefois, dans notre environnement naturel, l'exploitation du passé perceptif et la prévision de l'avenir peuvent être très importantes dans les situations perceptives où la qualité de l'apport sensoriel est faible, par exemple lorsque le stimulus est ambigu. Les stimuli du passé immédiat qui sont ambigus peuvent rendre les prédictions sur l'avenir perceptif immédiat moins fiables que les stimuli précédents non ambigus. Le paradigme expérimental introduit dans le projet 1 et le projet 2 ne permet toutefois pas d'étudier l'influence de stimuli de faible qualité sur les processus de prédiction. Dans la troisième partie de cette thèse, le paradigme est modifié de telle sorte que ces influences peuvent être systématiquement étudiées. La troisième question de recherche est donc la suivante : Un stimulus actuellement perçu est-il perçu et traité différemment si le stimulus précédent et le stimulus prédit sont ambigus par rapport au stimulus désambiguïsé ?

Résultats :

Projet 1 : Généralisation des effets d'ambiguïté de PE

Les effets d'ambiguïté de PE précédemment rapportés (P200, P400 Kornmeier and Bach, 2009; Kornmeier et al., 2016) ont révélé de grandes différences d'EEG en réponse aux figures ambigües classiques par rapport aux variantes désambiguïsé. Les différences ont été constatées en particulier dans deux composantes de l'EEG, 200 ms et 400 ms après le début du stimulus, avec de grandes amplitudes en réponse à des figures désambiguïsées et de petites amplitudes en réponse à des stimuli ambigus. Les effets PE ont été trouvés pour l'ambiguïté dans la géométrie, le mouvement et la perception de la Gestalt. En raison de l'apparition tardive - dans les échelles de temps de traitement perceptif - des composantes de PE à 200 ms et 400 ms après l'apparition du stimulus et de leur généralité à travers les types de stimulus, les effets sont interprétés comme le reflet de processus cognitifs de haut niveau, qui ne sont pas directement liés à l'information réelle sur le stimulus. Il a déjà été proposé par Kornmeier et al. que les effets d'ambiguïté de PE pourraient refléter des évaluations de haut niveau du résultat perceptuel avec de grandes amplitudes lorsque le résultat perceptuel est fiable (stimuli non ambigus) et avec de petites amplitudes lorsque le résultat perceptuel n'est pas fiable (stimuli ambigus). Si les effets reflètent réellement l'estimation de la fiabilité cérébrale du résultat perceptuel, alors la source de la (non) fiabilité ne devraient pas importer. En particulier, les effets d'ambiguïté PE précédemment constatés devraient être reproduits avec des stimuli à faible et à forte visibilité.

La vérification de cette hypothèse était l'un des objectifs de la présente étude. À cette fin, une autre source d'incertitude perceptuelle, à savoir la mauvaise visibilité, a été testée dans le cadre du paradigme d'ambiguïté de PE. Des stimuli très visibles ont été mis en contraste avec des stimuli moins visibles et on a cherché à savoir si les mêmes effets PE étaient présents dans ce cas par rapport à la (non) fiabilité évoquée par les grilles de Necker non ambiguës et ambiguës. L'identification des expressions émotionnelles dans les repères faciaux d'une autre personne représente une situation importante dans laquelle la visibilité est pertinente pour les interactions sociales. Les expressions émotionnelles des visages humains sont cependant d'une grande complexité et il peut être très difficile d'estimer toutes les sources de problèmes possibles pour détecter l'émotion correcte. Afin de quantifier facilement les aspects de la visibilité, j'ai réduit la complexité des stimuli au minimum en présentant des smileys. De plus, j'ai réduit la complexité de l'expression émotionnelle en ne présentant que des smileys heureux ou tristes. Les expressions émotionnelles ont été manipulées en ne faisant varier qu'un seul paramètre, à savoir la courbure de la bouche. La courbure de la bouche aurait pu être (1) très visible avec une expression clairement heureuse (bouche fortement penchée vers le haut) ou clairement triste (bouche fortement penchée vers le bas) afin d'induire une certitude perceptive. La courbure de la bouche aurait également pu être (2) moins visible avec des expressions peu claires de bonheur (bouche légèrement penchée vers le haut) ou de tristesse (bouche légèrement penchée vers le bas) afin d'induire des constructions perceptuelles peu fiables.

En plus des stimuli du smiley, des grilles de Necker ambiguës et désambiguïsés ont été présentées pour reproduire les résultats précédents (Kornmeier and Bach, 2009; Kornmeier et al., 2016). En outre, des stimuli abstraits ayant les mêmes caractéristiques de bas niveau que les stimuli smiley ont été présentés, mais ils ont été disposés différemment de sorte que pratiquement aucun visage ne pouvait être reconnu. Ces stimuli abstraits à faible visibilité et à haute visibilité ont été présentés pour deux raisons : (1) pour étudier un composant PE spécifique au visage (N170), dont on a supposé qu'il était présent dans les smiley mais absent dans les stimuli abstraits. Des amplitudes N170 plus importantes pour les smileys par rapport aux figures abstraites indiqueraient un traitement des smileys spécifique au visage. (2) Chercher à savoir si les mêmes effets PE n'ont été évoqués que par une différence de courbure des courbes présentes dans les stimuli abstraits.

Il a été constaté que les effets PE (P200 et P400) étaient évoqués de manière similaire par la grille de Necker, les smileys et également par des stimuli abstraits (voir Figure B.3). Étant donné la présence d'une composante PE sélective du visage en réponse aux smileys, mais pas aux stimuli abstraits, on a supposé que les smileys étaient effectivement traités comme des visages. En outre, les temps de réaction médians n'ont montré aucun effet de preuve sensorielle (ambiguë/basse visibilité vs. désambiguïsé/haute visibilité) ni de type de stimulus (grilles de Necker vs. smileys vs. figures abstraites).

