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Neural mechanisms underlying temporal modulation of visual perception

Neurale mechanismen die ten grondslag liggen aan temporele modulatie van visuele perceptie

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voor oma
Nelly de Jong-Uytdewilligen

to grandma
Nelly de Jong-Uytdewilligen

Contents

Chapter 1

Introduction

1.1 Introduction

Do you always believe your eyes? Sometimes your eyes can fool you. This is strikingly illustrated when we observe an ambiguous stimulus that allows two different perceptual interpretations, such as the one presented in Figure 1-1. Do you see a black vase or two red faces? The interesting thing is, you may see both, but never simultaneously (Blake & Logothetis, 2002). When faced with ambiguity in the visual input the brain chooses one interpretation, which is then experienced as if it were the only possible interpretation. You may alternate between the two interpretations, but this will appear as a change of the stimulus, while actually your own brain changed its perceptual interpretation. Ambiguous images can make us realize that, however confident we feel about the way we perceive the visual world around us, there is not a one-to-one relation between visual stimulation and visual perception.

Why does a percept feel so reliable when the stimulus is ambiguous? Maybe we cannot sense ambiguity, because visual input is always ambiguous to some extent. Our eyes register a reflection of the outside world and the brain is left with the difficult task of reconstructing ‘reality’ from this information. The units of information that the brain has to work with are patterns of electrical and chemical activity in nerve cells, signals that are noisy and probabilistic in nature. Thereby, visual information encoded in the brain is inherently ambiguous. The study of ambiguous images is of a broader interest and not only for understanding the perception of stimuli created in the laboratory, such as Figure 1-1. By studying these images we can learn how the brain interprets visual information.

The image in Figure 1-1 also shows us that perception is more than a registration of the visual world around us. While the image shows three homogeneously colored areas, the brain interprets it as two faces or a vase. This notion is important: the brain is wired to build a meaningful image of the world around us. One of the ways to make the content of our visual awareness more meaningful is contextual modulation, i.e. the elements of the visual scene are perceived within their spatial and temporal context. Figure 1-2A provides a compelling example of spatial contextual modulation, showing how profound the influence of context can be. As an adaptive system, the brain also modifies

Figure 1-1. Example of an ambiguous image.
Observers either perceive two red faces looking toward each other or a black vase in the center of the image. The two possible percepts can be experienced alternatingly, but never simultaneously, and differ in the way the perceived figure is separated from the background, a process referred to as figure-ground segregation. The image is known as Rubin's vase after its original designer Edgar Rubin, a Danish psychologist who developed the image around 1915 AD.

its processing based on prior activity, placing current activity within a temporal context. An example of temporal context can be perceived when you stare at the center of the image in Figure 1-1 for ten seconds and then look at a blank piece of paper. On the piece of paper you will see an afterimage of Figure 1-1, consisting of two cyan colored faces and a white vase.

In the above-described example prior visual experience has an adverse effect, meaning that the afterimage is perceptually opposite to the original image (cyan as opposed to red faces). Prior visual experience can also have a facilitative effect when a previously experienced percept is used as an assumption to guide the interpretation of later visual input. Some assumptions are common to all humans, such as the assumption that light comes from above, which results in the meaningful interpretation of shadows (see example in Figure 1-2B). Other facilitative aftereffects result from recent perceptual experience and can have a profound effect on the interpretation of ambiguous stimuli, as described below. Because of the influence of internal factors like individual perceptual experience, visual perception is your personal interpretation of the visual world around you.

This thesis presents a series of studies on how sensory brain regions process ambiguous visual information and how this processing is influenced by prior experience. We focus on two aspects of the perception of ambiguous images: 1) changes in visual awareness that occur spontaneously over time when an unchanging ambiguous stimulus is observed and 2) the influence of minutes-long experience with one of the perceptual interpretations on later perception of an ambiguous stimulus. As perception can change

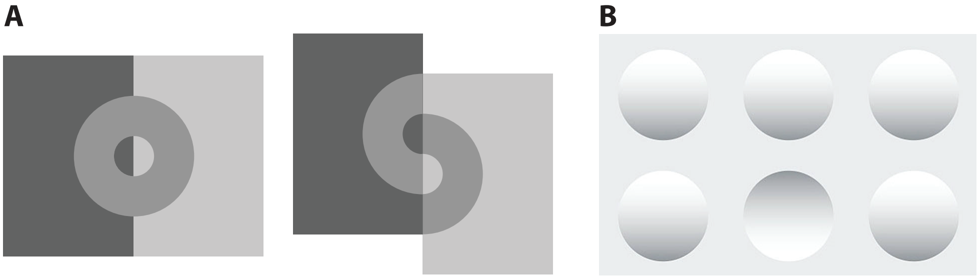

Figure 1-2. Examples of the influence of internal factors of visual perception.

A) Example of spatial contextual modulation. The ring in the image on the left is a uniform shade of gray and is usually perceived as such when intact, but when split in halves and slid vertically, as in the image on the right, the perceived shades of the half-rings are influenced by the background shades of gray, making the half-ring on the dark background appear lighter than the half-ring on the light background. The image is a modification of Koffka's ring, named after Kurt Koffka, a Gestalt psychologist who designed the image in 1935AD (further information in Huang et al., 2008).

B) Example of the influence of assumptions on visual perception. The gradient in the flat circular patches elicits the percept of bumps and a hole, because of the assumption that light comes from above (Ramachandran, 1988).

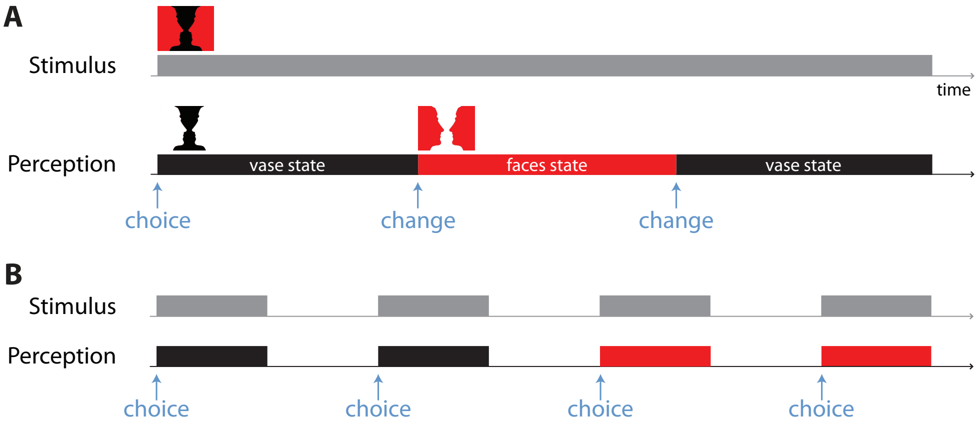

Figure 1-3. Presentation paradigms used in the study of visual perception of ambiguous images.

A) Continuous presentation of an ambiguous image has been argued to comprise three different attributes of the perception of ambiguous images that may be expressions of partially different neural mechanisms. The gray bar illustrates the continued presentation of an unchanging ambiguous stimulus such as Rubin's vase (Figure 1-1). The black and red bars illustrate periods in which the vase or the faces are perceived, respectively. Such periods of stable perception are referred to as *perceptual states*. After the onset of an ambiguous stimulus the processes leading to the initial perceptual interpretation are referred to as *perceptual choice* (investigated in chapters 4 and 5). *Perceptual change* refers to processes underlying spontaneous replacements of one percept by the other percept during continued viewing of the ambiguous stimulus. Perceptual changes occur spontaneously, while there is no concomitant change in the stimulus (investigated in chapters 2 and 3).

B) Intermittent presentation is well suited to study the mechanisms of perceptual choices at the onset of the stimulus. Due to the short presentations of the stimulus perceptual changes do not occur. Often the same perceptual interpretation is experienced on many consecutive presentations (not shown here). Colors as in panel A.

while the stimulus remains constant, these studies used ambiguous stimuli as a tool to disentangle processes involved in visual perception from those reflecting visual stimulation.

1.2 Existing knowledge about perception of ambiguous images

This thesis builds on a solid base of existing psychophysical knowledge, but the neural mechanisms associated with the perception of ambiguous images remain elusive. Literature described below has indicated three different attributes of the perception of ambiguous stimuli that may be expressions of partially different neural mechanisms. Firstly, a period of stable perception in which one of the percepts is experienced is known as *perceptual state*. Perceptual states are usually named after the experienced percept, e.g. the image in Figure 1-1 can give rise to a faces state or a vase state. Secondly, there are two non-state attributes dubbed perceptual choice and perceptual change (Figure 1-3A). *Perceptual choice* refers to the initial interpretation after the onset of an ambiguous stimulus, while *perceptual change* refers to spontaneous changes in perception during prolonged viewing of the stimulus. Following the idea of competition explained in the next paragraph, the neural processes underlying perceptual choices and perceptual changes can be visualized as a race between the neural representations of the two percepts: in the case of perceptual choices both start at the starting line (both neural representations activate from baseline level), whereas in the case of perceptual changes there is a change of lead during the race. Perceptual states are temporary periods with a stable lead (Figure 1-3A).

Based on psychophysical observations, a model has been proposed to explain competitive interactions between two possible interpretations of an ambiguous stimulus. The minimal version of the model includes reciprocal inhibition between two sensory neuron pools, each preferentially involved in one of the percepts (Lehky, 1988; Blake & Logothetis, 2002) and thus contains four cardinal neural components: two neuron pools and two directions of inhibitory connections between these neuron pools. Neural activity associated with the percept currently experienced suppresses neural activity associated with the other percept, although the latter is not completely silenced (Levelt, 1966; Wales & Fox, 1970; Blake & Camisa, 1979; Lehky, 1988; Hock et al., 1996; Blake & Logothetis, 2002). This model can explain several basic characteristics of the perception of ambiguous images, though not all. For example, it can reproduce the mutual exclusivity of the two percepts, but it neither explains the profound influence of perceptual memory on perceptual choices (Leopold et al., 2002; Pearson & Brascamp, 2008), nor the limited but existing influence of attention and intention on perceptual changes (Meng & Tong, 2004; van Ee et al., 2005; Brouwer & van Ee, 2006; Paffen & Alias, 2011).

The strength of the different components of the model is modulated by neural adaptation and neural noise (Cohen, 1959; Noest et al., 2007; Wilson, 2007; Shpiro et al., 2009). Neural noise is believed to be one of the determinants of perceptual choices at the onset of an ambiguous stimulus, when random fluctuation in activity favors one of the perceptual interpretations and concomitant inhibition of the other interpretation leads to augmentation of this imbalance. Another important determinant of perceptual choices is idiosyncratic bias (Carter & Cavanagh, 2007). Neural noise, but not idiosyncratic bias, is also thought to underlie perceptual changes during continued viewing of the stimulus, resulting in the stochastic nature of their timing (Blake et al., 1971). Furthermore, adaptation influences the likelihood of a perceptual change by attenuating activity associated with the dominant percept and/or weakening inhibition onto the neuron pool associated with the suppressed percept, a process commonly referred to as neural fatigue (Hochberg, 1950; Orbach et al., 1963; Long & Toppino, 2004).

The idea of reciprocal inhibition between sensory neuron pools as reflected in the minimal model is only partly supported by neuro-imaging and neurophysiological research. Corroborating the involvement of sensory neurons representing the two percepts, activity fluctuations in sensory brain regions have been found to reflect perceptual states (Polonsky et al., 2000; Tong & Engel, 2001; Gail et al., 2004; Wilke et al., 2006; Maier et al., 2008). Using functional magnetic resonance imaging (fMRI) in humans, it proved possible to predict which percept someone is experiencing from activity measured in brain regions specialized for processing of the used stimulus (Brouwer & van Ee, 2007; Haynes & Rees, 2005). However, casting doubt on the causal involvement of the signals measured with fMRI, electrophysiological recordings in monkeys revealed only a moderate amount of early visual neurons in which activity modulated with the perceptual state. Moreover, the observed modulations were small relative to stimulus preferences of the neurons (Leopold & Logothetis, 1996; Keliris et al., 2010).

Considering the non-state attributes of the perception of ambiguous images, surprisingly little neuro-imaging research has been reported with respect to perceptual choices. Contrary to the above-describe findings regarding perceptual states, perceptual changes have been associated with activations of cognitive rather than sensory brain regions (Basar-Eroglu et al., 1996; Kleinschmidt et al., 1998; Lumer et al., 1998; Isoglu-Alkac & Struber, 2006; Sterzer & Kleinschmidt, 2007; Sterzer et al., 2009; Kanai et al., 2011). Analogously, it has been argued that perceptual changes lacking a concomitant change in the stimulus are not initiated in sensory regions, but involve cognitive brain regions instead (Leopold & Logothetis, 1999; Tong et al., 2006; Sterzer et al., 2009).

A source in cognitive regions would require at least one additional level of neural processing in the above-explained minimal model of reciprocal inhibition between sensory neurons. As mentioned, there is consensus that this model cannot explain all characteristics of the perception of ambiguous images (Blake & Logothetis, 2002; Long & Toppino, 2004; Tong et al., 2006). Still, we use it here as a starting point for further exploration of neural mechanisms involved in spontaneous perceptual changes and minutes-long perceptual memory. While for both these phenomena a causal involvement of cognitive brain regions has been proposed by some researchers (see above), we here favor a more parsimonious explanation and consider the possibility that these phenomena originate from interactions within and between sensory neural networks preferentially involved in either of the two percepts.

1.3 Spontaneous changes in visual awareness

As noted earlier, continued viewing of an ambiguous stimulus elicits spontaneous perceptual changes while the ambiguous stimulus is constant. In chapter 2 we investigated whether these perceptual experiences that lack a concomitant sensory event involve sensory brain regions in the occipital cortex. Neural activity was recorded from intracranial electrodes placed directly on the surface of the human occipital cortex, while the participants experienced spontaneous perceptual changes. This technique measures neural activity at an intermediate level of resolution between multi-unit electrophysiology and scalp recordings, thereby bridging the gap between these techniques as well as linking monkey and human data. In chapter 3 we examined the influence of perceptual memory on perceptual changes, as described in the next section.

1.4 Memory for one of the percepts

Prior visual *stimulation* often has an adverse aftereffect, illustrated by the above-described afterimage that is experienced after staring at Rubin's vase for ten seconds. Contrarily, psychophysical investigations have shown a profound facilitative aftereffect of prior visual *perception* on perceptual choices, a phenomenon dubbed 'perceptual memory' (Orbach et al., 1963; Leopold et al., 2002; Pearson & Brascamp, 2008). Perceptual memory has been reported to develop involuntarily (Klink et al., 2008) and reflect perceptual history over at least the past several minutes (Brascamp et al. 2009; Pearson & Brascamp, 2008). The percept most likely experienced at stimulus onset is the percept experienced most in the recent past, regardless of which was the last-experienced percept (Brascamp et al. 2008; Pastukhov & Braun, 2008). Illustrating the facilitative aftereffect of prior perception on perceptual choices, intermittent presentation of an ambiguous stimulus can result in the same percept being experienced over and over again on many (up to hundreds) consecutive presentations (Pearson & Brascamp, 2008; Brascamp et al, 2009). Long sequences of short intermittent presentations are well suited to investigate mechanisms of perceptual choices, as each presentation instigates a perceptual choice, while perceptual changes do not occur due to the short stimulus durations (Figure 1-3B).

We have two research goals regarding perceptual memory. Firstly, we wanted to compare perceptual choices with perceptual changes regarding the influence of perceptual memory. An influence of perceptual memory has been established for perceptual choices but not perceptual changes. We do know that prolonged viewing of an ambiguous stimulus can give rise to small percept-invariant modulations, such as an increase in the number of changes per time unit (Cohen, 1959; Suzuki & Grabowecky, 2007), but the influence of memory for one of the percepts is unknown. Therefore, we performed a series of psychophysical investigations into the influence of perceptual memory for perceptual choices on perceptual changes during continued viewing of the stimulus (chapter 3).

Our second goal was to investigate neural activity associated with perceptual memory for perceptual choices. In chapter 4 we utilized the high spatial resolution and extended spatial coverage of fMRI to directly compare activity associated with perceptual memory in various brain regions. Importantly, due to the different perceptual interpretations that an ambiguous stimulus can elicit, we were able to dissociate the co-occurring influences of stimulus repetition and percept repetition. In chapter 5 we described the temporal dynamics of cortical activity associated with perceptual memory reflected in event-related potentials derived from scalp electro-encephalograms. This technique is superior to others in its temporal resolution, enabling study of the fast neural processing shortly after the onset of an ambiguous stimulus. We investigated whether stimulus repetition and percept repetition influence the same hierarchical level of processing, as reflected in the latency after stimulus onset that their separate influences become evident.

Chapter 2

Intracranial recordings of occipital cortex responses to illusory visual events

Submitted as:
de Jong MC, Hendriks RJM, Vansteensel MJ, Raemaekers M, Verstraten FAJ, Ramsey NF, Erkelens CJ, Leijten FSS, van Ee R. Intracranial recordings of occipital cortex responses to illusory visual events.

2.1 Abstract

Perception of a constant visual stimulus can change spontaneously in case the stimulus is ambiguous, creating the illusion that the stimulus changed. We investigate whether such spontaneous changes in visual perception involve occipital brain regions specialized for processing visual information, despite the absence of concomitant changes in stimulation. Spontaneous perceptual changes during binocular rivalry or ambiguous structure-from-motion were compared with stimulus-induced perceptual changes that occurred in response to an actual stimulus change. Intracranial recordings from human occipital cortex revealed that spontaneous and stimulus-induced perceptual changes were both associated with an early transient increase in high-frequency power that was more spatially confined than a later transient decrease in low-frequency power. We suggest that the observed high- and low-frequency modulations relate to initiation and maintenance of a percept, respectively. Our results are compatible with the idea that spontaneous changes in perception originate from competitive interactions within visual neural networks.

2.2 Introduction

When viewing an ambiguous stimulus an observer perceives changes back and forth between the different interpretations of the stimulus, while the stimulus is constant. These perceptual changes may be considered illusions, as they originate spontaneously in the mind of the observer, but are experienced as changes of the external stimulus. Here we investigate whether such spontaneous perceptual changes involve regions in the occipital cortex specialized for processing visual information, despite the lack of a concomitant change in the visual stimulus.