L'article ≪Large EEG amplitude effects are highly similar across Necker cube, smiley, and abstract stimuli ≫(Joos et al., 2020b) indique que les effets de PE sont les mêmes entre des catégories de stimulus très différentes, comme les figures classiques ambiguës et la visibilité des expressions faciales émotionnelles. Cette généralité des effets PE indique une évaluation de haut niveau du résultat perceptif, qui est indépendant des détails sensoriels. La modulation similaire de deux composantes PE distantes de 200 ms l'une de l'autre suggère que non seulement un événement dans le temps, mais plutôt un état cérébral de (in)certitude plus durable se produit à cause d'informations sensorielles de faible qualité (ambiguïté et faible visibilité). Par conséquent, le terme *effets d'incertitude de PE* pourrait être plus approprié que *effets d'ambiguïté de PE* et sera utilisé dans ce qui suit.

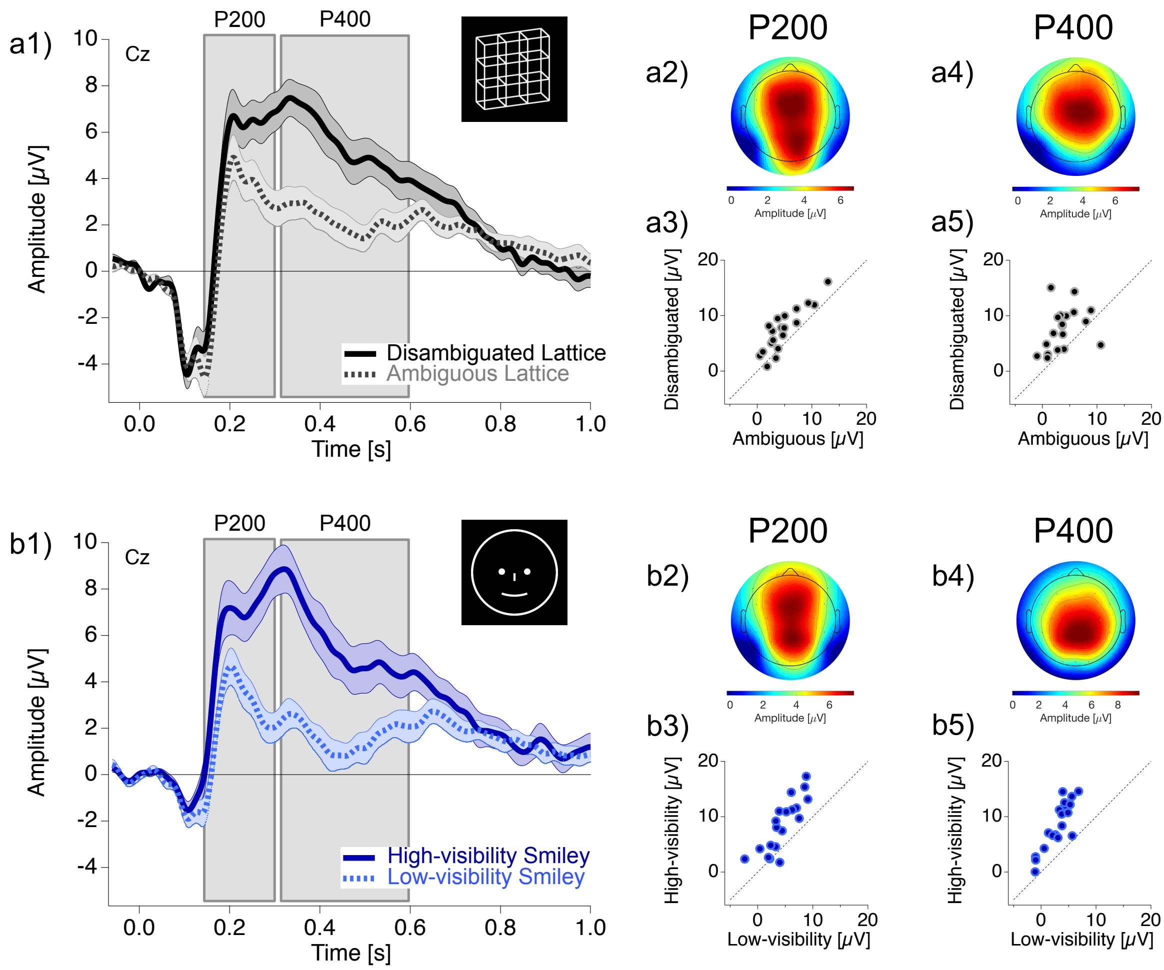

Figure B.3: Effets PE pour les grilles de Necker (a1-a5) et les smileys (b1-b5). Les graphiques (a1) et (b1) représentent les traces PE moyennes pour les stimuli désambiguïsées/à haute visibilité (lignes continues, couleurs sombres) et ambigus/faibles (lignes pointillées, couleurs claires). Les graphiques (a2, a4) et (b2, b4) montrent les cartes de tension moyenne générale des P200 (a2, b2) et des P400 (a4, b4) des stimuli respectifs. Les graphiques (a3, a5) et (b3, b5) montrent des diagrammes de dispersion pour les P200 (a3, b3) et les P400 (a5, b5) avec les amplitudes des participants individuels pour les stimuli désambiguïsées/à haute visibilité (ordonnée) par rapport aux stimuli ambigus/faible visibilité (abscisse). Dans tous les diagrammes de dispersion, la grande majorité des points de données se trouvent au-dessus de la bissectrice, ce qui indique des amplitudes plus importantes pour les variantes de stimulus désambiguïsées/à haute visibilité par rapport aux variantes de stimulus ambigus/faibles. Ce chiffre est tiré de (Joos et al., 2020b).