Rather than the occipital cortex, transient activations in the parietal and frontal cortices have been associated with spontaneous changes in the perception of a constant ambiguous stimulus (Doesburg et al., 2005; Isoglu-Alkac & Struber, 2006; Basar-Eroglu et al., 1996; Sandberg et al., 2014; Ehm et al., 2011; Kleinschmidt et al., 1998; Lumer et al., 1998; Sterzer & Kleinschmidt, 2007). Therefore, it has been argued that spontaneous perceptual changes are initiated in cognitive brain regions and not in occipital regions specialized for visual processing (Sterzer et al., 2009; Leopold & Logothetis, 1999). While viewing an ambiguous stimulus, activity in the occipital cortex has been found to fluctuate with the stable perceptual state rather than the changes between percepts, suggesting the occipital cortex is involved in the maintenance of a percept, but not in initiation of a new percept (Gail et al., 2004; Leopold and Logothetis, 1996; Maier et al., 2008; Wilke et al., 2006; Sandberg et al., 2013; 2014; de Jong et al., 2014; Brouwer & van Ee, 2007; Haynes & Rees, 2005; Polonsky et al., 2000; Tong & Engel, 2001; de Jong et al., 2012b; Scholvinck & Rees, 2010).

The putative non-involvement of the occipital cortex in spontaneous perceptual changes is somewhat surprising, considering this would be incompatible with the popular view that these changes rely on competitive interactions between visual neurons that are preferentially involved in one of the percepts (Blake & Logothetis, 2002). Therefore, we propose that spontaneous changes are associated with transient modulations in the occipital cortex that remained unnoticed in many previous studies because of two reasons. Firstly, up untill now investigations of occipital activity during ambiguous visual stimulation have focused on sustained modulations reflecting the perceptual state (e.g. Tong & Engel, 2001; Leopold & Logothetis, 1996), potentially overlooking transient modulations occurring at the moment of a perceptual change. Secondly, the recording techniques used on humans in previous studies, such as functional magnetic resonance imaging (fMRI) and scalp recordings (electro- and magneto-encephalography, abbreviated EEG and MEG) may not be well suited for detecting spatially localized transients in neural activity, particularly regarding high-frequency oscillatory activity (Privman et al., 2007; Jerbi et al., 2009; Lachaux et al., 2012; Crone et al., 2011).

Here we used recordings from intracranial electrodes implanted in three epilepsy patients to investigate the extent to which occipital activity is transiently modulated in association with spontaneous and stimulus-induced perceptual changes (i.e. 'illusory' and 'real' changes in the stimulus, respectively). The high spatial as well as temporal resolution of intracranial recordings provide a unique tool to study the relative roles of low-frequency (theta, alpha, beta range) and high-frequency (gamma range) oscillatory activity in these transient modulations. Involvement of low- but not high-frequency oscillations has been suggested in a few earlier investigations of posterior scalp recordings (Struber & Herrmann, 2002; Muller et al., 1999). Considering, however, that high-frequency oscillations are believed to reflect faster and more local processing than low-frequency oscillations (von Stein & Sarnthein, 2000; Donner & Siegel, 2011; Tallon-Baudry 2009; Buzsaki & Draguhn, 2004; Kopell et al., 2000) and may reflect the features of the visual input more reliably (Donner & Siegel, 2011; Siegel et al. 2007; Hall et al., 2005; Henrie & Shapley, 2005; Frien & Eckhorn, 2000; Liu & Newsome, 2006; Belitski et al., 2008), the proposed fast and localized interactions between visual neurons that could underlie spontaneous perceptual changes may be reflected particularly in high-frequency oscillations.

Indeed, in the current study we found that spontaneous perceptual changes were associated with transient modulations of occipital activity in both the low- and high-frequency range. Moreover, the modulations associated with spontaneous changes were similar to those associated with stimulus-induced changes in perception. This finding is remarkable considering spontaneous changes in perception occurred without a concomitant change in the visual input and thus reflected an illusion. We suggest that the observed transient modulations of occipital activity originate from stimulus-specific visual networks that serve a role in the initiation of spontaneous perceptual changes.

2.3 Methods

Participants

The study included three patients with intractable epilepsy who underwent chronic subdural electrocorticography that included coverage of the occipital lobe for clinical reasons (Figure 2-1). All participants had normal or corrected to normal vision and gave written informed consent prior to participation. The experiments were approved by the Medical Ethical Committee of the Utrecht University Medical Center and were carried out in accordance with the ethical guidelines in the Declaration of Helsinki (World Medical Association 2000). A fourth participant was excluded from the analysis because of excessive epileptiform activity and recording noise.

A

						performed experiments	
participant	age [years]	gender	hemisphere	handedness	used hand	binocular rivalry	3D-motion rivalry
A	31	F	R	R	R	yes	yes
B	28	M	R	L	R	yes	no
C	25	F	L	L	L	no	yes

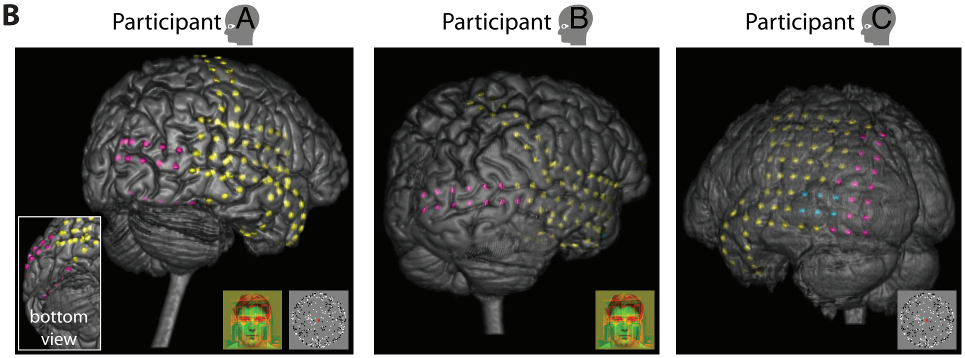

Figure 2-1. Participants.

A) Information on the participants. Hemisphere= sampled hemisphere, handedness= dominant hand, used hand = hand used to operate the button box, L= left, R= right, M= male, F= female. The small head icons represent the individual participants.

B) Placement of the electrodes. Pink dots indicate occipital electrodes, yellow dots indicate electrodes on other brain regions (that were not of interest in the present study), cyan dots indicate electrodes excluded from the analysis a priori (see methods). The cyan dots in participant C covered a temporo-occipital lesion. Miniature stimuli indicate for each participant which experiments were performed.

Procedure

We presented ambiguous visual stimuli that allowed two mutually exclusive perceptual interpretations, thereby enabling separate investigation of the neural underpinnings of visual perception and visual stimulation. To generalize our findings across stimuli we used two different types of ambiguous stimuli. The first was a binocular rivalry stimulus, including two different (incompatible) images presented to the two eyes (Blake & Logothetis, 2002; Tong et al., 2006), in this case a face and a house image (Figure 2-2A, left column). The second stimulus was a virtual rotating globe with ambiguous rotation direction. Here both eyes saw the same image, but there was a conflict in the three-dimensional (3D) interpretation of the motion in the stimulus (Braunstein, 1977; Wallach & O'Connell, 1953). We will refer to this as 3D-motion rivalry (Figure 2-2A, right column). When viewing an ambiguous stimulus an observer's perception spontaneously alternates even though the stimulus itself remains unchanged (Figure 2-2B).

To check whether our findings are specific for ambiguous stimulation we compared both ambiguous stimuli with unambiguous stimuli that were similar in appearance (Figure 2-2C). Alternating presentation of the two unambiguous stimuli, each resembling one of the interpretations of the ambiguous stimulus, elicited changes in perception that were designed to be almost indistinguishable in appearance to the spontaneous changes perceived in the ambiguous stimulus. The important difference is that now the stimulus actually changed, i.e. the perceived changes in the unambiguous stimulus were associated with a change in the physical stimulus (Figure 2-2D), whereas the changes in the ambiguous stimulus originated in the mind of the observer (Figure 2-2B). The participants were not informed about this difference in stimulation. They were instructed to report the identity of each new percept as soon as perception changed by pressing one of two corresponding buttons on a pressure-controlled button box held in the preferred hand (Figure 2-1A).

Before the start of the experiment the appearances of the two possible percepts were explained to the participant. The participants were instructed to stop the experiment when they could not differentiate between these two percepts, or when they perceived other percepts instead, such as intermediate or mixed percepts. This occurred one time, namely with participant B during the 3D-motion rivalry experiment. Therefore, participant B completed only the binocular rivalry experiment. Participant A completed both experiments. Participant C completed only the 3D-motion rivalry experiment, because the condition of the participant did not allow for more testing. During the experiments, participants sat in a semi-recumbent position in a hospital bed in a private room. A computer screen (60 Hz refresh rate) was positioned in front of the participant at a viewing distance of approximately 85 cm. The stimuli were presented in the center of the screen using Presentation (Neurobehavioral Systems).

An experimental session consisted of four 2-minute blocks of stimulation interleaved with 10 seconds rest, during which only the fixation stimulus was presented on the screen (see below). The blocks of stimulation were alternatingly ambiguous and unambiguous. In each experiment the participants completed two sessions of which the first started with an unambiguous block and the second with an ambiguous block. The stimuli are described in more detail in the following sections. The durations of the unambiguous stimuli were based on the percept durations during ambiguous stimulation reported by healthy volunteers in pilot tests.

Stimuli in binocular rivalry experiment

To achieve stereoscopic presentation we used a conventional red–green anaglyph technique with custom-made red and green filters of which the transmission spectrum matched the emission spectrum of the monitor. During the entire experiment the filters were placed before the eyes of the participants (as anaglyph glasses). The ambiguous stimulus subtended 2.9° horizontally and vertically, and consisted of a chromatically filtered image of a face and a house projected at the same location (Figure 2-2A, left column). By means of the anaglyph glasses one of the eyes was presented with the face image and the other eye with the house image, without visible ‘crosstalk’ between the eyes (images are courtesy of F. Tong, see Tong et al., 2006). The images were presented in the center of a binocular pattern of lines extending into the periphery of the visual field to facilitate proper alignment of the eyes (visible by both eyes, covering 15.8° horizontally and vertically). The binocular lines were presented continuously during the entire session, including during the rest periods. The perceptual conflict between the eyes resulted in the alternating dominance of the face and the house image (Blake & Logothetis, 2002; Levelt, 1966). The participants were instructed to fixate on the center of the face/house image and report the perceptual changes they experienced.

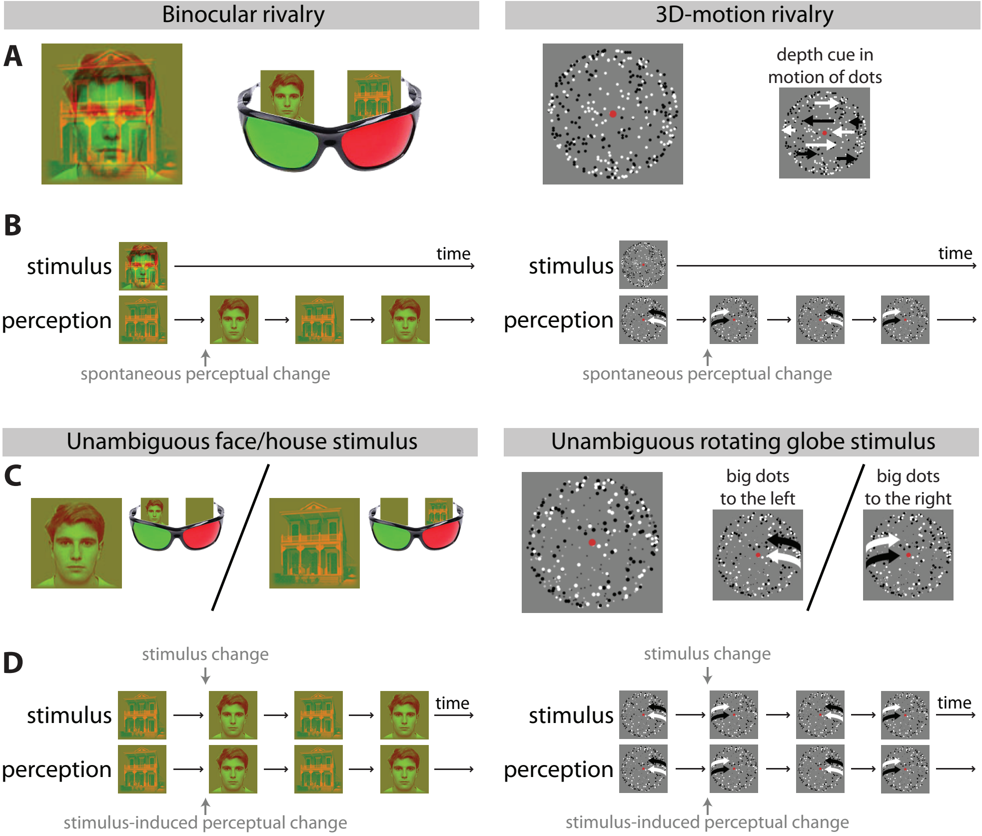

Figure 2-2. Stimuli.

A) Ambiguous stimuli. In the binocular rivalry experiment (left column) one of the eyes was presented with a face image and the other eye with a house image by means of anaglyph glasses. In the three-dimensional (3D-) motion rivalry experiment (right column) the 3D interpretation of a virtual globe was ambiguous, as it could be perceived rotating leftward or rightward.

B) Spontaneous perceptual changes (i.e. ‘illusory’ stimulus changes) between two equally likely interpretations of the ambiguous stimulus occurred while the stimulus was constant.

C) Unambiguous stimuli. To elicit stimulus-induced perceptual changes we alternatingly presented two unambiguous stimuli that each resembled one of the possible interpretations of the ambiguous stimuli. In the binocular rivalry experiment (left column) these were a face image and a house image. In the 3D-motion rivalry experiment we reversed the motion direction of the dots and added depth cues (size and contrast modulation).

D) Stimulus-induced perceptual changes occurred in response to the physical (‘real’) changes in the unambiguous stimulus. The spontaneous (see panel B) and stimulus-induced perceptual changes were similar in appearance, but only the latter was associated with an actual change in the visual input.

To disambiguate the binocular rivalry stimulus either the face or house image was temporarily removed from the stimulus (Figure 2-2C, left column). Observers perceived the remaining image, which, as with the ambiguous stimulus, was presented only to one eye. Stimulus changes occurred every couple of seconds (42 changes in total during 2 sessions) and consisted of the alternating presentation of either the face or the house image. The stimuli were created using Photoshop (Adobe).

Stimuli in 3D-motion rivalry experiment

The ambiguous virtual globe subtended 4.7° in diameter and consisted of 350 leftward and rightward moving dots presented on a gray background. The dots were black or white, subtended 0.11° in diameter, had unlimited lifetime and were perceived as random points on the surface of a virtual globe. The globe was perceived rotating about its vertical axis (every 6.3 seconds), but the direction of rotation was ambiguous: either the front surface was perceived to displace leftward and the back surface rightward or the other way around (Figure 2-2A, right column). This ambiguity arose by means of a phenomenon called structure-from-motion, which refers to a situation in which the three-dimensional shape of an object is reconstructed from local motion signals, in this case the motion of the dots (Braunstein, 1977; Wallach & O'Connell, 1953). Specifically, the speed of the dots on the screen was fastest in the middle of the stimulus and slowest near the left and right edges (where their motion direction reversed). The sinusoidal speed profile created the three-dimensional percept. However, there were no depth cues to differentiate the rightward moving surface from the leftward moving surface, so either direction could be perceived to be in front of the other.

Disambiguation was less straightforward for the 3D-motion rivalry stimulus than for the binocular rivalry stimulus. We chose to disambiguate the globe by adding two monocular depth cues (Figure 2-2C, right column), namely 1) a contrast imbalance: the contrast between the dots and the background was halved for the back surface of the globe compared to the front surface of the globe; and 2) a size imbalance: the size of the dots varied with virtual depth (between 0.05° and 0.15° in diameter, smaller dots on the back surface). A stimulus change consisted of instantly reversing the motion direction of all dots (44 changes in total during 2 sessions). During the entire session participants were instructed to maintain strict fixation on a red fixation dot (0.24° in diameter) in the center of the screen. The stimuli were created using Mathematica (Wolfram Research).

Behavioral analysis

In our analysis we compared the spontaneous changes reported during the ambiguous blocks with the stimulus-induced changes reported during the unambiguous blocks. If reports followed each other within 1000 ms we excluded the second report, because neural activation related to the earlier report could contaminate the epoch of the second report. If the same report was given twice consecutively, we also excluded the second report. For these reasons, 3 reports of participant A (binocular rivalry experiment, ambiguous blocks), 2 reports of participant B (ambiguous blocks) and 1 report of participant C (unambiguous block) were excluded. We also excluded the very first report of each block, because this report is associated with the perceived onset of the stimulus rather than a perceived change in the stimulus.

Regarding the unambiguous blocks we only included correct reports, defined as reports within 3500 ms after a stimulus change indicating the stimulus was perceived as intended by the applied disambiguation method. During the unambiguous blocks of the binocular rivalry experiment all reports were correct for both participants. During the unambiguous blocks of the 3D-motion rivalry experiment 3 reports of participant A were incorrect (>3500 ms) and 30 reports of participant C were incorrect and these were excluded from the analysis. Participant C experienced spontaneous changes in addition to the stimulus-induced changes during the unambiguous blocks, despite the intended disambiguation of the stimulus.

Electrocorticographic recording and processing

The subchronic electrocorticographic recordings were part of a pre-surgical assessment to localize the epileptic focus for surgical removal. Electrode grids were implanted subdurally (2.3 mm exposed diameter, inter-electrode distance 1 cm, Ad-Tech, Racine, USA). Recording was done continuously using a 128-channel Micromed system (Treviso, Italy, 22 bits, band pass filter 0.15 - 134.4Hz) at a sampling frequency of 512Hz. The recorded data were analyzed using in-house developed Matlab code and the open source Matlab toolbox EEGlab (Delorme & Makeig, 2004). The signals of all electrodes were visually inspected for artifacts. One anterior electrode of participant B was excluded from the analysis because of technical failure (Figure 2-1B). Electrodes affected by a temporo-occipital lesion in participant C were also excluded (Figure 2-1B). All remaining electrode signals were then referenced to their grand average signal. The precise positioning of the electrodes was determined using an anatomical MRI scan made prior to implantation and a computed tomography (CT) scan made after implantation, following a method described by Hermes et al. (2010). We used anatomical landmarks to assess which electrodes were located on the surface of the occipital lobe, namely: all electrodes posterior of the imaginary line between the pre-occipital notch and the parieto-occipital sulcus were classified as occipital electrodes (Figure 2-1B). Unless indicated otherwise, we analyzed the averaged activity of all occipital electrodes.

Experimental epochs were extracted from the continuous data. A time–frequency transformation was applied over a frequency range of 2-130 Hz (using a 3-97.5 cycle Morlet wavelet, respectively, tapered with a Hanning window and taking frequency steps of 1 Hz and time steps of 25 ms). There was no true baseline period, because we do not know precisely when the spontaneous changes were initiated. Therefore, we normalized the power per epoch, per frequency, relative to the mean power across a broad time window (normalized power = power / mean power; normalization window was 5 seconds wide and centered on the moment of the report). After the time-frequency transformation we aligned the epochs in time to the moment of the report (button press) and averaged across epochs. We then averaged the perturbations across two frequency bands of interest derived from previous studies into stimulus-induced perceptual changes: 3-30 Hz and 50-130 Hz (Lachaux et al., 2005; Donner & Siegel, 2011; Tallon-Baudry & Bertrand, 1999; Tallon-Baudry, 2009; Siegel et al., 2007; Hoogenboom et al., 2006; Maier et al., 2008; Wilke et al., 2006).

Peak-locked perturbations and power change surface area

Considering that the averaged perturbations aligned to the report may be affected by jitter in reaction times (i.e. variation in the time period between the perceptual change and the buttonpress, see results), we performed two additional analyses insensitive to such jitter. For these analyses we chose a time window of interest spanning -1500 to +500 ms relative to the report, since activity related to perceptual changes may be expected around or preceding the report. Firstly, we determined, per epoch, per frequency band, the latency of the peak in the power modulation (minimum or maximum amplitude within the time window of interest for negative and positive power fluctuations, respectively) and aligned the epochs in time to latencies of these peaks before averaging across epochs (see peak-locked perturbations in Figures 2-4 and 2-5). Secondly, we calculated, per epoch, per frequency band, the surface area of the power modulations across the time window of interest (area below or above the grand average for negative and positive power fluctuations, respectively). To correct for noise-related fluctuations, we applied the same method to a reference time window spanning +500 to +2000 ms after the report (see schematic illustration in Figure 2-4B). We subtracted the reference surface area from the surface area in the time window of interest (after scaling both areas to the width of the used time windows) and then averaged across epochs. Statistical analysis was performed using SPSS Statistics 20 (IBM).

2.4 Results

Behavioral results

Participants A and B reported spontaneous changes in perception of the binocular rivalry stimulus every 5.9 (4.1) seconds and every 7.0 (4.6) seconds on average (medians in parenthesis), respectively. Participants A and C reported spontaneous changes in perception of the 3D-motion rivalry stimulus every 13.7 (14.0) and 9.2 (8.7) seconds on average (medians in parenthesis), respectively. We compared spontaneous changes observed in ambiguous stimuli with stimulus-induced changes observed in unambiguous stimuli (Figure 2-2). The unambiguous stimulus durations were set to 10.0 (5.9) and 10.0 (9.8) seconds on average (medians in parenthesis) in the binocular rivalry and 3D-motion rivalry experiment, respectively. The mean reaction times (delay between stimulus change and report) of participant A and B in the binocular rivalry experiment and participants A and C in the 3D-motion rivalry experiment were 830 (829), 741 (627), 1196 (984) and 1308 (1094) ms (medians in parenthesis), respectively. The number of analyzed epochs for these participants (in the same order) was 42, 42, 41 and 18 regarding stimulus-induced changes, and 78, 60, 32 and 46 regarding spontaneous changes, respectively. Only accurate reports were analyzed (see methods).

Analysis of electrocorticographic recordings

The exact moment that the spontaneous perceptual changes occurred is unknown, because they originated in the mind of the participants. Therefore, we aligned the epochs in time to the moment of the manual report (button press) in our first analysis. Even though the spontaneous changes were perceptual - and not sensory - in nature, the occipital recordings showed clear event-related responses in both experiments and all participants. Preceding the button press there was a broadband decrease in the power of low frequencies (3-30 Hz; theta, alpha and beta band) and a broadband increase in the power of high frequencies (50-130 Hz; higher gamma band; Figure 2-3A). A similar event-related spectral perturbation was observed for stimulus-induced perceptual changes (Figure 2-3B). In further analyses we averaged the spectral perturbations within the 3-30 Hz and 50-130 Hz bands.

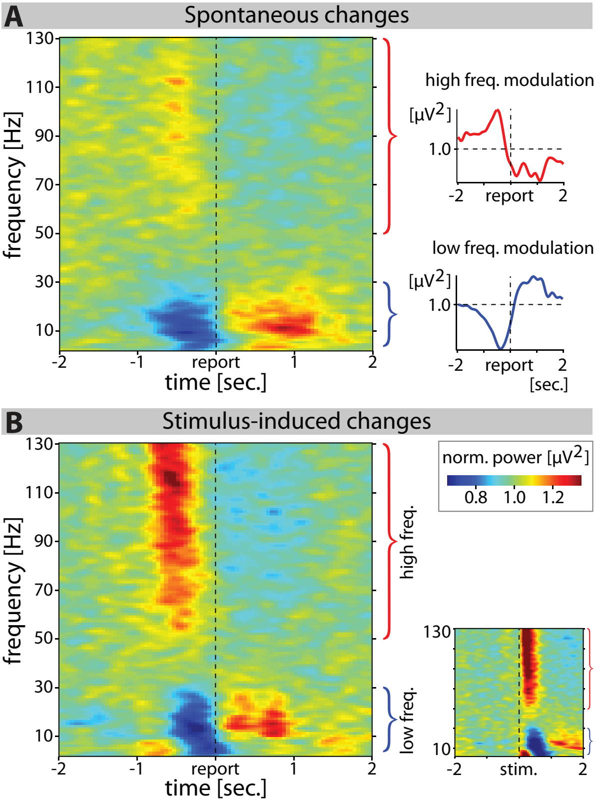

Figure 2-3. Event-related spectral perturbation recorded from occipital subdural electrodes**.**

A) Occipital event-related spectral perturbation for spontaneous perceptual changes averaged across all occipital electrodes, all participants and both experiments. The epochs were time-locked to the moment the participant reported the spontaneous change (indicated as 'report' on the time axis). Colors indicate the normalized power (see scale in upper right corner of panel B). Despite the lack of a concomitant change in the visual input, spontaneous perceptual changes were accompanied by transient modulations in the occipital cortex, a part of the brain specialized for processing visual information. Preceding the report there was an increase in the power of high frequencies (higher gamma band; see red accolade and red line graph) and a slightly later decrease in the power of low frequencies (theta, alpha en beta band; see blue accolade and blue line graph). Further analysis was performed on the average perturbation across these two broad frequency bands (as in the line graphs on the right). Norm.= normalized, freq.= frequencies, sec.= seconds.

B) Occipital event-related spectral perturbation for stimulus-induced perceptual changes (details as in panel A), resembling the perturbation for spontaneous changes presented in panel A. Small figure on the right: presents the same data time-locked to the change in the unambiguous stimulus instead of the report, indicated as 'stim.' and 'report' on the time axes, respectively. Contrary to the report-locked perturbation, the stimulus-locked perturbation is not affected by jitter in reaction times.

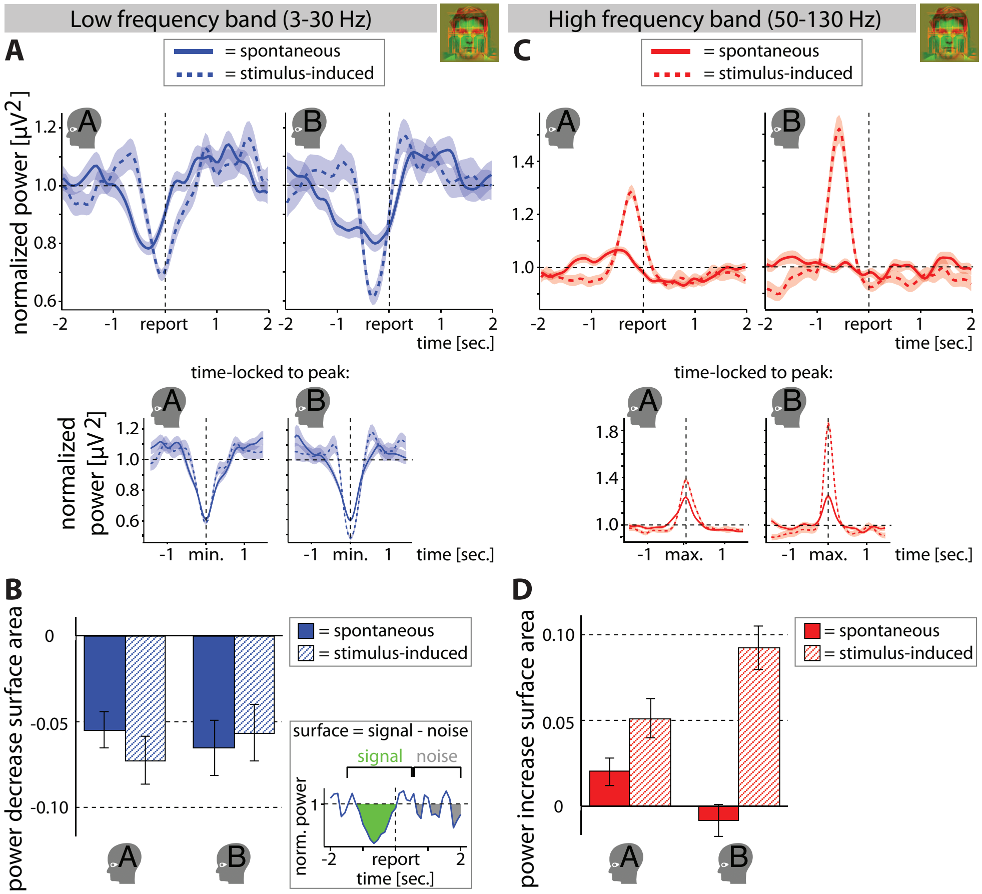

Figure 2-4. Spectral perturbations during the binocular rivalry experiment.

A) Spectral perturbations averaged across the low-frequency band of interest (3-30 Hz; see blue accolades in Figure 2-3) for participant A (graphs on the left) and participant B (graphs on the right) in the binocular rivalry experiment. Top row: perturbations time-locked to the moment a spontaneous (solid lines) or stimulus-induced (dashed lines) change was reported (indicated as 'report' on the time axis). Bottom row: perturbations time-locked to latency of the peak amplitude per epoch (minimum within time-window of interest, see methods; indicated as 'min.' on the time axis), thereby eliminating the influence of reaction-time jitter. In comparison with the report-locked perturbations (top row), the peak-locked perturbations (bottom row) were similar for spontaneous and stimulus-induced changes, suggesting that 1) jitter in reaction times influenced the report-locked perturbations and 2) the spontaneous and stimulus-induced changes were associated with a similar occipital low-frequency power decrease, even though the stimulus was changed in the latter, but not in the former. Shading indicates ±SEM. Small head icons indicate participants.

B) Surface area of the drop in low-frequency power in the binocular rivalry experiment (±SEM; see methods and schematic illustration on the right), showing that spontaneous (solid bars) and stimulus-induced (striped bars) changes were associated with a similar drop in low-frequency power. Small head icons indicate participants.

C) Spectral perturbations averaged across the high-frequency band of interest (50-130 Hz; see red accolades in Figure 2-3) for participant A (graphs on the left) and participant B (graphs on the right) in the binocular rivalry experiment. Top row: perturbations time-locked to the report. Bottom row: perturbations time-locked to latency of peak amplitude per epoch

(maximum; indicated as 'max.' on the time axis). Preceding the report a clear increase in high-frequency power for stimulus-induced changes (dashed lines) was less clear for spontaneous changes (solid lines). Editing and symbols as in panel A.
D) Surface area of the high-frequency power increase in the binocular rivalry experiment (±SEM). Editing and symbols as in panel B. The high-frequency power increase was smaller for the spontaneous than for the stimulus-induced changes.

The perturbations reflecting stimulus-induced changes appeared more spread out in time when they were time-locked to the report than when they were time-locked to the stimulus change (small inset in Figure 2-3B). This could reflect jitter in reaction times (interval between stimulus change and perceptual report of the change), affecting the report-locked and not the stimulus-locked perturbations. To assess the influence of reaction-time jitter on the averaged perturbations reflecting spontaneous changes we aligned the epochs to the latency of the peak in either the low- or high-frequency modulation before averaging across epochs (see methods; peak within time window of interest; minimum or maximum amplitude for the low- and high-frequency modulations, respectively). We compared the resulting peak-locked perturbations with the report-locked perturbations for spontaneous as well as stimulus-induced changes (Figure 2-4 and 2-5).

The report-locked perturbations for the low- and high-frequency modulations were more spread out in time for spontaneous than for stimulus-induced changes, particularly in the binocular rivalry experiment (large graphs in Figures 2-4A, 2-4C, 2-5A and 2-5C). Conversely, the drop in low-frequency power in the peak-locked perturbations was similar for spontaneous and stimulus-induced changes in both experiments (small graphs in Figures 2-4A and 2-5A), suggesting that reaction-time jitter produced the difference observed in the report-locked perturbations. Regarding the high-frequency power increase, the peak-locked perturbations were similar for spontaneous and stimulus-induced changes in the 3D-motion rivalry experiment (small graphs in Figure 2-5C), whereas in the binocular rivalry experiment they were larger for stimulus-induced than for spontaneous changes, indicating a difference between the two changes that was unrelated to reaction-time jitter (small graphs in Figure 2-4C).

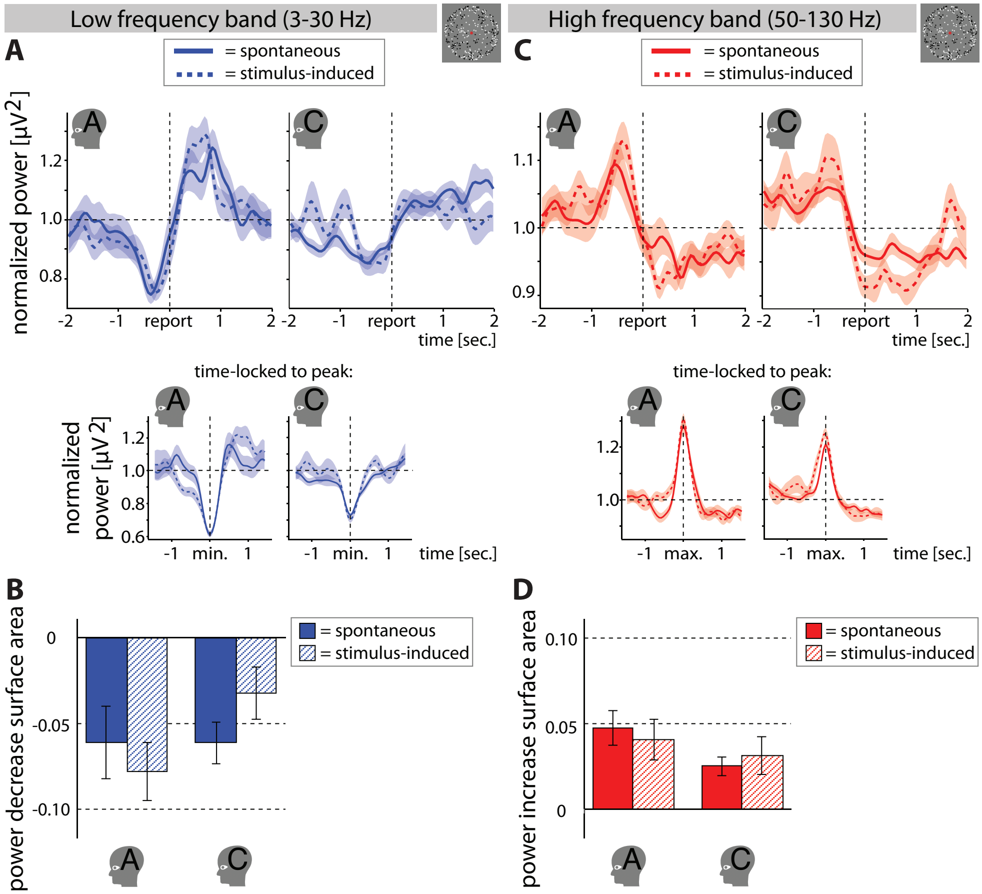

Figure 2-5. Spectral perturbations during the 3D-motion rivalry experiment**.**

A) Spectral perturbations averaged across the low frequencies of interest (see blue accolades in Figure 2-3) for participant A (graphs on the left) and participant C (graphs on the right) in the 3D-motion rivalry experiment. Report-locked and peak-locked perturbations are presented in the top and bottom row, respectively (see legend of Figure 2-4A for details). As in the binocular rivalry experiment (Figure 2-4A), spontaneous as well as stimulus-induced changes elicited a decrease in low-frequency power.

B) Surface area of the drop in low-frequency power in the 3D-motion rivalry experiment (±SEM), showing that spontaneous (solid bars) and stimulus-induced (striped bars) changes were associated with a similar drop in low-frequency power.

C) Spectral perturbations averaged across the high frequencies of interest (see red accolade in Figure 2-3) for participant A (graphs on the left) and participant C (graphs on the right) in the 3D-motion rivalry experiment. Report-locked and peak-locked perturbations are presented in the top and bottom row, respectively (see legend of Figure 2-4A for details). Spontaneous and stimulus-induced changes were associated with a similar high-frequency power increase in the 3D-motion rivalry experiment, whereas in the binocular rivalry experiment the increase was smaller for spontaneous than for stimulus-induced changes (compare with Figure 2-4C).

D) Surface area of the high-frequency power increase in the 3D-motion rivalry experiment (±SEM). Spontaneous (solid bars) and stimulus-induced (striped bars) changes were associated with a similar high-frequency power increase. Small head icons indicate participants.

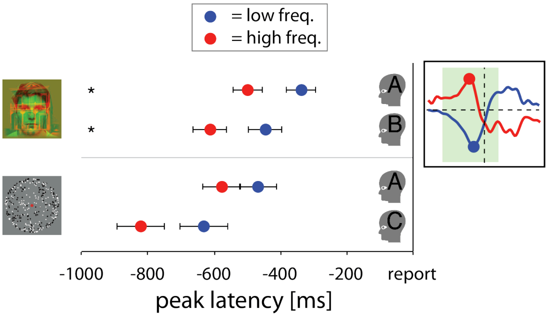

Figure 2-6. Additional characteristics of the low- and high-frequency modulations.
Average latency (±SEM) of maximum high-frequency power (red dots) and minimum low-frequency power (blue dots) within the time-window of interest (see methods and schematic illustration on the right), showing that the high-frequency power increase peaked earlier than the low-frequency power decrease. Values for spontaneous and stimulus-induced changes are averaged as they did not differ. Asterisk indicates p< 0.05.

The increase in high-frequency power peaked earlier than the decrease in low-frequency power in the binocular rivalry experiment (Figure 2-6; peak within time window of interest, see methods; effect of frequency band: both *F*> 5.6, both p< 0.02; frequency band x type of change ANOVA performed per participant). In the 3D-motion rivalry experiment the same trend was present (both *F*≤ 3.5, both p< 0.06). In both experiments there was no significant difference between spontaneous and stimulus-induced changes regarding this latency difference (frequency band x type of change: all *F*≤ 2.6, all p> 0.1).