Projet 2 : Effets de l'incertitude PE chez les patients atteints de troubles du spectre de la schizophrénie

Le trouble du spectre de la schizophrénie (SSD) représente un ensemble complexe de troubles neurodéveloppementaux ayant de graves implications à la vie des patients et de leurs familles. Les diagnostics sont basés sur des paramètres comportementaux (American Psychiatric

Association, 2013), alors que des marqueurs physiologiques fiables n'existent pas encore.
Les patients atteints de SSD présentent une altération du traitement perceptuel (Silverstein et al., 2015) et des déficiences dans l'intégration des informations ≪bottom-up ≫avec les informations ≪top-down ≫(Notredame et al., 2014; van Assche and Giersch, 2011). Cela pourrait entraîner un traitement différent du problème de l'inférence perceptuelle chez les patients atteints de SSD par rapport aux contrôles. Les effets d'incertitude de PE (Kornmeier and Bach, 2009; Kornmeier et al., 2016; Joos et al., 2020b) sont proposés pour refléter une estimation de la fiabilité du résultat perceptuel, qui se fonde sur la résolution du problème d'inférence perceptuelle. Les effets d'incertitude de PE sont donc supposés être modifiés chez les patients atteints de SSD. En outre, les patients atteints de SSD présentent des déficits dans le traitement des émotions (Dlabac-de Lange et al., 2018; Turetsky et al., 2007; Kohler et al., 2003). Par conséquent, le paradigme et les stimuli émotionnels de l'project 1 (Joos et al., 2020b) ont été appliqués aux patients atteints de SSD dans le cadre du présent projet. Les effets de PE ont des tailles d'effet importantes et sont visibles chez les participants individuels, ce qui en fait des candidats prometteurs pour différencier de manière fiable les patients atteints de SSD des contrôles. En raison de la situation sanitaire liée au Coronavirus, je n'ai pas pu terminer la collecte de données pendant la durée de mon doctorat. Pour l'analyse EEG, j'ai pu inclure 11 patients et 12 contrôles dans l'analyse. La collecte des données se poursuit jusqu'à ce que la taille de l'échantillon atteigne N = 20 par groupe. Cette étude n'étant pas suffisamment puissante statistiquement à ce stade-ci, les résultats actuels pourraient différer après d'avoir inclus d'autres ensembles de données et les interprétations fondées sur l'ensemble actuel de données doivent être faites avec prudence. La capacité à identifier les expressions émotionnelles peu visibles devait révéler une grande variabilité interindividuelle et a donc été déterminée séparément pour chaque participant. Pour ce faire, une série de smileys avec différents niveaux de visibilité a été présentée dans une expérience comportementale 1 et pour chaque individu, les stimuli qui évoquaient la plus grande incertitude perceptive ont été déterminés. Les stimuli sélectionnés n'ont pas systématiquement différé entre les groupes. Les contrôles ont révélé des temps de réaction plus longs en réponse aux stimuli moins visibles et des temps de réaction plus courts aux stimuli plus clairement visibles. Les patients, en revanche, ont révélé (1) des temps de réaction généralement longs indépendamment de la visibilité des stimuli et (2) des temps de réaction très similaires à ceux des contrôles en réponse aux stimuli moins visibles (voir Figure B.4).

Dans une expérience électrophysiologique 2, les stimuli à faible visibilité déterminés pour chaque individu dans l'expérience 1 ont été présentés dans une condition expérimentale. Dans une autre condition expérimentale, des smileys à haute visibilité ont été présentés. Les résultats contrastés des deux conditions ont révélé que les effets d'incertitude de PE étaient reproduits (voir Joos et al., 2020b) avec de grandes amplitudes de PE dans le cas d'une haute visibilité des expressions émotionnelles dans les smileys et de petites amplitudes de PE dans le cas d'une faible visibilité. Il y avait une tendance observable à des effets d'incertitude de PE plus faibles chez les patients atteints de SSD par rapport aux contrôles, mais cette différence n'était pas statistiquement significative. Dans une analyse exploratoire de l'expérience 2, les différences de