Low-frequency power decrease

To quantify the magnitude of the low-frequency modulation independent of reaction-time jitter we calculated, per epoch, the surface area of the drop in low-frequency power and then averaged across epochs (surface area across a time window of interest relative to the report; see methods and schematic illustration in Figure 2-4B). In both experiments the surface area of the low-frequency power decrease was highly significant (type of change x participant ANOVA performed per experiment; intercept: both *F*> 11,117.7, both p≈ 0) and similar in magnitude for spontaneous and stimulus-induced changes (Figures 2-4B and 2-5B; effect of type of change: both *F*≤ 0.1, both p> 0.7; effect of participant: both *F*≤ 1.6, both p> 0.2; type of change x participant interaction: both *F*≤ 1.6, both p> 0.2). Spontaneous and stimulus-induced changes were thus associated with a similar transient drop in low-frequency power in the occipital cortex, even though the stimulus was changed in the latter but not in the former. Additional analyses showed that the similarity was widespread across electrodes and unrelated to cancelling-out of opposing effects between electrodes. When low-frequency sub-bands were tested separately, we also found no differences between spontaneous and stimulus-induced changes (bands tested: theta, 3-8 Hz; alpha, 9-13 Hz; lower beta, 14-20 Hz; higher beta, 21-30 Hz).

High-frequency power increase

The surface area of the increase in high-frequency power was similar in magnitude for spontaneous and stimulus-induced changes in the 3D-motion rivalry experiment (Figure 2-5D; type of change x participant ANOVA performed per experiment; effect of type of change: $F_{(1,133)}= 0.0$, $p= 1$; effect of participant: $F_{(1,133)}= 3.2$, $p= 0.1$; type of change x participant interaction: $F_{(1,133)}= 0.4$, $p= 0.5$; intercept: $F_{(1,133)}= 38{,}743.0$, $p\approx 0$). In the binocular rivalry experiment, on the contrary, the surface area of the high-frequency modulation was larger for the stimulus-induced than for the spontaneous changes (Figure 2-4D; effect of type of change: $F_{(1,128)}= 40.0$, $p\approx 0$; effect of participant: $F_{(1,128)}= 0.4$, $p= 0.5$). In participant A the power increase for spontaneous changes was fairly small but significant, whereas in participant B it was not significant (type of change x participant interaction: $F_{(1,128)}= 11.1$, $p= 0.001$; participant A, type of change: $F_{(1,118)}= 5.1$, $p= 0.026$; participant B, type of change: $F_{(1,100)}= 41.2$, $p\approx 0$; participant A, spontaneous changes: $t_{(77)}= 2.5$, $p= 0.015$; participant B, spontaneous changes: $t_{(59)}= -0.9$, $p= 0.4$). Analyses of the individual occipital electrodes showed that generally active electrodes in the binocular rivalry experiment were extra active for stimulus-induced compared with spontaneous changes, while in the 3D-motion rivalry experiment individual-electrode activations were similar for both changes.

Inter-electrode relations

The surface areas of the modulations across electrodes tended to correlate between spontaneous and stimulus-induced changes for all participants and for the low- as well as the high-frequency modulation, suggesting co-localization of the activations associated with spontaneous and stimulus-induced changes (Figure 2-7A, right graph). There was no such systematic relation between the low- and high-frequency modulations, indicating that electrodes with a large drop in low-frequency power not necessarily had a large increase in high-frequency power (Figure 2-7A, left graph, spontaneous and stimulus-induced changes were taken together; correlations between high-frequency power increases as is and low-frequency power decreases multiplied by -1).

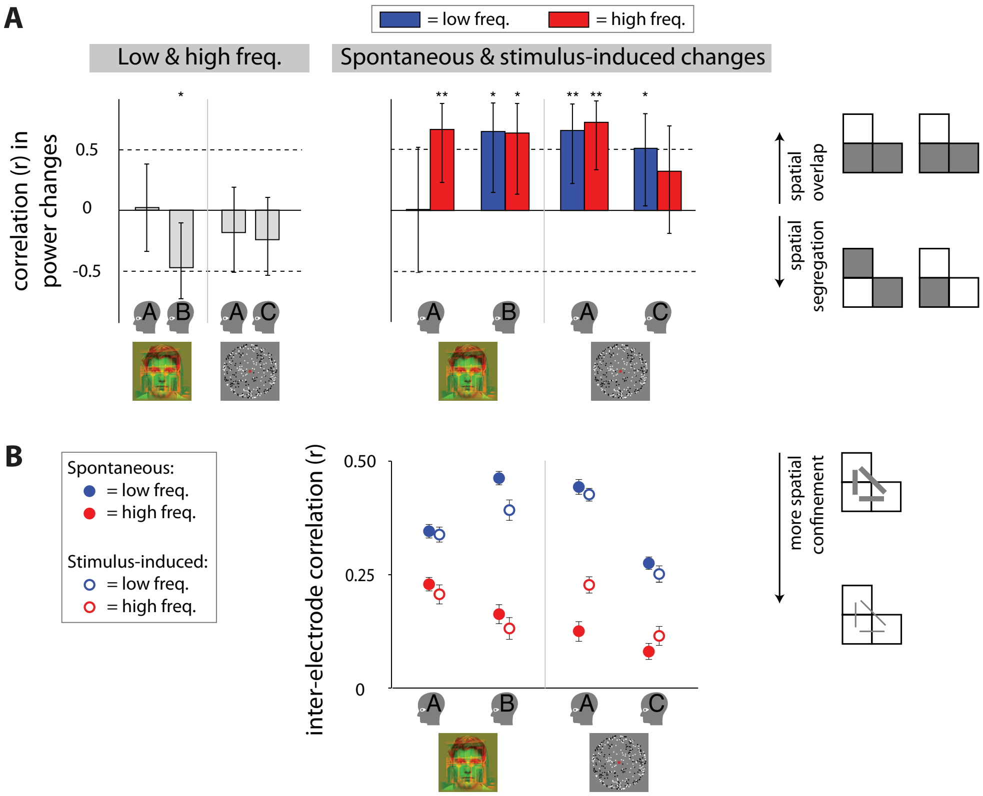

Figure 2-7. Measures of similarity in spatial organization.

A) On the left: Correlation between the low- and high-frequency modulation in the surface areas of the modulations per occipital electrode (correlation coefficients, r ±95%CI; high-frequency power increase as is, low-frequency power decrease multiplied by -1; spontaneous and stimulus-induced changes taken together). A negative correlation coefficient indicates that electrodes with a large high-frequency modulation tended to have a small low-frequency modulation. On the right: Correlation between spontaneous and stimulus-induced changes in the surface areas of the modulations per electrode. Positive correlation coefficients indicate that the pattern of activity across electrodes was similar (co-localized) for spontaneous and stimulus-induced changes (see schematic illustration on the right, icons symbolize activations of three neighboring electrodes). Miniatures of the stimuli indicate the respective experiments. Small head icons indicate the participants. Double asterisk indicates $p< 0.01$; single asterisk $p< 0.05$. Freq.= frequencies.

B) Inter-electrode correlations in the surface areas of the modulations per epoch (correlation coefficients, r ±SEM, of correlations between all possible occipital electrode pairs), showing that correlations were stronger in the low- (blue circles) than in the high- (red circles) frequency modulation. This finding was observed for spontaneous (filled circles) as well as the stimulus-induced (open circles) changes and suggests that for both changes the high-frequency modulation reflected more spatially confined activity than the low-frequency modulation. Icons on the right symbolize three electrodes with correlations (grey lines) between pairs of electrodes.

For all possible occipital electrode pairs we calculated the correlation in the surface areas of the modulations across epochs (per participant, per type of change, per frequency band). For spontaneous as well as stimulus-induced changes the inter-electrode correlations were stronger regarding the low- than regarding the high-frequency modulation, supporting the idea that high-frequency activity is more spatially confined than low-frequency activity (Figure 2-7B; type of change x frequency band ANOVA performed per participant; effect of frequency band: all $F \geq 40.4$, all $p \approx 0$).

2.5 Discussion

The present study had two main aims. Firstly, we compared the extent to which regions in the occipital cortex sensitive to visual stimulation are transiently modulated in association with spontaneous and stimulus-induced perceptual changes (i.e. 'illusory' and 'real' changes in the stimulus, respectively). Secondly, we assessed the relative roles of low- and high-frequency oscillations in these modulations. In line with previous literature, *stimulus-induced* perceptual changes were associated with a decrease in the power of low frequencies (theta, alpha, beta range) and an increase in the power of high frequencies (gamma range) in occipital cortex activity (Lachaux et al., 2005; Donner & Siegel, 2011; Tallon-Baudry & Bertrand, 1999; Tallon-Baudry, 2009; Siegel et al., 2007; Hoogenboom et al., 2006; Maier et al., 2008; Wilke et al., 2006). Interestingly, *spontaneous* perceptual changes were associated with a similar transient modulation of occipital activity (Figure 2-3), despite the fact that these perceptual changes originated in the minds of the participants and lacked a concomitant change in the visual input.

In many previous studies spontaneous perceptual changes were associated with transient responses in the parietal and frontal cortices and not the occipital cortex (see introduction). The discrepancy between the present and previous findings regarding occipital responses could relate to a difference in recording techniques, as most previous studies used scalp recordings or fMRI, whereas we used intracranial recordings in humans (Privman et al., 2007; Jerbi et al., 2009; Lachaux et al., 2012; Crone et al., 2011; but see Matsuzaki et al., 2012).

Transient decrease in low-frequency power

In the binocular rivalry experiment (Figure 2-4A) as well as the 3D-motion rivalry experiment (Figure 2-5A) we observed a transient drop in low-frequency power (3-30 Hz) preceding the report of both spontaneous and stimulus-induced perceptual changes. Following existing literature, we initially aligned the epochs to the moment that the participant reported the perceived change. In the averaged perturbations time-locked to the report, the power decrease appeared to be smaller and wider for spontaneous compared with stimulus-induced changes (similar to scalp recordings reported by Struber & Hermann, 2002). This suggests that synchronizing the epochs to the report imposed temporal uncertainty on the averaged perturbations as a result of jitter in reaction times. The perturbations associated with spontaneous changes may be affected more by such temporal uncertainty (Naber et al., 2011; Knapen et al., 2011; Kornmeier & Bach, 2006), because the transition periods between percepts can be less discrete in time for spontaneous than for stimulus-induced changes (Anstis et al., 1985; Hollins & Hudnell, 1980),

To assess the influence of reaction-time jitter, we performed two additional analyses insensitive to temporal jitter: we calculated the surface areas of the drop in low-frequency power and we re-aligned the perturbations to the peak in the observed power fluctuation before averaging across epochs (see methods). Both the surface area (Figures 2-4B and 2-5B) and the peak-locked perturbation (small graphs in Figures 2-4A and 2-5A) of the drop in low-frequency power were similar for spontaneous and stimulus-induced changes. We thus presume that the difference observed in the report-locked perturbations resulted from increased temporal uncertainty in the reports of the spontaneous compared with the stimulus-induced changes, although we cannot exclude the possibility that the neural modulations themselves were more variable in time for the spontaneous changes. We conclude that the transient drop in occipital low-frequency power was indistinguishable in magnitude between spontaneous and stimulus-induced changes. To us, this finding indicates that spontaneous changes are initiated within rather than beyond the occipital cortex.

Transient increase in high-frequency power

The occipital intracranial recordings revealed that spontaneous as well as stimulus-induced changes in perception were associated with an increase in the power of high frequencies (50-130 Hz). Previously reported scalp recordings revealed no high-frequency modulations for spontaneous changes (Struber & Herrmann, 2002; Muller et al., 1999). However, the dispersion of neural signals measured on the scalp by dura, skull, and skin may have precluded detection of local high-frequency activity in these studies (Jerbi et al., 2009; Lachaux et al., 2012; Crone et al., 2011).

In the binocular rivalry experiment the high-frequency modulation was smaller for spontaneous than for stimulus-induced changes (Figures 2-4C and 2-4D). This difference was unrelated to a difference in temporal uncertainty, because it was also observed in the surface areas of the modulations (Figure 2-4D) and in the averaged peak-locked perturbations (small graphs in Figure 2-4C). Whereas the stimulus-induced changes probably elicited a ubiquitous bottom-up response, spontaneous changes may have recruited a subset of the involved visual neurons, particularly those specialized for the features of the stimulus (de Jong et al., 2012b; Haynes & Rees, 2005), resulting in a smaller measured response when an electrode covers activated as well as silent neurons.

In the 3D-motion rivalry experiment spontaneous and stimulus-induced changes were associated with a similar high-frequency power increase (Figures 2-5C and 2-5D). Whereas in the binocular rivalry experiment a stimulus-induced change involved the actual removal of the perceived image and appearance of a new image, the stimulus-induced changes in the 3D-motion rivalry experiment were quite subtle, involving only a change in motion direction in the perceived image (Figure 2-2C). It could be that the spontaneous and stimulus-induced changes engaged the same regions sensitive to global motion and motion in depth in the 3D-motion rivalry experiment (Brouwer & van Ee, 2007; de Jong et al., 2012b; Paradis et al., 2000), hence the similar high-frequency modulations. This is explanation tentative, considering that it is difficult to infer which functional regions were sampled in the present study. Also, different results might have been obtained from parts of the occipital cortex that were not sampled.

Functional dissociation between low and high frequencies

It has often been reported that high- and low-frequency modulations reflect local and global processes, respectively (see introduction). In accordance, we found that the high-frequency modulation correlated less between occipital electrodes than the low-frequency modulation (Figure 2-7B). The high- and low-frequency modulation further differed regarding which electrodes showed a large or small modulation (Figure 2-7A), evidencing that the neural networks involved in the high- and low-frequency modulations were differently localized.

In addition to differences in spatial organization, there was also a temporal dissociation between the high- and low-frequency modulations, as the former peaked earlier than the latter (Figure 2-6; similar to findings by Wilke et al., 2006). Taking the above into consideration, we propose the following functional dissociation between the frequency bands: whereas the high-frequency modulation reflects the initiation of perceptual changes in specialized visual networks, the low-frequency modulation reflects distribution of change-related activity to a wider range of visual networks, thereby mediating the maintenance of the perceptual state. Interestingly, neural modulations reflecting (the maintenance of) the perceptual state have primarily been reported in low- and not high-frequency activity (Maier et al., 2008; Gail et al., 2004; Sandberg et al., 2014). Considering the transient nature of the current low-frequency modulation it is probably not involved in the maintenance itself, but it could instigate coordinated distributed activity needed to maintain a percept. The proposed role of the high-frequency modulation is congruent with findings that features of the visual input are more reliably reflected in high- than in low-frequency activity (see introduction).

Compatible with a distinction between local initiation and more widespread maintenance of the percepts, a previous fMRI study that decomposed spatial patterns of occipital activity reported that patterns locally in V4 corresponded with the prevalence of spontaneous changes, whereas patterns in multiple occipital regions (areas V1 up to V3) corresponded with the duration of the percepts (Donner et al., 2013). Interestingly, a previous study of intracranial recordings in monkeys reported that low-frequency modulations propagated primarily in the feedback direction in occipital visual regions, while high-frequency modulations propagated in the feedforward direction (van Kerkoerle et al., 2014), suggesting that the high-frequency modulation might govern the low-frequency modulation through feedback in the present study.

Spatial overlap between spontaneous and stimulus-induced changes

At the spatial scale of the current intracranial recordings the spontaneous and stimulus-induced changes were associated with remarkably similar and in many aspects indistinguishable transient occipital modulations. In addition, in both the binocular rivalry and 3D-motion rivalry experiment there was a spatial overlap between spontaneous and stimulus-induced changes regarding which electrodes were strongly or weakly activated (Figure 2-7A), indicating the observed modulations associated with spontaneous and stimulus-induced changes were largely co-localized.

Outstanding questions

Future investigations at a finer spatial scale are needed to gain knowledge about the neural interactions underlying the observed modulations and may reveal critical differences between spontaneous and stimulus-induced changes. Importantly, the present results suggest that such studies may restrict their search to stimulus-specific visual regions. It might be that within these regions spontaneous changes are associated with more competitive neural interactions than stimulus-induced changes, possibly through the activation of inhibitory interneurons (Blake & Logothetis, 2002; Long & Toppino, 2004).

In addition, the role of regions beyond the occipital cortex in spontaneous perceptual changes needs further investigation. Transient activations of parietal and frontal regions reported previously in association with spontaneous changes (see introduction) may not reflect the initiation of perceptual changes, but instead could be associated with cognitive processes associated with perception, such as attention, intention, introspection or perceptual uncertainty (Frassle et al., 2014; Knapen et al., 2011; Raemaekers et al., 2009; de Graaf et al., 2011). Also, following the above-mentioend idea that the observed occipital high-frequency modulation might govern the low-frequency modulation via feedback connections, additional sources within and beyond the occipital cortex could play a governing role as well.

Conclusion

Our results suggest that spontaneous changes in perception that lack a concomitant change in the visual stimulus are initiated within (rather than beyond) the visual cortex. We propose that the observed increase in occipital high-frequency power reflects the initiation of perceptual changes, whereas the drop in occipital low-frequency power that was later in time and less spatially confined reflects their distribution. Accordingly, we speculate that new percepts are initiated locally in the occipital cortex, after which perceptual change-related activity is distributed to a wider range of visual networks in order to mediate maintenance of the percept.

Chapter 3

Opposite influence of perceptual memory on initial and prolonged perception of sensory ambiguity

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3.1 Abstract

Observers continually make unconscious inferences about the state of the world based on ambiguous sensory information. This process of perceptual decision-making may be optimized by learning from experience. We investigated the influence of previous perceptual experience on the interpretation of ambiguous visual information. Observers were pre-exposed to a perceptually stabilized sequence of an ambiguous structure-from-motion stimulus by means of intermittent presentation. At the subsequent re-appearance of the same ambiguous stimulus perception was initially biased toward the previously stabilized perceptual interpretation. However, prolonged viewing revealed a bias toward the alternative perceptual interpretation. The prevalence of the alternative percept during ongoing viewing was largely due to increased durations of this percept, as there was no reliable decrease in the durations of the pre-exposed percept. Moreover, the duration of the alternative percept was modulated by the specific characteristics of the pre-exposure, whereas the durations of the pre-exposed percept were not. The increase in duration of the alternative percept was larger when the pre-exposure had lasted longer and was larger after ambiguous pre-exposure than after unambiguous pre-exposure. Using a binocular rivalry stimulus we found analogous perceptual biases, while pre-exposure did not affect eye-bias. We conclude that previously perceived interpretations dominate at the onset of ambiguous sensory information, whereas alternative interpretations dominate prolonged viewing. Thus, at first instance ambiguous information seems to be judged using familiar percepts, while re-evaluation later on allows for alternative interpretations.

3.2 Introduction

The visual input registered by our eyes is inherently ambiguous. To maintain a stable perceptual representation of the state of the world the brain has to make inferences. This means that observers continually, yet unconsciously, make perceptual choices based on ambiguous sensory information (Helmholtz, 1911). It is easily envisaged how such perceptual decision-making mechanisms may shape their performance by learning from experience (Sasaki et al., 2010; Kristjansson & Campana, 2010; Kourtzi, 2010). In this study we investigated how our current perceptual interpretation of the outside world is influenced by previous perception. In order to dissociate prior *perception* from prior *stimulation* we used ambiguous visual input, i.e. stimuli that allow for several, mutually exclusive ('rivalrous'), perceptual interpretations (example in Figure 3-1A). Under these conditions of ongoing ambiguity in the visual input we tested whether perceptual decisions from the recent past influence the detailed time-course of current perceptual decisions.

Visual input is generally associated with a definite perceptual state, even when the input is ambiguous. At the onset of an ambiguous stimulus only one of the possible perceptual interpretations is perceived ('rivalry at onset'). Subsequently, a process of continuous perceptual alternations between the different interpretations sets in ('ongoing rivalry'). Although these two aspects of rivalry are believed to involve the same neural populations, the processes of perceptual decision-making exhibit several differences. For example, the frequency of perceptual alternations is much lower when short presentations of an ambiguous stimulus are interleaved with blank intervals than when a single, longer-lasting, presentation of the stimulus is viewed continuously (Brascamp et al., 2009). An intermittent paradigm can be thought of as the repeated occurrence of rivalry at onset, while a continuous paradigm reflects the mechanisms of ongoing rivalry. Other differences between rivalry at onset and ongoing rivalry concern the influence of perceptual biases (Carter & Cavanagh, 2007; Hupé & Rubin, 2003) and the influence of attention (Chong et al., 2005; Chong & Blake, 2006).

The slow frequency of perceptual alternations during intermittent viewing is often referred to as 'perceptual stabilization' and is argued to reflect perceptual memory (Orbach et al., 1963; Leopold et al., 2002; Pearson & Brascamp, 2008). Here we utilized this phenomenon to build-up minutes-long perceptual experience with only one of the interpretations of an ambiguous stimulus, while the other perceptual interpretation was suppressed. This enabled us to investigate the influence of biased perceptual experience on current perception of ambiguous visual input. The buildup of biased perceptual experience would not have been possible using continuous presentation of an ambiguous stimulus, because in such a paradigm ongoing perceptual alternations occur. Perceiving such alternations can result in percept-invariant modulations of perception, for example an increase or decrease in perceptual alternation-rate (e.g. Cohen, 1959; Suzuki & Grabowecky, 2007; Long et al., 1992), but it does not reveal percept-specific effects of perceptual experience. An alternative method to bias perceptual experience is to use pre-exposure to an unambiguous stimulus. However, we preferred ambiguous pre-exposure, because the features used to bias an unambiguous stimulus may induce feature-specific neuronal adaptation independent of their intended perceptual effect. In the case of perceptually biased, i.e. stabilized, ambiguous pre-exposure any percept-specific 'memory' or adaptation is related to the perceptual interpretation of the information and not to an imbalance in stimulation.

We investigated the influence of minutes-long, perceptually stabilized, ambiguous pre-exposure on subsequent continuous perception of the same stimulus. Earlier studies have investigated the perceptual dynamics within a period of intermittent presentation (e.g. Pearson & Brascamp, 2008; Klink et al., 2008) or reported the first couple of seconds/percepts after the onset of rivalry (Brascamp et al., 2008; Pastukhov & Braun, 2008), but such short presentations of the stimulus mostly reflect the dynamics of rivalry at onset. A detailed analysis of the durations of the two percepts during ongoing rivalry can reveal the intimate properties of prolonged ambiguous perception. In line with the phenomenon of perceptual stabilization, which has been attributed to perceptual memory (Orbach et al., 1963; Leopold et al., 2002; Pearson & Brascamp, 2008), we may expect a facilitation of the pre-exposed percept during ongoing rivalry, for example reflected in an increase in the average duration of the pre-exposed percept (facilitation hypothesis, Figure 3-2B).

Previous studies into *rivalry at onset* have reported either facilitation or suppression of the pre-exposed percept. Facilitation has been found particularly after ambiguous or faint/brief unambiguous pre-exposure, or with long intervals between the pre-exposure and the test stimulus (Orbach et al., 1963; Leopold et al., 2002; Long et al., 1992; Klink et al., 2008; Kanai & Verstraten, 2005; Brascamp et al., 2007; Daelli et al., 2010; Pearson & Clifford, 2005). Suppression of the pre-exposed percept, reflected in the tendency to see the alternative percept, is common with short intervals between the ambiguous pre-exposure and the test stimulus (e.g. Klink et al., 2008) or after strong unambiguous pre-exposure (Virsu, 1975; Harris, 1980; Petersik et al., 1984; Long & Toppino, 2004). It has been attributed to ‘adaptation’, ‘satiation’ or ‘neural fatigue’ (e.g. Hochberg, 1950; Long & Toppino, 2004; Thompson & Burr, 2009). Accordingly, an alternative hypothesis regarding our paradigm is that the average duration of the pre-exposed percept is decreased during ongoing rivalry, rather than increased, after ambiguous pre-exposure (suppression hypothesis, fig, 2B). We expect the duration of the alternative percept to be unaffected by pre-exposure, because this percept is not seen during the pre-exposure (‘no transfer’-hypothesis, Figure 3-2B). However, manipulations of one of the percepts can affect the duration of the opposite percept (second proposition of Levelt, 1966; see also Brascamp et al., 2006), thus we should consider the possibility that the effect of pre-exposure transfers to the alternative percept (Leveltian hypothesis, Figure 3-2B).

Our results indicate that the pre-exposed percept was facilitated during rivalry at onset, but was not much affected during ongoing rivalry. Interestingly, the duration of the alternative percept, i.e. the percept that was suppressed during intermittent pre-exposure, increased during subsequent ongoing rivalry, supporting the Leveltian hypothesis (illustrated in Figure 3-2B). This effect occurred similarly for ambiguous structure-from-motion and binocular rivalry. During binocular rivalry the eye-bias was not affected by pre-exposure. In additional experiments we elaborate on the effects of specific characteristics of the pre-exposure, such as the comparison between ambiguous and unambiguous pre-exposure.

3.3 Methods

Participants

The number of participants was 10, 6, 13, and 6 for Experiments 1, 2, 3, and 4, respectively. Seven participants participated in more than 1 experiment. The remaining 18 participated only in 1 experiment. Most participants (20 out of 25) had no experience with psychophysical experiments. Participants who reported particular difficulty in perceiving the three-dimensional structure of the stimulus or differentiating the two possible percepts were excluded (8 out of 33). All participants gave verbal informed consent before participation and had normal or corrected to normal vision. All experiments were conducted in agreement with (not specifically approved by) the ethics and safety guidelines of the Science Faculty of Utrecht University.

Experiment 1: Ambiguous pre-exposure

Stimulus and task

We used a structure-from-motion stimulus (Braunstein, 1977; Wallach & O'Connell, 1953) consisting of 450 leftward or rightward moving dots (each 0.077° in diameter). The dots represented random points on the surface of a virtual globe (5.0° in diameter). The globe rotated around its vertical axis with a period of 7.8 seconds. Stimuli were created using custom software and presented in the center of a gray computer-screen (75 Hz LaCie monitor, 1600x1200 pixels, a gamma shaped luminance correction was applied). The direction of rotation was ambiguous (leftward or rightward), because no depth cues differentiated the rightward moving surface from the leftward moving surface (Figure 3-1A). Observers alternately perceived either of two possible percepts for several seconds at a time. Participants were instructed to maintain strict fixation on a static green dot (0.18° in diameter) placed in the center of the globe. Head movements were constrained using a chin-rest. Participants indicated the direction of motion of the surface perceived to be in front by holding down one of two corresponding buttons on a keyboard, and releasing the buttons when the stimulus disappeared or when they could not differentiate the front from the back surface. During the intermittent presentations the participants were required to respond to every single presentation of the stimulus. Without explaining why, participants were informed that the rotation directions they were going to see were unpredictable and that their percepts were never 'incorrect'.

Upon debriefing afterwards most participants reported that they had been unaware of the perceptual ambiguity of the stimulus.

Procedure

Each trial consisted of two phases. In the pre-exposure phase the ambiguously rotating globe was presented intermittently to stabilize perception and build up 'experience' with one of the two possible percepts (duration of one presentation of the globe: 720 ms; duration of intervening blank periods: random value between 800 and 1200 ms). In the following test phase the ambiguously rotating globe was presented continuously to test the effect of the pre-exposure on prolonged viewing (Figure 3-1B). There were five conditions with distinct pre-exposure durations, being 16, 31, 64, 130, and 260 seconds

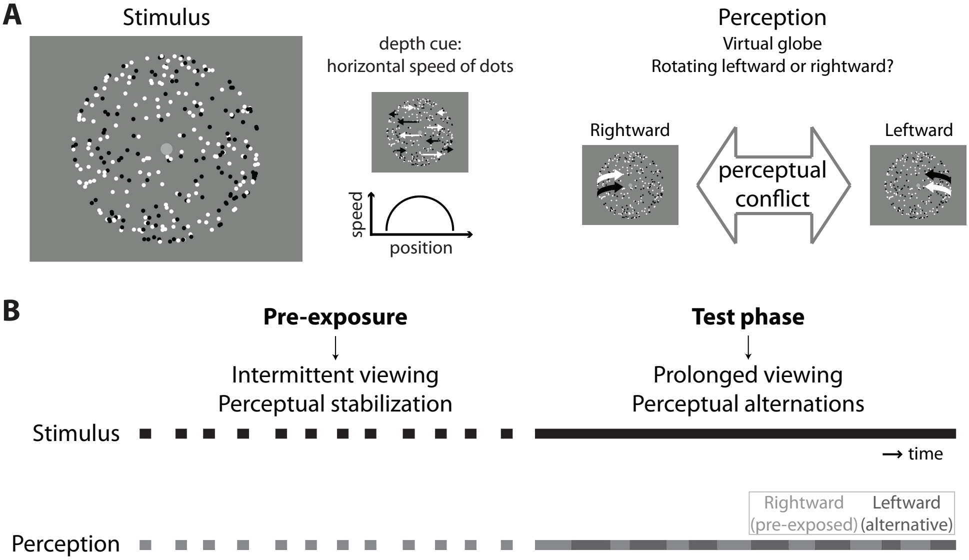

Figure 3-1. Stimulus and paradigm.

A) The stimulus consisted of black and white leftward and rightward moving dots placed such that they represented points on the surface of a virtual globe. Depth was signaled by the sinusoidal speed profile of the dots, i.e. the dots moved faster as they were closer to the vertical meridian of the globe, thereby creating the illusion of a 3-dimensional globe in depth. The virtual globe was perceived rotating around its vertical axis, but the direction of the rotation was ambiguous: either the rightward or the leftward moving surface was perceived in front of the other surface.

B) A trial started with an intermittent presentation period of variable duration (up to 4.3 minutes) during which the ambiguous globe perceptually stabilized. Subsequently, the ambiguous globe was presented continuously for a prolonged duration (up to 10 minutes). During this period perceptual alternations occurred every few seconds. The stabilized percept is referred to as the 'pre-exposed' percept throughout this manuscript. We investigated the effect of the pre-exposure on the durations of the pre-exposed and alternative percept, during continuous test period.

(which is 0.3, 0.5, 1.1, 2.2, and 4.3 minutes, respectively). The corresponding durations of the test phase were 1.2, 1.7, 2.7, 5.0, and 10.1 minutes, respectively. The durations of the test phase were based on pilot experiments. These pilot experiments revealed no cyclic or late effects of pre-exposure after the effect seen in the beginning of the test phase. Two baseline measurements were added that lacked the pre-exposure phase (duration of test phase: 5.0 and 10.1 minutes; data were analyzed in conjunction). Most participants completed 4 trials per condition. Some participants completed fewer trials due to reduced availability of the participant or because of technical issues (on average 3.9 trials were completed). Of the completed trials a total of 4.0% was excluded from the analysis. Inclusion criteria for trials were: 1) during the pre-exposure phase one percept should be seen at least three times more often than the other percept, i.e. there should have been proper perceptual stabilization, and 2) during the pre-exposure as well as the test phase the subject should have reported either one of the two possible percepts in at least 75% of the time that the stimulus was displayed (subjects refrained from responding when they could not distinctly identify the rotation direction of the globe).

Experiment 2: Unambiguous pre-exposure

The pre-exposure phase of each trial (lasting 260 seconds / 4.3 minutes) contained either an ambiguous, a 'monocular-unambiguous' or a 'binocular-unambiguous' globe, while the test phase (lasting 10.1 minutes) always contained an ambiguous globe (Figure 3-3A). The unambiguous globes were identical to the ambiguous globe, with the exception that cues were added to indicate an ordering in depth of the leftward and rightward moving dots. For the binocular-unambiguous globes we used *disparity*, a binocular depth cue. With a mirror stereoscope two slightly different images were presented to the two eyes, mimicking the different viewing angles that the two eyes would have on a globe in depth. The monocular-unambiguous globes were viewed with both eyes, but contained only monocular depth cues: 1) *contrast imbalance*: the contrast between the dots and the background was halved for the back surface of the globe compared to the front surface of the globe; 2) *size imbalance*: the size of the dots varied with virtual depth (between 0.051° and 0.198° in diameter, smaller dots on the back surface). These manipulations reliably disambiguated the rotation direction of the globe, as was confirmed by the responses of the participants. The experiment consisted of the two described unambiguous conditions, one ambiguous condition and a baseline condition. The participants completed 3 or 4 trials per condition (3.6 trials on average) of which 3.5% was excluded from the analysis. Inclusion criteria were those described for Experiment 1 and, additionally, perception of the unambiguous globes should stabilize into the percept intended by the disambiguation. All other characteristics of Experiment 2 were the same as those of Experiment 1.

Experiment 3: Intermittent and continuous pre-exposure

The pre-exposure phase of each trial consisted of either intermittent presentation, like in Experiments 1 and 2, or continuous presentation. The total presentation duration of the globe was the same for the intermittent and the continuous pre-exposure procedure, i.e. the sum of all short presentations during the intermittent procedure (which took 64 seconds / 1.1 minutes, including the blanks) equaled the duration of one long presentation (of 27 seconds / 0.45 minutes) during the continuous procedure (Figure 3-4A). As stabilization cannot be achieved with continuous presentation of the ambiguous stimulus, only the monocular-unambiguous and binocular-unambiguous globes (as described for Experiment 2) were used in the pre-exposure phases of this experiment. There were four experimental conditions (disambiguation method *x* stabilization procedure) and one baseline condition. The test phase of each trial always contained an ambiguous globe and took 2.7 minutes. From experiment 1 we knew that the effect of pre-exposure is smaller when the duration of pre-exposure is smaller. In anticipation of the smaller effect size we used more subjects and more trials. Most participants completed 8 trials per condition (occasionally less, 7.9 trials on average). Based on the inclusion criteria described above 7.0% of the trials was excluded from the analysis.

Experiment 4: Pre-exposure in binocular rivalry

In this experiment we tested the effect of pre-exposure on two orthogonal black-and-white grating patterns, each grating presented to one eye. When two conflicting images are presented to the two eyes observers perceive only one of them at any given time (Levelt, 1966). We used sine-wave gratings of 1.95 cycles per degree that were titled 45 degrees from vertical to either the left or right and subtended a circular patch of 1.4° in diameter. Participants were instructed to fixate on the centre of the patch (Figure 3-5A). To enable proper alignment of the eyes a binocular pattern of lines was presented in the periphery of the stimulus. For the individual participants the stimulus and blank durations during intermittent viewing were based on psychophysical pilot-tests (to ensure perceptual stabilization) and averaged to 625 ms and 1581 ms, respectively. The very first intermittent stimulus presentation lasted 8000 ms in all participants, because pilot work showed this reduced the occurrence of mixture percepts (piecemeal combinations of both gratings). There was a baseline condition and two experimental conditions with a pre-exposure duration of either 30 or 150 seconds (which is 0.5 or 2.5 minutes, respectively). The test phase of each trial lasted 50 seconds. Per trial it was randomly determined which grating (leftward or rightward tilted) was presented to which eye. Additionally, in 50% of the trials in the experimental conditions the grating stimuli were swapped between the eyes in the test phase compared to the pre-exposure phase. In this way the grating corresponding to the stabilized *percept* was either in the stabilized *eye* or in the other eye during the second phase. As a consequence, averaging the trials with and without a swap yielded the effect of *percept*-stabilization per se, without any effect of *eye*-stabilization. All other characteristics of Experiment 4 were the same as those of Experiment 1. The participants usually completed 6 trials per parameter-settings, which amounts to 24 trials per condition (occasionally less were completed, 23.4 on average), since there were 4 parameter-settings (being: all combinations of swap/nonswap and leftward/rightward grating in left eye). Based on the criteria described above 4.3% of the trials was excluded from the analysis.

Analysis of percept durations

The durations of the percepts were derived from the recorded button presses and, considering the generally skewed distribution of percept-durations, were log-transformed (logarithm to base 10) before averaging to avoid a disproportionate contribution of excessively long percepts. Idiosyncratic (subject-specific) bias in the occurrence of the leftward and rightward percepts was taken into account by calculating a weighted average of the data from the baseline condition (without pre-exposure). The purpose of the weighing was to make sure that each percept (leftward or rightward) is counted as 'pre-exposed' equally often in the baseline condition and the pre-exposed conditions, so that the idiosyncratic bias between the ‘pre-exposed’ and ‘alternative’ percept, if any, was visible in the baseline condition. For example, if in 75% of the trials with pre-exposure (3 out of 4) the leftward percept was stabilized/pre-exposed during the intermittent phase, the weights of the leftward and rightward percept of the baseline condition were 0.75 and 0.25, respectively. The baseline measure was calculated per percept and per condition (and per eye for the grating stimulus in Experiment 4), for each participant individually. Statistical testing was done using a

Greenhouse-Geisser corrected repeated-measures analysis of variance (ANOVA) (unless indicated otherwise). For all tests a two-tailed α of 0.05 was adopted.

Analysis of percept predominance

The predominance of the alternative percept within a given time-window was calculated as the total time spent seeing the alternative percept divided by the total time perceiving any percept (= alternative / (pre-exposed+alternative)). Periods in which neither of the two response buttons were pressed were thus excluded from the analysis. The statistical testing and definition of the baseline measure were the same as for the percept durations.