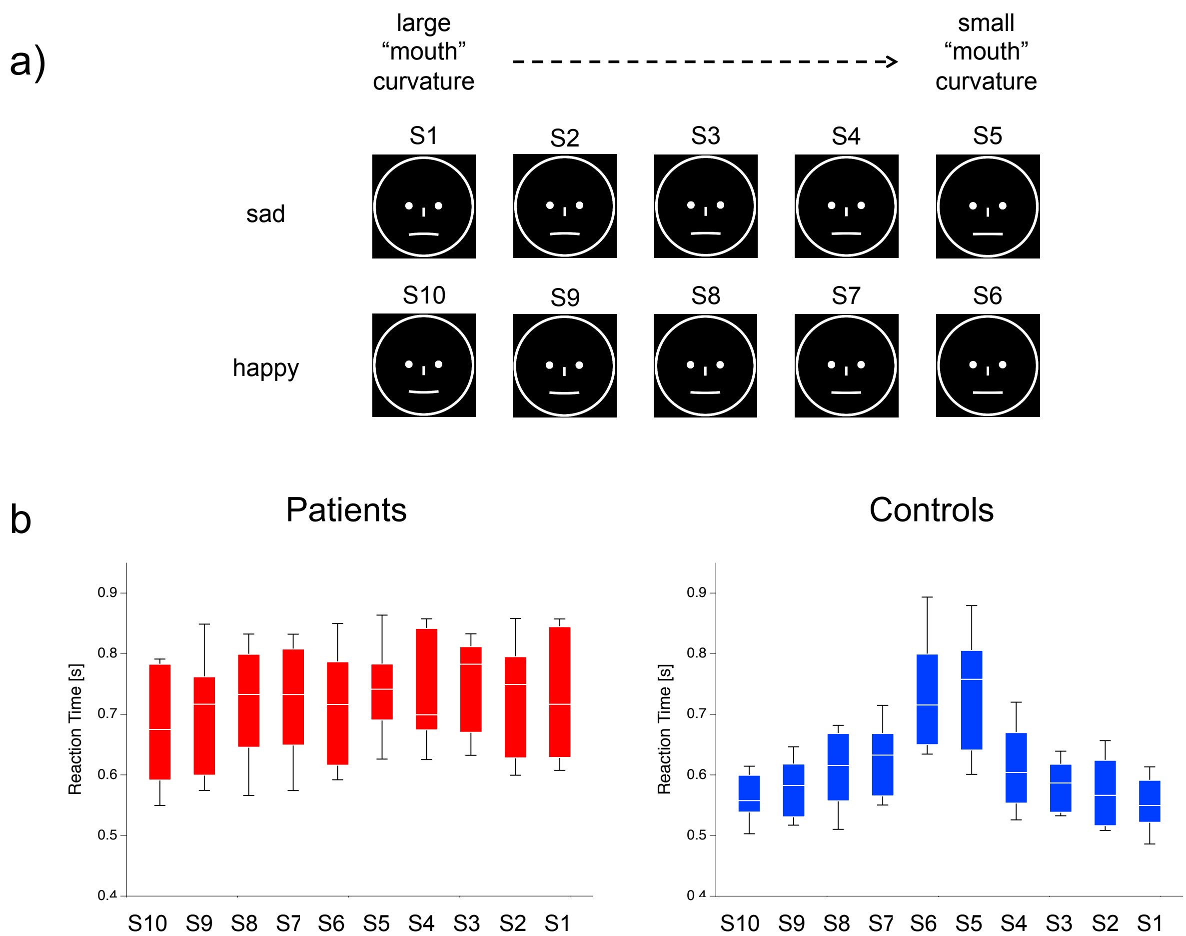

Figure B.4: Expérience comportementale du projet 2 : (a) Représente les 10 variantes de stimulus du smiley (S1-S10). L'expression émotionnelle des stimuli du smiley n'est créée qu'à travers les différents rayons de courbure de la bouche et était soit heureuse (S1-S5) soit triste (S6-S10). Les stimuli étaient présentés dans un ordre aléatoire et les participants devaient indiquer l'expression émotionnelle perçue (heureuse ou triste) en appuyant sur une touche respective en réponse à chaque stimulus. (b) présente les données sur le temps de réaction médian au niveau du groupe en réponse aux différentes variantes de stimulus, les données des patients étant présentées à gauche (rouge) et celles des contrôles à droite (bleu). Les participants du groupe control présentent clairement des temps de réaction plus longs en réponse aux variantes de stimulus S6 et S5, c'est-à-dire aux stimuli les plus neutres, tandis que les patients présentent des réponses plus longues et également plus similaires à toutes les variantes de stimulus. Compte tenu de la corrélation positive précédemment constatée entre la durée du temps de réaction et les cotes de certitude (Henmon, 1911), on peut supposer que les patients atteints de SSD perçoivent généralement plus de (in)certitude perceptive que les contrôles.

traitement perceptif en réponse à la (in)certitude perceptive entre les patients et les contrôles ont été étudiées au moyen de différences topographiques. À cette fin, une analyse des micro-états basée sur les données a été réalisée. Il a été constaté que les effets de l'incertitude des micro-états différaient entre les patients atteints de SSD et les contrôles appariés. Il est intéressant de noter le fait que les micro-états qui différaient entre les groupes n'étaient présents que dans une partie des groupes, ce qui suggère l'existence de sous-groupes au sein du groupe de patients et du groupe control. En outre, le premier moment après l'apparition du stimulus o le traitement de la (in)certitude perceptive différait entre les patients atteints de SSD et les contrôles a été

constaté dès 115 ms après l'apparition du stimulus au niveau des électrodes occipitales.
L'étude fondamental du manuscrit non publié ≪Uncertainty Effects in the Schizophrenia Spectrum Disorder - an EEG study ≫chapter 3 indique que le traitement de la (in)certitude est modifié chez les patients atteints de SSD par rapport aux contrôles. Les fondements des sous-groupes, comme l'indiquent les effets d'incertitude des micro-états, ne sont actuellement pas clairs et ne peuvent être consultés qu'avec des ensembles de données plus nombreux. En outre, il sera intéressant de démêler les sources anatomiques des différents micro-états dans les études futures (en incluant de façon optimale les scans IRM anatomiques pour diminuer le problème de l'inverse dans l'analyse des sources EEG) et ainsi en apprendre davantage sur le rôle fonctionnel de ces micro-états. La constatation que les patients révèlent des temps de réaction similaires pour une gamme de stimuli différents dans l'expérience 1 suggère un niveau d'incertitude généralement plus élevé chez les patients que chez les contrôles. En outre, le trouble du spectre de la schizophrénie est généralement considéré comme une maladie cognitive de haut niveau. En revanche, la différence d'EEG très précoce entre les groupes indique également des altérations de faible niveau chez les patients atteints de SSD par rapport aux contrôles. En fin de compte, des études antérieures ont montré que les patients atteints de SSD révèlent des mécanismes de codage prédictif altérés (Notredame et al., 2014). L'altération des mécanismes prédictifs pourrait entraîner une altération des attributions de fiabilité des résultats perceptifs et donc une altération des réponses comportementales et neuronales à la (in)certitude, comme le montre l'étude actuelle sur les patients atteints de SSD.

Projet 3 : Effets du contexte temporel sur le traitement perceptuel

Le problème d'inférence perceptuelle est résolu à l'aide d'informations provenant de l'histoire perceptuelle immédiate, des expériences vécues au cours de la vie et des prédictions sur les informations sensorielles à venir qui en découlent. Les études précédentes concernant ces aspects temporels de la perception se sont soit principalement concentrées sur l'influence des expériences passées sur les processus perceptifs du présent, soit principalement sur l'influence des prédictions concernant les stimuli futurs sur les processus perceptifs actuels. La présente étude établit un pont entre ces différentes lignes de recherche en reconnaissant l'interaction entre les expériences et les prédictions antérieures et son influence combinée sur la perception du présent. Dans ce qui suit, cette interaction sera appelée *contexte temporel*.
Les stimuli utilisés dans les études précédentes sur les aspects de l'intégration du contexte temporel étaient généralement sans ambiguïté, très visibles et différaient principalement par leur fréquence d'apparition. La résolution du problème de l'inférence perceptuelle peut cependant être plus difficile lorsque le stimulus est de faible qualité, par exemple lorsqu'il est ambigu. En outre, des stimuli ambigus dans le passé immédiat peuvent donner lieu à des prédictions moins fiables sur l'avenir perceptif immédiat que des stimuli non ambigus antérieurs. Dans la présente étude, des variantes de grilles ambiguës et non ambiguës ont été présentées (comme Kornmeier and Bach, 2009; Kornmeier et al., 2016), l'ambiguïté étant la variable indépendante de stimulus pour étudier les effets du contexte temporel pendant la perception. Le paradigme d'incertitude

PE (Kornmeier and Bach, 2009; Kornmeier et al., 2016; Joos et al., 2020b), cependant, n'était pas adapté aux analyses systématiques des effets du contexte temporel, car le niveau d'ambiguïté était maintenu constant dans les conditions (conception en bloc). Le paradigme a donc été modifié de telle sorte que les stimuli étaient présentés par paires, o le stimulus S1 était suivi du stimulus S2. Quatre conditions expérimentales différentes ont été créées avec un plan par paires (2x2) avec des niveaux d'ambiguïté différents de S1 et S2 (ambiguë contre non ambiguë). Cela a permis d'étudier les réponses neuronales provoquées par les mêmes stimuli S1 sur différents niveaux d'ambiguïté dans son contexte temporel, c'est-à-dire précédant S2 de la paire précédente et prédisant S2 de la paire actuelle.
On suppose que le contexte temporel est automatiquement intégré dans le traitement du présent sensoriel et dans l'exécution d'une tche présente. Dans la première expérience de cette étude, les temps de réaction et les effets d'ambiguïté PE (P200 et P400) ont été comparés entre deux conditions : la condition 1 avait un contexte temporel constitué de stimuli non ambigus et la condition 2 avait un contexte temporel constitué de stimuli ambigus. Les amplitudes de PE étaient plus importantes avec un contexte temporel non ambigu qu'avec un contexte temporel ambigu, c'est-à-dire les *effets du contexte temporel de PE* (voir Figure B.5). Les temps de réaction ont également été affectés par les stimuli du contexte temporel. En détail, les temps de réaction étaient courts lorsque le niveau d'ambiguïté était le même dans S1 et S2 alors que les temps de réaction étaient longs lorsque le niveau d'ambiguïté était différent dans S1 et S2.

Dans la deuxième expérience, on a cherché à savoir si les mêmes résultats que dans l'expérience 1 pouvaient être trouvés lorsque l'information permettant de prédire l'avenir perceptif est fournie sous forme de symbole abstrait, et non sur la base de l'expérience perceptive directe des régularités sensorielles dans le passé. À cette fin, les stimuli S2 précédents ont été remplacés par une représentation symbolique des stimuli à venir présentée au début de chaque bloc. La durée des blocs a été considérablement réduite, passant de 9 minutes à 9 secondes (trois présentations par paire) et les répétitions de blocs ont été augmentées. Cela a permis d'analyser séparément la première, la deuxième et la troisième présentation des stimuli. Les résultats ont montré que l'exposition aux informations sensorielles est en effet une condition préalable nécessaire pour les effets du contexte temporel de PE. Ce n'est que dans la troisième présentation du stimulus qu'un effet significatif a été observé pour une différence d'PE entre les stimuli désambiguïsés et ambigus dans le contexte temporel. Les différences de temps de réaction, en revanche, étaient déjà présentes dans la deuxième présentation du stimulus, c'est-à-dire après l'exposition à une expérience sensorielle.
L'article ≪Using the perceptual past to predict the perceptual future influences the perceived present - a novel ERP paradigm ≫(Joos et al., 2020a) indique que les informations sensorielles précédentes et prédites ont une forte influence sur le traitement du présent et peuvent être mesurées à la fois sur le plan comportemental et électrophysiologique. Il est important de noter le fait que c'est le cas même si la tche ne dépendait pas d'informations provenant du contexte temporel. Cela indique une intégration automatique des informations précédentes et prédites sur la certitude des résultats perceptifs. Le cerveau estime toujours la fiabilité des informations sensorielles précédentes ainsi que prédites et les intègre dans l'information actuelle, malgré leur pertinence réelle. Cependant, l'expérience directe des informations sensorielles réelles est