3.4 Results

The present study was designed to test whether pre-exposure to a perceptually stabilized ambiguous stimulus modifies the perception of ongoing ambiguity in visual information (Figure 3-1). We attempted to build-up perceptual experience for one of two interpretations of an ambiguously rotating globe (rightward or leftward rotation) by interleaving short presentations with blank periods, which stabilized the perception of the globe. Only trials with proper stabilization (see methods for definition) were included in further analysis of the data (being 97.1%, 93.8%, 96.6% and 93.9% of the trials in Experiments 1, 2, 3 and 4, respectively). To preview our main result: during subsequent continuous viewing of the ambiguous globe the durations of the pre-exposed percept were comparable to a situation without pre-exposure, whereas the durations of the alternative percept were much increased.

Experiment 1: Ambiguous pre-exposure

We varied the amount of pre-exposure by changing the duration of the intermittent period. During this period the same percept was seen repeatedly at almost all of the presentations of the stimulus (97.5%, 99.4%, 97.6%, 97.7% and 97.2% of the presentations for the extra short to extra long pre-exposures, respectively). Regardless of the duration of the pre-exposure the tendency to perceive the pre-exposed percept at the onset of the test phase was stronger after pre-exposure (96.7%, 95.0%, 100%, 85.8%

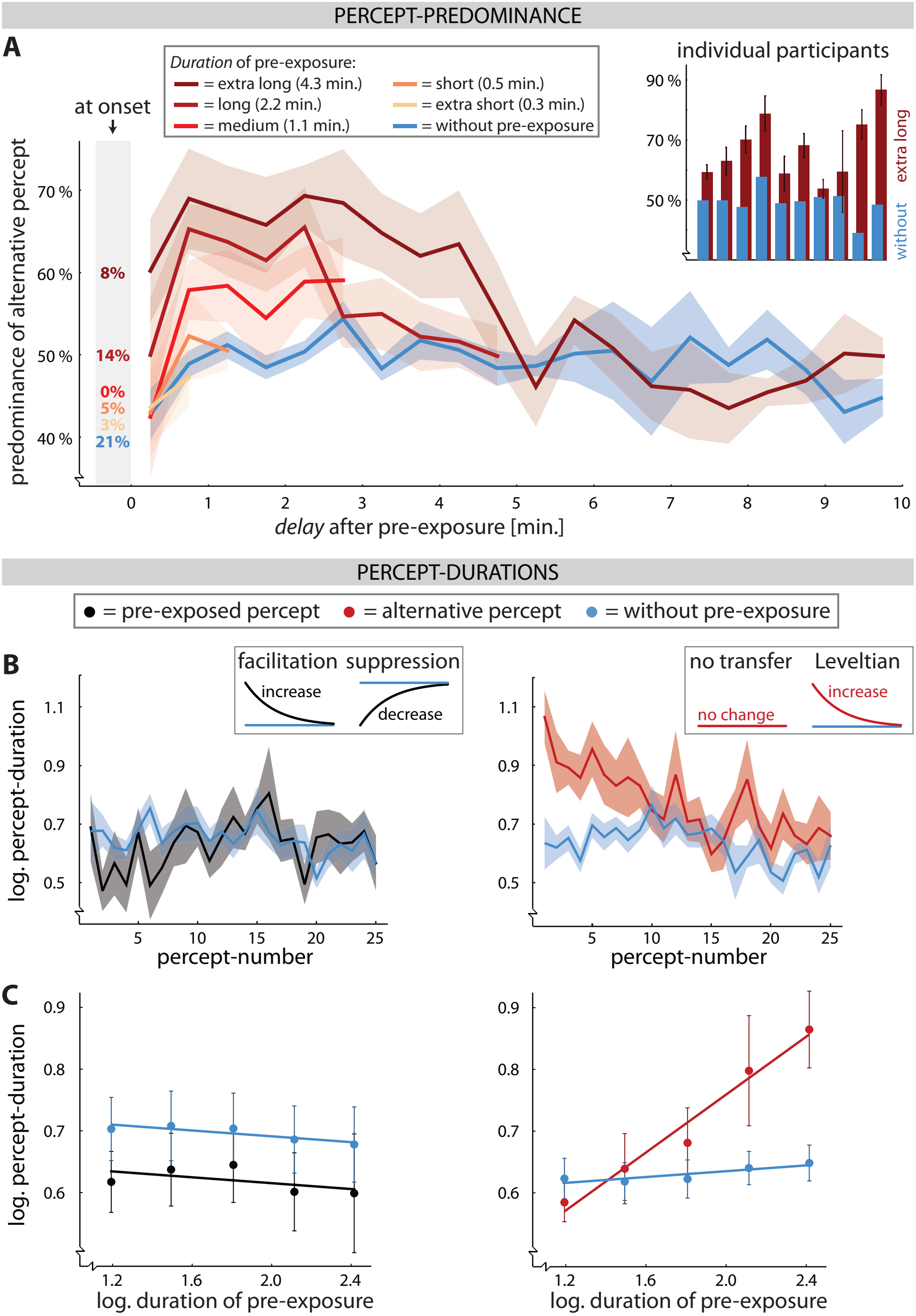
PERCEPT-PREDOMINANCE
A
Duration of pre-exposure:
= extra long (4.3 min.)
= long (2.2 min.)
= medium (1.1 min.)
= short (0.5 min.)
= extra short (0.3 min.)
= without pre-exposure
at onset
individual participants
90 %
70 %
50 %
extra long
without
predominance of alternative percept
70 %
60 %
50 %
40 %
8%
14%
0%
5%
3%
21%
0
1
2
3
4
5
6
7
8
9
10
delay after pre-exposure [min.]
PERCEPT-DURATIONS
● = pre-exposed percept
● = alternative percept
● = without pre-exposure
B
facilitation
suppression
increase
decrease
no transfer
Leveltian
no change
increase
log. percept-duration
1.1
0.9
0.7
0.5
5
10
15
20
25
percept-number
C
0.9
0.8
0.7
0.6
1.2
1.6
2.0
2.4
log. duration of pre-exposure

Figure 3-2. Results of Experiment 1: Ambiguous pre-exposure.
A) Predominance of the alternative percept at the onset of the test phase (numbers in grey shading reflect identity of the first percept) and during subsequent ongoing rivalry (±SEM; width of time-bins is 30 sec.) in five conditions with increasing duration of the pre-exposure (from *yellow* to *dark red*). During continuous viewing the predominance of the alternative percept was larger after longer pre-exposure durations and decreased over time. Such an effect was not present at the onset of the test phase. The *blue* line reflects the averaged baseline measure (without pre-exposure; statistics reported in the text were done on the individual baseline measures). Inset on the top right: Predominance of the alternative percept for individual participants after a pre-exposure period lasting 4.3 minutes (predominance over a time-window of 0.5 to 3.5 minutes after pre-exposure, which was the period in which the pre-exposure condition differed from the baseline measure).
B) The average duration (±SEM) of the first to the 25th percept without pre-exposure (*blue*) and after 4.3 minutes of pre-exposure (pre-exposed percept in *black*, left graph; alternative percept in *red*, right graph). The duration of the pre-exposed percept was not increased, even while this percept was facilitated in the sense that it was likely to occur at stimulus onset. The results for the pre-exposed percept resemble the suppression hypothesis (proposing a 'fatigue-like' effect) more than the facilitation hypothesis (proposing a 'memory-like' effect) (see inset in left graph). Although the alternative percept was not seen during pre-exposure, its duration shows a clear increase after pre-exposure, which might relate to Levelt's 2nd proposition (Levelt, 1967).
C) The average duration (±SEM) of the percepts that occurred within 1.5 minutes after the pre-exposure (pre-exposed percept in *black*, left graph; alternative percept in *red*, right graph) or within the first 1.5 minutes of the condition without pre-exposure (*blue*). Data are shown for five different durations of the pre-exposure. The duration of the alternative percept increased when the duration of the pre-exposure increased, whereas the duration of the pre-exposed percept remained unchanged.

and 91.7% of trials for the extra short to extra long pre-exposure durations, respectively) than without pre-exposure (79.2%, this baseline value is also relatively high due to relatively large idiosyncratic biases, Figure 3-6B).

The predominance of the alternative percept during the test phase was calculated in successive time-bins with a width of 30 seconds (Figure 3-2A). The predominance was defined as the percentage of time that the percept was seen within the time-bin. From 0.5 till 3.5 minutes after extra long pre-exposure (4.3 minutes) the predominance of the alternative percept was significantly larger than the baseline measure (time-bins 2-5 and 7: all $t>3.0$, all $p< 0.05$; time-bin 6 was marginally significant: $t=2.2$, $p= 0.06$). During this time-window the increase in predominance of the alternative percept was visible in the data of every individual participant that we tested (Figure 3-2A, right graph). The effect of pre-exposure was not significant in the first time-bin, presumably because of the first percept at the onset of the test-phase was almost invariably the one seen during intermittent presentation.

After long pre-exposure (2.2 minutes) the predominance of the alternative percept was increased in a time-window ranging from 0.5 till 2.5 minutes (time-bins 2-5: all $t> 2.8$, all

$p < 0.05$) and after medium-length pre-exposure (1.1 minutes) this was true for a time-window spanning 0.5 till 1.0 minutes (time-bin 2: $t = 2.5$, $p < 0.05$). The effect of pre-exposure thus lasted longer when the pre-exposure itself took longer (1.0, 2.5 and 3.5 minutes after a pre-exposure of 1.1, 2.2 and 4.3 minutes, respectively; Figure 3-2A, left graph). Additionally, the magnitude of the effect depended on the duration of the pre-exposure. In a time-window ranging from 0 till 2.5 minutes after pre-exposure (all $F > 4.3$, all $p < 0.05$) the longer pre-exposure durations resulted in a larger predominance of the alternative percept and this trend was also visible in a time-window ranging from 2.5 till 4 minutes after pre-exposure (all $F > 3.4$, all $p \leq 0.08$). Thus, the pre-exposed percept was reliably seen at the onset of the test phase for all pre-exposure durations, whereas the alternative percept predominated during continuous viewing. The magnitude and duration of the predominance of the alternative percept increased when the duration of pre-exposure was longer (Figure 3-2A).

To see what the influence of pre-exposure is on the duration of the perceptual epochs we analyzed the individual durations of the pre-exposed and alternative percept after extra-long exposure to intermittent presentation (4.3 minutes; fig 2B and 2C). To avoid a disproportionate contribution of excessively long percepts we further analyzed the logarithmic transformation of the percept durations. Compared to a condition without pre-exposure, continuous viewing after pre-exposure was characterized by long durations of the alternative percept, whereas the duration of the pre-exposed percept was not much affected. The duration of the alternative percept was longest shortly after pre-exposure and gradually decayed to baseline afterwards (Figure 3-2B, right graph; 1st-5th occurrence of the alternative percept: all $t > 2.6$, all $p < 0.05$). For the pre-exposed percept there was a trend toward a slight decrease in duration compared with baseline (Figure 3-2B, left graph; only significant for 2nd and 6th occurrence of the pre-exposed percept: both $t \leq -2.6$, both $p < 0.05$; see methods for definition of baseline). In a pilot experiment we used a pre-exposure duration of 2.2 minutes and a test period of 15 minutes and we found no late or cyclic effects of pre-exposure after this initial effect starting early in the test-phase.

To investigate how the modulation of the percept duration depended on the duration of the pre-exposure we compared the average of all percepts ending within 1.5 minutes after pre-exposure across the different pre-exposure durations. Within this time-window the effect of pre-exposure was maximal for all pre-exposure durations (Figure 3-2A). A 2-way repeated-measures ANOVA over *pre-exposure duration* and *condition* (i.e. with/without pre-exposure) revealed that the decrease in the duration of the pre-exposed percept was not significant ($F_{(1,9)}$= 3.3, p= 0.1; Figure 3-2C). Also, the duration of the pre-exposed percept was not modulated by the duration of the pre-exposure (main effect and interaction effect were not significant: both $F \leq 0.7$, both $p \geq 0.6$). A least-squares repeated-measures regression confirmed that the duration of the pre-exposed percept was not influenced by the duration of the pre-exposure (Figure 3-2C, left graph; slope= -0.02, t= -0.4, p= 0.3; slope for baseline measure: -0.02, t= -1.0, p= 0.2).

For the duration of the alternative percept, on the other hand, a 2-way repeated-measures ANOVA revealed a significant interaction effect ($F_{(2.4,\,21.9)}$= 4.6, $p < 0.05$; Figure 3-2C, right graph). Further testing showed that the duration of the alternative percept changed with the duration of the pre-exposure ($F_{(2.1,\,19.1)}$= 6.1, $p <= 0.01$), while the baseline measure did not ($F_{(1.4,\,12.7)}$= 0.8, p= 0.4). A repeated-measures regression indicated that the duration of the alternative percept increased with the duration of the pre-exposure in a near-linear fashion (slope= -0.23, t= 5.4, $p < 0.001$; slope for baseline measure: 0.02, t= 1.0, p= 0.2). There was thus no evidence of saturation of the effect with longer durations of pre-exposure.

Taken together, the results of Experiment 1 revealed a functional link between perceptual stabilization of an intermittently presented ambiguous stimulus and later continuous viewing of the same stimulus: the percept that was suppressed during intermittent viewing (i.e. rivalry at onset) predominated during continuous viewing. The time-span and strength of the effect on ongoing rivalry (but not the effect on rivalry at onset) depended on the amount of prior exposure to the perceptually stabilized stimulus (Figure 3-2).

Experiment 2: Unambiguous pre-exposure

The effects of pre-exposure found in Experiment 1 could reflect an influence of previous perceptual state, i.e. the content of perceptual awareness, or they could be specifically related to perceptual decision-processes under conditions of visual ambiguity. To differentiate these two factors we compared ambiguous pre-exposure with unambiguous pre-exposure. In this latter condition the perceptual state is the same, but

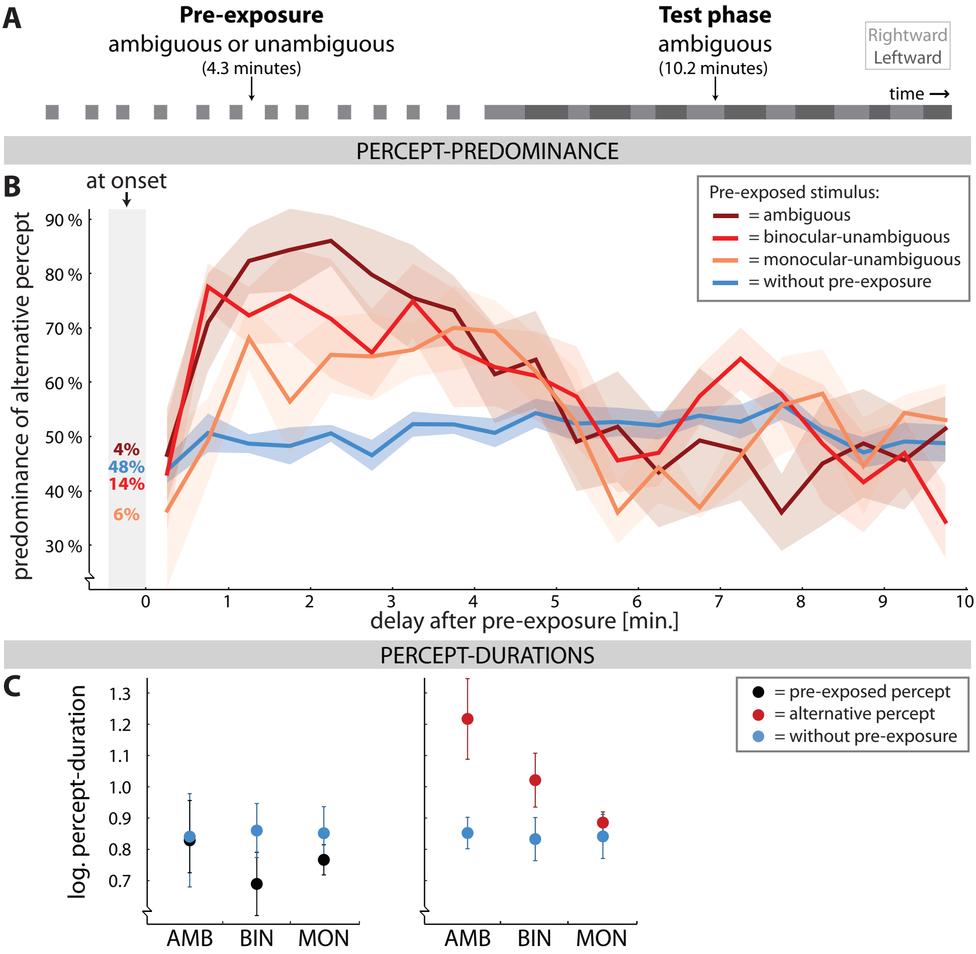

Figure 3-3. Paradigm and results of Experiment 2: Unambiguous pre-exposure.

A) The paradigm. The pre-exposure period had a fixed duration (4.3 minutes) and contained either an ambiguous globe, a globe disambiguated using binocular depth-cues (disparity) or a globe disambiguated using monocular depth-cues (contrast- and size-imbalance). The subsequent test period always contained an ambiguous globe.

B) The predominance of the alternative percept at the onset of the test phase (numbers in grey shading) and during subsequent ongoing rivalry (±SEM; bin-width: 30 sec.) in the condition without-pre-exposure (*blue*; averaged baseline measure) and after ambiguous (*dark red*), binocular-unambiguous (*red*) and monocular-unambiguous (*orange*) pre-exposure. After pre-exposure the predominance of the alternative percept was increased during continuous viewing (but not at onset) in all 3 conditions. This increase was successively larger for the monocular-unambiguous, binocular-unambiguous and ambiguous condition.

C) The average duration (±SEM) of the percepts that occurred between 0.5 and 4.5 minutes after pre-exposure (pre-exposed percept in *black*, left graph; alternative percept in *red*, right graph; no pre-exposure in *blue*). The increase in the duration of the alternative percept was successively larger when the pre-exposed stimulus was monocular-unambiguous (MON), binocular-unambiguous (BIN) or ambiguous (AMB). The slight decrease in the duration of the pre-exposed percept did not significantly differ between the 3 conditions.

it is determined by exogenous stimulus manipulations as opposed to endogenous decision-making mechanisms. We used an ambiguous stimulus in all test phases, but in the intermittent pre-exposure phase we presented either one of three stimuli: an ambiguous globe, a globe disambiguated with disparity ('binocular-unambiguous') or a globe disambiguated with a contrast- and size-imbalance ('monocular-unambiguous') (Figure 3-3A). These three cases were similar with respect to the stabilization of perception during pre-exposure (99.2%, 99.8% and 99.5% of the presentations, respectively), as well as the tendency to perceive the pre-exposed percept at the onset of the test phase (94.4%, 86.1%, 95.8%, respectively, compared with 51.9% in the condition without pre-exposure).