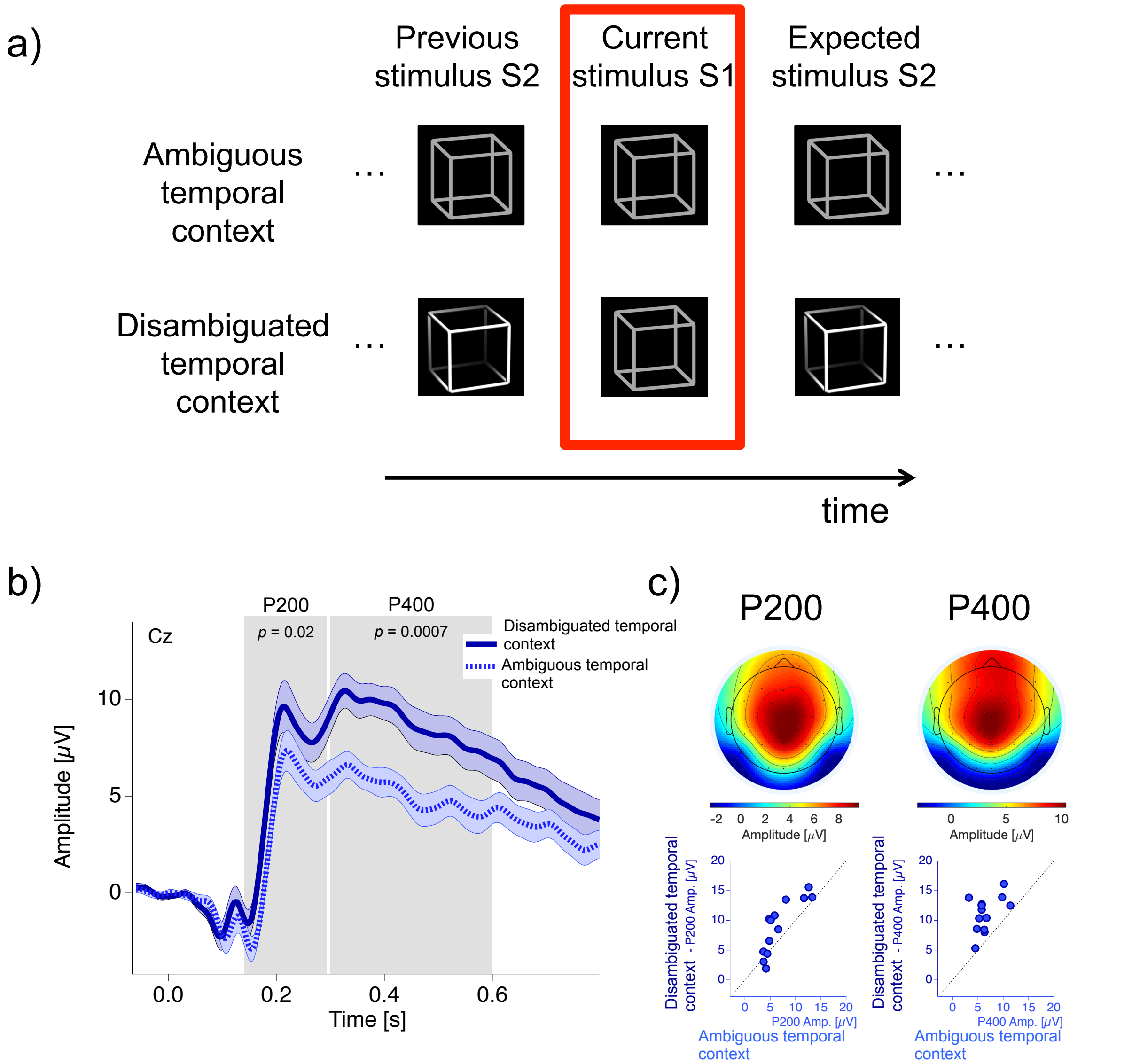

Figure B.5: Paradigme simplifié du projet 2. Les stimuli précédents et attendus sont soit seulement ambigus (contexte temporel ambigu), soit seulement désambiguïsés (contexte temporel désambiguïsé). Les stimuli identiques actuellement observés (cadre rouge) sont comparés en fonction de leur contexte temporel. Notez que la tâche liée au stimulus actuel ne nécessitait aucune information du contexte temporel et se concentrait uniquement sur le stimulus actuel. (b) représente les traces PE grandes moyennes correspondantes montrant de grandes différences PE dans la fenêtre temporelle P200 et P400. Des stimuli actuels identiques et ambigus révèlent des amplitudes nettement plus importantes en réponse à un contexte temporel désambiguïsé par rapport à un contexte temporel ambigu. c) affiche séparément la distribution spatiale et les données de crête individuelles pour les composantes P200 (à gauche) et P400 (à droite).

nécessaire pour former ces prédictions sur l'avenir perceptif, alors qu'une information symbolique sur l'avenir n'est pas suffisante.

Dans les maladies psychiatriques telles que le trouble du spectre de la schizophrénie, il est proposé de modifier les processus prédictifs par rapport aux contrôles (Shergill et al., 2005; Fletcher and Frith, 2009; Notredame et al., 2014; Schmack et al., 2015; Sterzer et al., 2019). Les résultats actuels pourraient aider à étudier les processus prédictifs aberrants chez les patients psychiatriques au moyen des effets du contexte temporel de PE.