After ambiguous as well as unambiguous pre-exposure the predominance of the alternative percept (calculated per 30 seconds) was increased compared with the baseline condition without pre-exposure (Figure 3-3B). The time-span of this effect overlapped between the three different pre-exposure stimuli (Ambiguous ⇒ time-bins 3-6: all $t > 3.1$, all $p < 0.05$; Binocular-unambiguous ⇒ time-bins 2-4 and 7: all $t > 3.3$, all $p < 0.05$; time-bins 5-6 were marginally significant; Monocular-unambiguous ⇒ time-bins 3, 8 and 9: all $t > 2.6$, all $p < 0.05$; time-bins 5-7 were marginally significant; time-bin 14 showed significant decrease: $t = -9.5$, $p < 0.001$).

From 0.5 till 4.5 minutes after pre-exposure (time-bins 2-9) there were significant increases in the predominance of the alternative percept for at least one of the three pre-exposure stimuli. We performed a repeated-measures ANOVA over this time-window and found a significant main effect of the pre-exposure stimulus ($F_{(1.7, 8.6)} = 5.5$, $p < 0.05$; the time-bins did not differ from each other in this respect). Partial testing revealed that the increase in predominance of the alternative percept was significantly larger after ambiguous pre-exposure than after monocular-unambiguous pre-exposure ($F_{(1, 5)} = 15.6$, $p < 0.05$). The binocular-unambiguous case was an intermediate, as it did not significantly differ from either of the other two stimuli (both $F_{(1, 5)} \leq 3.7$, both $p > 0.1$; there were no effects of time-bin in the partial tests). The difference between monocular- and binocular-unambiguous pre-exposure was further explored in Experiment 3 and did reach statistical significance there.

The log-transformed duration of the alternative percept showed the same pattern of results. As in Experiment 1, the duration of the pre-exposed percept was slightly decreased after pre-exposure ($F_{(1,5)} = 8.1$, $p < 0.05$), but was not influenced by the type of stimulus that was pre-exposed ($F_{(1.8, 8.7)} = 0.7$, $p = 0.5$). The duration of the alternative percept, on the other hand, differed for the different pre-exposure stimuli ($F_{(1.5, 7.7)} = 4.9$, $p < 0.05$) and was significantly longer after ambiguous compared with monocular-unambiguous pre-exposure ($F_{(1,5)} = 9.4$, $p < 0.05$; Figure 3-3C). The baseline measures also did not differ between the 3 conditions ($F_{(1.1, 5.3)} = 0.2$, both $p = 0.7$).

In overview, the effect of pre-exposure was qualitatively the same for the ambiguous and unambiguous cases. However, monocular-unambiguous pre-exposure had a smaller influence on ongoing rivalry than ambiguous pre-exposure, both in terms of the predominance of the alternative percept and the durations of the alternative percept. Binocular pre-exposure showed intermediate values. Such a difference between the pre-exposure stimuli was not observed for rivalry at onset.

Experiment 3: Intermittent and continuous pre-exposure

In this experiment we introduced a continuous pre-exposure procedure that consisted of a single continuous presentation of the globe and compared this with an intermittent pre-exposure paradigm. The blank periods in an intermittent procedure may allow the system to partially return to baseline, thereby attenuating the effect of pre-exposure. Alternatively, by forcing the visual system to repeatedly make perceptual decisions at each stimulus onset, effect of pre-exposure may be stronger after intermittent than after continuous pre-exposure. Importantly, we kept the total duration of exposure to the stimulus equal for both paradigms (i.e. 0.45 minutes; Figure 3-4A). Considering that ambiguous and unambiguous pre-exposure have qualitatively similar effects (see Experiment 2) we used unambiguous globes in all pre-exposure periods, as these ensured stable perception during the continuous as well as the intermittent pre-exposure. The percentage of time that the same percept was seen during pre-exposure was 99.5% and 99.7% in the intermittent and continuous binocular-unambiguous conditions, and 99.9% and 98.8% in the intermittent and continuous monocular-unambiguous conditions, respectively.

Whereas rivalry at onset was not influenced by the duration of pre-exposure in Experiment 1 or the pre-exposure stimulus in Experiment 2, we did find an effect of the pre-exposure procedure on rivalry at onset in Experiment 3. After continuous pre-exposure the first percept was shorter than the baseline measure ($F_{(1, 12)} = 6.1$, $p < 0.05$), whereas this was not the case after intermittent pre-exposure (Figure 3-4C, top row; $F_{(1, 12)} = 0.5$, $p < 0.5$; difference from baseline *x* pre-exposure procedure: $F_{(1, 12)} = 15.3$, $p < 0.01$). In trials where the test phase started with the alternative percept instead of the pre-exposed percept the duration of the first percept was not influenced by pre-exposure procedure ($F_{(1, 12)} = 0.9$, $p = 0.4$). Only the duration of the first pre-exposed percept was influenced. The intermittent and continuous procedure did not differ much in the percentage of trials in which the test phase started with the pre-exposed percept (87% and 77%, respectively; small difference may be related to shorter percepts being harder to track with button presses).

From 0 till 80 seconds after pre-exposure (time-bins 1-4) there were significant changes in the predominance of the alternative percept (compare with the baseline measure) for at least one of the four conditions (Figure 3-4B). We performed a repeated-measures ANOVA over this time-window and found that the effect of the pre-exposure procedure was different in the first time-bin after pre-exposure (= first 20 seconds) compared with 20-80 seconds after pre-exposure (time-bin 2-4), reflecting the difference in rivalry at onset between the procedures (described above). Between 20 and 80 seconds after pre-exposure the predominance of the alternative percept was larger after intermittent pre-exposure than after continuous pre-exposure (main effect of *procedure*: $F_{(1, 12)} = 9.1$, $p < 0.05$; Figure 3-4B). Also, the predominance of the alternative percept was larger when the binocular-unambiguous stimulus was used than when the monocular-unambiguous pre-exposure stimulus was used (main effect of *pre-exposure stimulus*: $F_{(1, 12)} = 7.9$, $p < 0.05$; in line with Experiment 2). Regarding the percept durations, the duration of the alternative percept was increased compared with the baseline measure ($F_{(1, 12)} = 4.8$, $p < 0.05$; Figure 3-4C, bottom row), but the effect of pre-exposure procedure was not significant ($F_{(1, 12)} = 0.9$, $p = 0.4$). The duration of the pre-exposed percept did not differ from the baseline measure ($F_{(1, 12)} = 0.02$, $p = 0.9$; first percept of test-phase excluded from analysis).

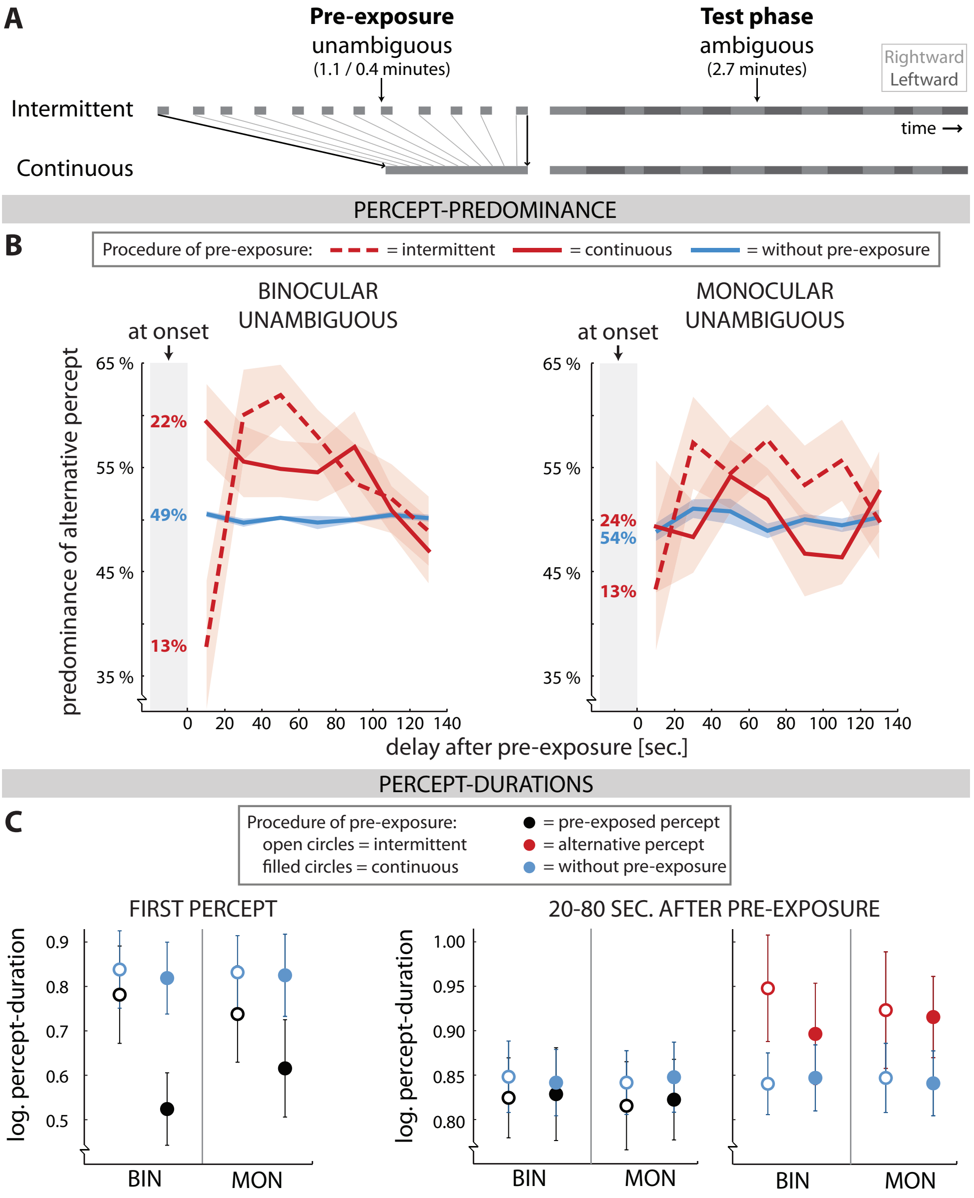

Figure 3-4. Paradigm and results of Experiment 3: Intermittent and continuous pre-exposure.

A) We test the influence of the blank periods during the intermittent pre-exposure we compared intermittent pre-exposure with continuous pre-exposure. Both pre-exposure procedures included the same total amount of exposure to the stimulus (i.e. 0.4 minutes). To ensure stable perception during the continuous pre-exposure we used unambiguous stimuli.

B) The predominance of the alternative percept at the onset of the test phase (number in grey shading) and during subsequent ongoing rivalry (±SEM; bin-width: 20 sec.) for the binocular-unambiguous (*left* graph) and monocular-unambiguous (*right* graph) pre-exposure stimulus. Averaged baseline measure in *blue* (without-pre-exposure). For both stimuli the predominance was larger after the intermittent procedure (*dashed red* lines) than after the continuous procedure (*solid red* lines) in a time-window ranging 20-80 seconds after pre-exposure. In the first time-bin (0-20 sec.) the reverse was true, because the first pre-exposed percept lasted shorter after continuous pre-exposure than after the intermittent pre-exposure (see upper graph in panel C).

C) *Left graph:* The average duration (±SEM) of the first percept in trials that started with the pre-exposed percept (*black*) and trials without pre-exposure (*blue*). For the binocular-unambiguous (BIN) as well as the monocular-unambiguous (MON) stimulus the duration of the first percept was reduced after continuous pre-exposure and not after intermittent pre-exposure. *Middle and right graph:* The average duration (±SEM) of percepts that occurred between 20 to 80 seconds after pre-exposure (pre-exposed percept in *black*, middle graph; alternative percept in *red*, right graph; no pre-exposure in *blue*). The duration of the alternative percept was increased, whereas the duration of the pre-exposed percept was not. Abbreviations: BIN= binocular-unambiguous, MON= monocular-unambiguous.

To summarize, the effect of pre-exposure on ongoing rivalry was qualitatively the same, but smaller when the pre-exposure consisted of one continuous presentation (continuous procedure) compared with a situation where blanks were included in the pre-exposure phase (intermittent procedure). In line with Experiments 1 and 2 the duration of alternative percept was increased, whereas the duration of the pre-exposed percept was not affected. Additionally, the first occurrence of the pre-exposed (but not the alternative) percept after continuous pre-exposure was shorter in duration than during the condition without pre-exposure, whereas this was not the case after intermittent pre-exposure.

Experiment 4: Pre-exposure in binocular rivalry

To see whether the effect of pre-exposure is specific for the rotating globe, or whether it extends to other ambiguous stimuli, we also tested binocular rivalry (orthogonal gratings; Figure 3-5A). During binocular rivalry we can identify a pre-exposed percept, but also a ‘pre-exposure eye’, i.e. the eye that was presented with the pre-exposed percept during pre-exposure. To be able to dissociate the effects of the percept of pre-exposure from the eye of pre-exposure we switched the grating patterns between the eyes in half of the trials as soon as the test phase had ended. As with the rotating globe, perception was stabilized during the intermittent pre-exposure phase (the percentage of presentations with the same percept was 97.2% and 97.7% for the short and long pre-exposure duration, respectively).

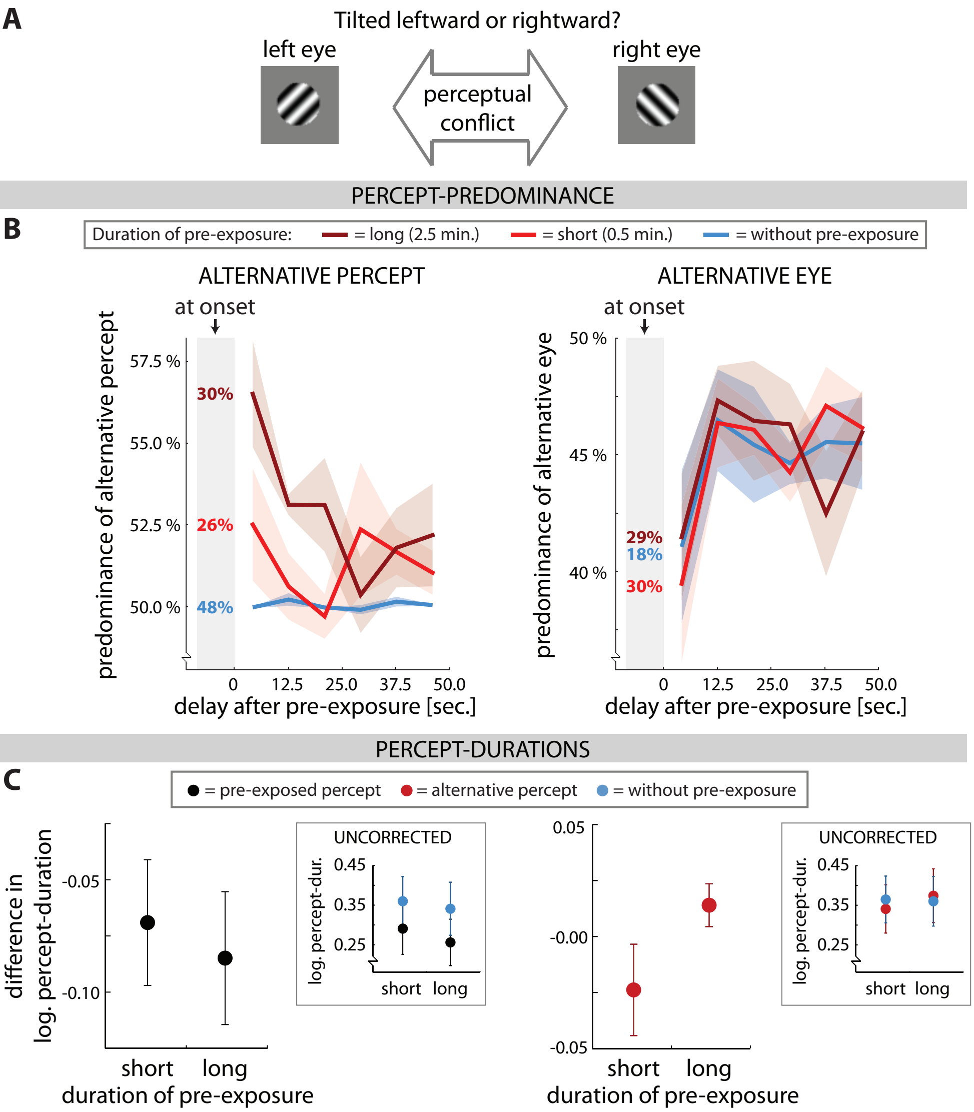

Figure 3-5. Stimulus and results of Experiment 4 'Pre-exposure in binocular rivalry.

A) We investigated the perception of binocular gratings to test whether the effects of pre-exposure reflect a general phenomenon among ambiguous stimuli, or whether they are specific to the rotating globe. When a leftward and a rightward tilted grating pattern are presented to the two eyes observers perceive them alternating for several seconds at a time. We used the paradigm presented in Figure 3-1B, with the intermittent viewing period lasting either 0.5 or 2.5 minutes and the test period lasting 50 seconds. In 50% of the trials the grating stimuli were swapped between the eyes at the beginning of the test phase (compared to the intermittent phase of that trial), to be able to dissociate the effects of percept-stabilization from those of eye-stabilization.

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B) The predominance of the alternative percept (*left* graph) and the 'alternative eye', i.e. the eye that was suppressed during the pre-exposure (*right* graph) at the onset of the test phase (numbers in grey shading) and during subsequent ongoing rivalry (±SEM; bin-width: 8.3 sec.). In line with the previous experiments in which we used the rotating globe (see Figure 3-2E), the predominance of the alternative percept during ongoing rivalry was increased after pre-exposure (*red*) compared with a condition without pre-exposure (*blue*). This increase was larger after long pre-exposure (2.5 minutes; *dark red*) than after short pre-exposure (0.5 minutes; *light red*). Rivalry at onset was not influenced by the duration of the pre-exposure. Pre-exposure did not affect the predominance of the alternative eye. In all conditions the predominance of the alternative eye was low initially and near 50% later on.

C) Small graphs labeled 'uncorrected': Average duration (±SEM) of percepts that occurred between 0 to 16.7 seconds after pre-exposure (pre-exposed percept in *black*, left graph; alternative percept in *red*, right graph; without pre-exposure in *blue*). Large graphs: Same data, but now showing the average *difference in percept duration* between the conditions with and without pre-exposure. The effect of pre-exposure duration is better viewed with this correction, because the variability between the participants in the overall mean percept duration was rather large. The decrease of the duration of the pre-exposed percept is not influenced by the duration of the pre-exposure, whereas the duration of the alternative percept is longer after long pre-exposure than after short pre-exposure (in line with the result for the rotating globe, see Figure 3-2C).