Discussion

Dans cette thèse, des différents aspects de la résolution du problème de l'inférence perceptuelle par le cerveau sont étudiés. Dans l'projet 1 (Joos et al., 2020b), je montre que la représentation neuronale de la (in)certitude perceptive est la même pour l'ambiguïté et la visibilité. Cela indique qu'il existe une estimation généralisée de la (in)certitude des résultats perceptifs à un niveau cognitif au-delà des détails sensoriels. Cela pourrait aboutir à ce que les amplitudes des composantes de PE constituent les effets d'incertitude de PE. Dans l'projet 2 (chapter 3), je montre que les patients atteints du trouble du spectre de la schizophrénie (SSD) révèlent des étapes à la fois similaires mais aussi différentes au cours du traitement de (in)certitude par rapport aux participants du contrôle apparié, tant sur le plan comportemental qu'électrophysiologique. Cela suggère que la résolution du problème d'inférence perceptive est partiellement altérée chez les patients atteints de SSD, ce qui est censé reposer sur des processus prédictifs aberrants. Dans l'projet 3 (Joos et al., 2020a), je modifie le paradigme d'ambiguïté PE utilisé précédemment (Kornmeier and Bach, 2009; Kornmeier et al., 2016) de manière à pouvoir étudier les processus prédictifs. Je montre que le cerveau utilise les informations du contexte temporel, c'est-à-dire les informations du passé perceptif qui évoquent des prédictions sur le futur perceptif, afin de résoudre le problème d'inférence perceptive d'une information sensorielle donnée de manière hautement automatique. Cela confirme les théories antérieures (basées sur von Helmholtz, 1867) utilisant des mesures électrophysiologiques des réponses neuronales et permet d'étudier les fondements des altérations du traitement perceptif en termes de mécanismes de codage prédictifs liés à la faible qualité de l'information sensorielle.

Une cause possible des altérations comportementales et électrophysiologiques entre (1) les stimuli à faible visibilité et à haute visibilité, ainsi qu'entre (2) le patient atteint de SSD et les contrôles, peut être trouvée à la lumière de la probabilité bayésienne (Kersten and Yuille, 2003) et des mécanismes de codage prédictif (Friston, 2012; Kok and de Lange, 2015). Selon ces théories, le cerveau forme un modèle sur le monde extérieur et compare les informations sensorielles réelles avec le modèle précédemment formé. La différence entre le modèle et les informations sensorielles est ensuite calculée au moyen d'une erreur de prédiction. La mise à jour du modèle en fonction des informations sensorielles minimise l'erreur de prédiction. Dans le cas des smileys à haute visibilité, les différences de faible niveau sont importantes entre les expressions joyeuses et tristes, c'est-à-dire une forte flexion vers le haut et une forte flexion vers le bas de la courbure de la bouche. La comparaison d'un smiley joyeux prédit et d'un smiley triste effectivement présenté devrait donc évoquer de grandes erreurs de prédiction. Dans le cas de stimuli à faible visibilité, les différences de faible niveau entre les émotions sont faibles et l'erreur de prédiction devrait donc également être faible. Les amplitudes des effets d'incertitude de PE peuvent refléter cela avec de grandes amplitudes de PE dans le cas d'une petite erreur de prédiction et de petites amplitudes de PE dans le cas d'une grande erreur de prédiction.
Pendant le processus de formation du modèle, l'erreur de prévision est minimisée afin de mettre à jour le modèle le plus efficacement possible. Dans le cas d'une haute visibilité, les

informations sensorielles peuvent être considérées comme suffisamment fiables pour intégrer toutes les informations sensorielles dans la formation des prévisions. Dans le cas d'une faible visibilité, en revanche, les informations sensorielles peuvent être considérées comme peu fiables et toutes les informations ne sont pas intégrées dans la formation des prévisions. L'idée sous-jacente a été proposée par Friston (2010), c'est-à-dire que l'erreur de prédiction est pondérée en fonction de sa précision estimée. Il est important de noter le fait que la formation des prédictions est perturbée chez les patients atteints de SSD (Notredame et al., 2014; Fletcher and Frith, 2009; Sterzer et al., 2019; Schmack et al., 2015; Shergill et al., 2005). Une des conséquences pourrait être que les informations sensorielles ne sont jamais considérées totalement fiables chez les patients. Cela pourrait expliquer les altérations observées chez les patients atteints de SSD par rapport aux les personnes neurotypiques, telles qu'elles ont été constatées et examinées dans l'projet 2.

Le paradigme de l'incertitude PE, tel qu'il est utilisé dans l'projet 1 (Joos et al., 2020b) et dans l'projet 2, ne permet pas une investigation systématique des processus prédictifs dans les effets de l'incertitude PE. Dans ces études, il n'est possible d'analyser que le traitement neuronal lié à un stimulus actuellement perçu, tandis que les influences des informations sen sorielles prédites à venir n'étaient pas mesurables. Par conséquent, le paradigme expérimental est modifié dans l'projet 3 (Joos et al., 2020a) de manière à pouvoir étudier les influences du passé immédiat et les prédictions qui en résultent concernant l'avenir perceptif immédiat sur le traitement perceptif du présent. Il est constaté que le contexte temporel (passé perceptif immédiat mémorisé et futur perceptif immédiat prédit) modifie le traitement du présent perceptif en fonction de la qualité des informations sensorielles dans le contexte temporel, c'est-à-dire les effets du contexte temporel PE. Il est intéressant de constater que cela se produit indépendamment de la pertinence de ces informations contextuelles temporelles pour une tche présente. L'intégration des informations du contexte temporel est donc proposée pour agir de manière hautement automatique. La durée de cette influence n'a pas fait l'objet de cette étude. L'étude systématique de l'influence de la distance temporelle entre les stimuli d'intérêt sur l'intégration du contexte temporel serait une prochaine étape très intéressante. Dans les théories de codage prédictif, il n'existe qu'un seul facteur couvrant les informations perceptuelles précédentes, à savoir le postérieur. Les souvenirs perceptifs sur différentes échelles de temps pourraient être intégrés avec des pondérations différentes, par exemple en fonction de leur distance temporelle et/ou de leur importance. En outre, il est constaté que l'expérience directe des régularités passées est nécessaire pour prédire l'avenir perceptif, alors qu'une représentation symbolique n'évoque pas de telles prédictions. Les conclusions de l'projet 3 (Joos et al., 2020a) soulignent l'importance des informations dans le contexte temporel d'un stimulus donné pour son traitement perceptif. Il est important de noter le fait que les effets de PE sont fortement modulés par cette intégration du contexte temporel, ce qui permet de mieux comprendre leurs rôles fonctionnels.

Ces résultats doivent être pris en compte lorsque l'on utilise les effets d'incertitude de PE pour étudier les altérations chez les patients atteints de maladies psychiatriques. Les processus prédictifs aberrants proposés chez les patients atteints de SSD (Notredame et al., 2014; Fletcher and Frith, 2009; Sterzer et al., 2019; Schmack et al., 2015; Shergill et al., 2005) devraient donc être étudiés en utilisant les effets de contexte temporel de PE tels qu'ils figurent dans l'article

3 (Joos et al., 2020a). Cette manipulation expérimentale permettrait d'étudier plus en détail les aspects temporels des altérations des mécanismes de prédiction chez les patients atteints de SSD. En outre, la présente thèse montre que la (in)certitude perceptive se reflète dans les effets d'incertitude de PE également par des stimuli socialement pertinents, comme les expressions faciales émotionnelles, qui s'avèrent particulièrement difficiles à traiter pour les patients atteints de SSD. La combinaison du paradigme du contexte temporel de PE avec les stimuli du smiley constituerait une prochaine étape très prometteuse pour étudier les processus prédictifs aberrants proposés chez les patients atteints de SSD, ce qui pourrait être particulièrement important pour traiter l'incertitude dans les interactions sociales.

En conclusion, l'étude des effets d'incertitude PE et des effets de contexte temporel PE exceptionnellement importants en ce qui concerne les processus prédictifs pourrait aider à démêler les étapes et mécanismes de traitement fondamentaux normaux et modifiés pendant le processus de résolution du problème d'inférence perceptuelle.

C. Short summary

Résumé

Le cerveau construit des interprétations fiables à partir de données sensorielles limitées. La comparaison entre figures ambigües et figures univoques permet d'étudier les processus neuronaux sous-jacents et montre des différences importantes au niveau de l'EEG (Kornmeier and Bach, 2009; Kornmeier et al., 2016). Ici, il a été montré que (1) non seulement l'ambiguïté, mais aussi une faible visibilité évoquent ces effets, suggérant que les processus de haut niveau liés à un état d'incertitude en sont la cause. (2) Les patients atteints de schizophrénie perçoivent plus d'incertitude et leurs processus neuronaux associés diffèrent de ceux de contrôles. (3) Les données présentées auparavant et celles pouvant être prédites influencent automatiquement la perception actuelle. Il a été postulé que cette influence pouvait être altérée chez les patients. Les résultats présents permettront d'étudier les mécanismes prédictifs et les processus perceptifs fondamentaux chez les patients et les personnes neurotypiques.

Mots-clés : Neuroscience cognitive, EEG, ambiguïté, visibilité, trouble du spectre de la schizophrénie, mécanismes prédictifs

Résumé en anglais

The brain constructs reliable interpretations from the limited sensory input. Contrasting ambiguous figures with disambiguated variants allows investigating the underlying neural processes and shows large EEG differences (Kornmeier and Bach, 2009; Kornmeier et al., 2016). Here, I showed that (1) not only ambiguity, but also low visibility evokes those effects, suggesting that high-level processes related to a state of uncertainty evoke the effects. (2) Patients with schizophrenia perceive more uncertainty and have different related neural processes than controls. (3) Previous and predicted input automatically influence the perceptual present. It was proposed before that this influence is altered in patients. The present findings will help to study predictive mechanisms and fundamental perceptual processes in patients and in neurotypicals.

Keywords: Cognitive neuroscience, EEG, ambiguity, visibility, Schizophrenia Spectrum Disorder, predictive mechanisms

D. Erklärung

Ich erkläre hiermit, dass ich die vorliegende Arbeit ohne unzulässige Hilfe Dritter und ohne Benutzung anderer als der angegebenen Hilfsmittel angefertigt habe. Die aus anderen Quellen direkt oder indirekt übernommenen Daten und Konzepte sind unter Angabe der Quelle gekennzeichnet. Insbesondere habe ich hierfür nicht die entgeltliche Hilfe von Vermittlungs- beziehungsweise Beratungsdiensten (Promotionsberater oder anderer Personen) in Anspruch genommen. Niemand hat von mir unmittelbar oder mittelbar geldwerte Leistungen für Arbeiten erhalten, die im Zusammenhang mit dem Inhalt der vorgelegten Dissertation stehen. Die Arbeit wurde bisher weder im In- noch im Ausland in gleicher oder ähnlicher Form einer anderen Prüfungsbehörde vorgelegt.

Die Bestimmungen der Promotionsordnung der Fakultät für Biologie der Universität Freiburg sind mir bekannt; insbesondere weiß ich, dass ich vor Vollzug der Promotion zur Führung des Doktortitels nicht berechtigt bin.

Strasbourg, 07.04.2021

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Ort, Datum Ellen Joos

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Ellen JOOS

EEG correlates of normal and altered processing strategies to solve the perceptual inference problem

Résumé

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