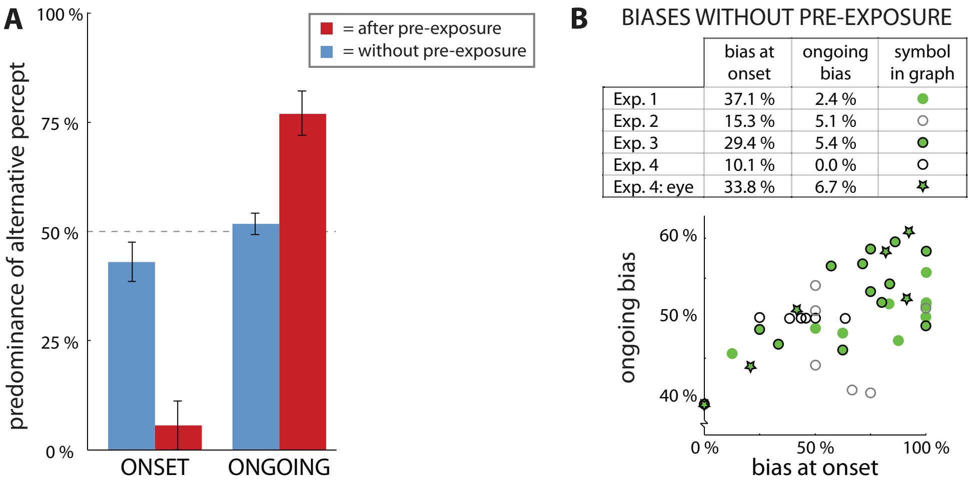
During ongoing rivalry the predominance of the *eyes* was not influenced by pre-exposure (difference from condition without pre-exposure: all $t>1.9$, all $p> 0.1$; overall ANOVA: $F_{(1,5)} = 0.1$, $p= 0.7$). We calculated the predominance over 6 equally sized time-bins (test phase lasted 50 sec., bin-width was 8.3 sec.). In both pre-exposure conditions there was a strong tendency to see the grating in the 'pre-exposure eye' at the start of the test phase (in 69.6% and 71.3% of the trials for the short and long pre-exposure durations, respectively; Figure 3-5B, right graph). The same eye was also predominant at the start of the trials without pre-exposure (i.e. in 82.2% of the trials). This was due to idiosyncratic eye-biases, i.e. most subjects tend to see the image presented to one specific eye at the beginning of any trial. This eye becomes the 'pre-exposure eye' in the conditions with pre-exposure and it is also the eye that is initially used in the condition without pre-exposure. The numbers suggest that this eye-bias was slightly reduced at onset of the test-phase after pre-exposure (from 82.2% to about 70%), but this difference was not significant ($F_{(1,5)}= 0.1$, $p= 0.7$; Figure 3-5B right graph). Regarding the *perceptual* bias (i.e. pattern bias), there was a significant effect of pre-exposure on rivalry at onset, indicating that perceptual stabilization occurred ($F_{(1,5)}= 7.6$, $p< 0.05$; Figure 3-5B left graph).

In all experiments with the rotating globe we found an opposite influence of pre-exposure on rivalry at onset and ongoing rivalry (Figures 3-2A, 3-3B, 3-4B). At onset the alternative percept is suppressed (i.e. there is perceptual stabilization), whereas during ongoing rivalry the alternative percept is facilitated. In line with this, the predominance of the alternative percept was also increased during *ongoing* binocular rivalry after pre-exposure compared with the condition without pre-exposure (Figure 3-5B, left graph). After long pre-exposure this increase in predominance was significant within a delay of 0 to 16.7 seconds (time-bins 1-2: both $t > 3.9$, both $p < 0.05$). In this time-window this effect of pre-exposure was stronger after long pre-exposure than after short pre-exposure ($F_{(1,5)} = 7.8$, $p < 0.05$). We also analyzed the average duration of the percepts that occurred between 0 and 16.7 seconds after pre-exposure. The pre-exposed and alternative percept were differentially influenced by pre-exposure ($F_{(1,5)} = 8.3$, $p < 0.05$). Based on the results for the rotating globe we expected the duration of the alternative percept to be longer after long pre-exposure than after short pre-exposure. There was indeed a trend toward this difference ($F_{(1,5)} = 4.4$, $p = 0.09$; compare Figure 3-5C to Figure 3-2C), but the overall increase was not significant ($F_{(1,5)} = 0.1$, $p = 0.8$). The duration of the pre-exposed percept was decreased compared with the condition without pre-exposure ($F_{(1,5)} = 7.0$, $p < 0.05$), but was not influenced by the duration of the pre-exposure ($F_{(1,5)} = 0.4$, $p = 0.5$).

In comparison with the rotating globe, the effect of pre-exposure was qualitatively the same for binocular rivalry. The pre-exposed percept was initially seen at the onset of the test phase, whereas the alternative percept predominated during subsequent ongoing rivalry. The duration of the alternative percept during ongoing rivalry was longer when the pre-exposure had lasted longer. The duration of the pre-exposed percept, on the other hand, was decreased during ongoing rivalry following pre-exposure, but this decrease was not influenced by the duration of the pre-exposure. The effect for binocular rivalry appeared to be smaller in size and less long-lasting than the effect for the rotating globe (compare Figure 3-5B to Figure 3-2D). Pre-exposure did not affect the predominance of the eye that was dominant during pre-exposure.

Idiosyncratic perceptual bias

In the absence of bias the predominance of both the rightward and the leftward percept would be 50%. However, we found that idiosyncratic biases were present in the condition without pre-exposure in all of the experiments. Interestingly, the biases were much more extreme at the onset of rivalry (initial percept) than during ongoing rivalry. In Experiment 1, for example, there was on average a 37% distance from 50% in the predominance of the rightward percept at onset of the condition without pre-exposure, whereas this distance was only 2.4% during ongoing rivalry without pre-exposure. A similar pattern was found for the other experiments (Figure 3-6B). Although the ongoing biases were small, there was a significant positive correlation between onset bias and ongoing bias for Experiment 1 (regression coefficient = 0.07, t= 3.2, p< 0.05), Experiment 3 (regression coefficient = 0.15, t= 3.4, p< 0.01) and eye bias in Experiment 4 (regression coefficient = 0.19, t= 4.8, p< 0.01). The presence of these biases stresses the importance of the weighted baseline measure used in the analyses described above (see Methods), which ruled out any contribution of idiosyncratic bias to the effects of pre-exposure.



BIASES WITHOUT PRE-EXPOSURE

	bias at onset	ongoing bias	symbol in graph
Exp. 1	37.1 %	2.4 %	●
Exp. 2	15.3 %	5.1 %	○
Exp. 3	29.4 %	5.4 %	◉
Exp. 4	10.1 %	0.0 %	○
Exp. 4: eye	33.8 %	6.7 %	✶

Figure 3-6. Ongoing rivalry compared with rivalry at onset.

A) In all four experiments we found an opposite influence of pre-exposure on rivalry at onset and ongoing rivalry (Figures 3-2A, 3-3B, 3-4B and 3-5B). At onset the alternative percept is suppressed (i.e. there is perceptual stabilization), whereas during ongoing rivalry the alternative percept is facilitated. As an illustration, the graph shows data from Experiment 2, condition with 4.3 minutes of ambiguous pre-exposure (see also Figure 3-3B).

B) Idiosyncratic perceptual biases in the baseline condition without pre-exposure, given as the percentage that the rightward percept is seen, or, concerning the eye bias in Experiment 4, the right eye is used. The table presents the mean difference from 50% of the individual biases (i.e. a value of 10% in the table refers to a bias of either 40% or 60%). Biases were high at onset and very small during ongoing rivalry. The graph shows the bias at onset and during ongoing rivalry for the individual participants in all four experiments. The ongoing biases are all small (ranging from 39% to 61%), but correlated positively with the bias at onset (which ranged from 0% to 100%) for Experiment 1, Experiment 3 and the eye bias in Experiment 4 (indicated with green symbols).

3.5 Discussion

We investigated ongoing conscious perception of ambiguous visual information after observers were pre-exposed to a perceptually stabilized sequence of the same stimulus. The subsequent ongoing rivalry between the possible interpretations of the ambiguous stimulus was biased toward the alternative percept, i.e. the percept that was suppressed during the pre-exposure. In contrast, the initial interpretation of the stimulus showed a bias toward pre-exposed instead of the alternative percept (Figure 3-6A; perceptual stabilization, see Orbach et al., 1963; Leopold et al., 2002; Pearson & Brascamp, 2008). Rivalry at onset thus had a different dependence on pre-exposure than ongoing perceptual rivalry. Furthermore, the bias at onset was only reflected in the perceptual choice and not in the duration of the first percept, whereas a modification of percept durations was responsible for the bias toward the alternative percept during ongoing rivalry. Previous research has indicated that rivalry at onset and ongoing rivalry also differ in the dynamics of the perceptual choices (Brascamp et al., 2009; Hupé & Rubin, 2003), the influence of idiosyncratic perceptual biases (Carter & Cavanagh, 2007) and the influence of attention (Chong et al., 2005; Chong & Blake, 2006; Klink et al., 2008). Taken together, our results reaffirm the difference between gaining dominance at the onset of an ambiguous stimulus and *re*gaining dominance during ongoing rivalry.

The facilitative effect of pre-exposure at the onset of an ambiguous stimulus is not overwritten by unrelated intervening stimulus-presentations (Brascamp et al., 2008; Pearson & Clifford, 2005; Maier et al., 2003) and can be influenced by complex task-characteristics (Klink et al., 2008; Chopin & Mamassian, 2011). It may be mediated by a greater neural sensitivity to the pre-exposed percept, i.e. a greater ‘readiness to respond’. For example, a change in sensitivity, rather than a change in activity, is particularly suited to produce a steeper upstroke in the neural activity for that percept at the onset of the stimulus (Brascamp et al., 2009; Noest et al., 2007). A change in sensitivity may not be very effective during ongoing rivalry, because there is already neural activity for both percepts, albeit sub-threshold for the suppressed percept (Noest et al., 2007; Hock et al., 1996). In this situation the mutual inhibition between the neurons or the saturation level of the neural activity are more likely candidates for mediating the effect of pre-exposure. Specifically, we had hypothesized either a fatigue-like decrease in the duration of the pre-exposed percept during ongoing rivalry (suppression) or a 'memory-like' increase (facilitation). For the alternative percept we initially expected no effect, but considering Levelt's second proposition of binocular rivalry the effect of pre-exposure may also transfer to the perceptual durations of the alternative percept (see hypotheses in Figure 3-2B; Levelt, 1966; Brascamp et al., 2006).

Our results indicate that the duration of the alternative percept was increased after pre-exposure, while the duration of the pre-exposed percept remained largely unaffected (Figure 3-2C), which supports a Leveltian transfer of the suppression hypothesis. It is not likely that this is caused by fatigue in the neurons coding for the pre-exposed percept, since that would logically lead to shorter durations of the pre-exposed percept. Nonetheless, considering that the effect of pre-exposure is specific for retinotopic location (Knapen et al., 2009; Harrison & Backus, 2010), it seems reasonable that sensory neurons tuned to the feature-differences between the percepts are involved. A role of sensory brain regions is further supported by a recent transcranial magnetic stimulation study (Brascamp et al., 2010) and several models of perceptual rivalry (Brascamp et al., 2009; Noest et al., 2007). Therefore, we speculate that the neurons coding for the alternative percept may have been primed – without being fatigued - as a consequence of subthreshold activation during pre-exposure (Knapen et al., 2009). An alternative, but not mutually exclusive, suggestion is that the cross-inhibition between the neurons coding for the two percepts is affected by the pre-exposure, rather than the activity in the neurons themselves. Long-term adaptation in this inhibitory mechanism has been reported recently for binocular rivalry (Klink et al., 2010).

Pre-exposure also had a nonspecific, i.e. percept-invariant, effect on all percept-durations. After pre-exposure the durations were slightly shorter compared with a situation without pre-exposure (Figure 3-2C), in line with the increase in the perceptual alternation-rate reported previously (Cohen, 1959; Suzuki & Grabowecky, 2007). The duration of the pre-exposed percept was affected only by this small and nonspecific effect, which reached significance just in 2 out of our 4 experiments. Our results suggest that for the alternative percept the nonspecific decrease in duration is masked by a facilitative effect (increase in duration) that becomes increasingly larger with longer pre-exposure. This interpretation would explain why there was a slight decrease in duration with very short (≤ 30 seconds) durations of the pre-exposure: the decrease outweighed the increase (Figure 3-2C and 3-5C). For binocular rivalry as well as ambiguous structure-from-motion the facilitative effect outweighed the nonspecific decrease by far when the pre-exposure lasted longer. Consequently, the predominance of the alternative percept, defined as the percentage of time that this percept was seen, was much larger after pre-exposure than without pre-exposure. There were no signs of saturation or ceiling of this effect when the duration of the pre-exposure was extra long (max. 4.3 minutes in our experiments; Figure 3-2C), suggesting that the duration of the alternative percept becomes even longer with pre-exposure durations that exceed those measured in the present study.

Not only the magnitude of the effect of pre-exposure (see above), but also its lifetime scaled with the duration of the pre-exposure. The lifetime of the ‘perceptual memory’ was thus proportional to the duration of the relevant perceptual experience (for related findings with onset-rivalry see Pearson & Brascamp, 2008; Brascamp et al., 2008). Moreover, the prevalence of the alternative percept was surprisingly long lasting (4.5 minutes in Experiment 2, after 4.3 minutes of pre-exposure). Previously reported interdependencies between consecutive percepts during *ongoing rivalry* were short-lived (regarding percept duration: van Ee, 2009; survival probability: Mamassian & Goutcher, 2005; and percept identity: Naber et al., 2010; Suzuki & Grabowecky, 2002). For *rivalry at onset* effects of unambiguous pre-exposure have been reported that lasted hours/days (Harrison & Backus, 2010). The present results shows that the *ongoing* perception of visual ambiguity is also subjected to longer-term effects of prior perception, at the least on the scale of minutes.

During binocular rivalry (Experiment 4; Figure 3-5) the predominance of the two eyes was not affected by pre-exposure, while the predominance of the two percepts showed a pattern similar to what was found for the ambiguous rotating globe. This finding is surprising given previous reports that perceptual stabilization during intermittent binocular rivalry is more eye-based than percept-based (Pearson & Clifford, 2004). However, at the onset of binocular rivalry there is a large influence of idiosyncratic eye-bias and this eye-bias is not affected by pre-exposure (Figure 3-5B and 3-6B). The tendency to repeatedly see the image presented to the same eye during intermittent binocular rivalry, even when the images are swapped between the eyes (see Pearson & Clifford, 2004), was thus driven by idiosyncratic eye-bias and not by a gain in dominance of that eye. There was even a small (but not significant) decrease in eye-bias after pre-exposure, instead of an increase (Figure 3-5B). By swapping the images between the eyes at the start of the continuous test phase in 50% of the trials we could average out this eye-based effect and we found that there is a small, but significant, effect of *perceptual* stabilization after pre-exposure (in line with Pearson & Clifford, 2004). The pre-exposed percept was more likely to be seen at onset of the stimulus after pre-exposure than without pre-exposure (Figure 3-5B). During subsequent ongoing binocular rivalry the predominance of the alternative percept was increased, in line with the results for the ambiguous structure-from-motion stimulus. There were almost no idiosyncratic eye-biases during ongoing binocular rivalry (see related findings in Carter & Cavanagh, 2007; Bartels & Logothetis, 2010), regardless of whether the condition included pre-exposure or not (Figure 3-5B and 3-6B).

Our findings were not specific to ambiguous pre-exposure. We found that unambiguous pre-exposure resulted in a qualitatively similar effect. In our paradigm the pre-exposed percept was facilitated at onset of the test phase after ambiguous as well as unambiguous pre-exposure. Suppression of the pre-exposed percept at onset of the stimulus has often been reported after unambiguous pre-exposure (Virsu, 1975; Harris, 1980; Petersik et al., 1984; Long & Toppino, 2004), but facilitation is common after long blank intervals (Long et al., 1992; Kanai & Verstraten, 2005; Brascamp et al., 2007). During ongoing rivalry there was facilitation of the alternative percept after ambiguous as well as unambiguous pre-exposure (see also predominance ratios described in Nawrot & Blake, 1991; Von Grünau & Dubé, 1993; Jackson & Blake, 2010), indicating that the effect of pre-exposure is not reliant on perceptual decision-processes under conditions of ambiguity. However, the magnitude of the effect was smaller when the pre-exposed stimulus was disambiguated with monocular depth-cues (i.e. a contrast- and size-imbalance) than when it was ambiguous or disambiguated with a binocular depth-cue (disparity). The disparity-defined stimulus also seemed to have a smaller effect than the ambiguous stimulus, but this difference was not significant (Figure 3-3B and 3-4B). We interpret this as an indication that the site of neural processing where ambiguous structure-from-motion is resolved has more overlap with the site where disparity information is processed than with the processing-level of basic stimulus features such as size and contrast. During the perception of ambiguous structure-from-motion perceptual decisions are indeed reflected in the activations of brain regions that are sensitive to disparity (Brouwer & van Ee, 2007).

One could also suggest that the effect of unambiguous pre-exposure was smaller because unambiguous stimuli lead both to stimulus-based adaptation and percept-based ‘memory’, which counteract each other. However, given that the former is likely to have a suppressive effect on the pre-exposed percept, while the latter facilitates the alternative percept, these effects would strengthen rather than counteract each other in terms of the predominance of the percepts. Also, it is unlikely that these effects would last equally long, considering that the suppressive effect on the pre-exposed percept that we found after continuously (but not intermittently) presented unambiguous pre-exposure lasted for only one perceptual epoch. In other words, it merely influenced rivalry at onset. In line with our results regarding ongoing rivalry, it was previously reported that rivalry at onset is also influenced more strongly by ambiguous than by unambiguous pre-exposure in a specific location-contingent perceptual learning paradigm (Harrison & Backus, 2010; van Dam & Ernst, 2010). Interestingly, using the same paradigm, pre-exposure with a combination of binocular and monocular depth-cues had a stronger effect on rivalry at onset than by pre-exposure with monocular depth-cues only (Harrison et al., 2011).

If the cross-inhibition between the two percepts is indeed modified by pre-exposure, as proposed above, there is an additional explanation of our results regarding unambiguous pre-exposure. One could propose that less inhibition of the suppressed percept is needed when there is more low-level percept-specific information as evidence for the dominant percept. This weaker inhibition *during* pre-exposure might result in a weaker modulation of the inhibition *after* pre-exposure. A similar reasoning might explain why we found a smaller effect of continuously presented unambiguous pre-exposure than intermittently presented unambiguous pre-exposure, even though the total presentation-time was kept constant between the two procedures (Figure 3-4B). It could be that the repeated onset of stimulation during the intermittent pre-exposure more strongly activated mutual inhibition than the continuous presentation.

Conclusion

The present data show that previously perceived interpretations dominate at the onset of ambiguous sensory information, whereas alternative perceptual interpretations tend to dominate with prolonged viewing. This effect of previous experience on the perception of ongoing sensory ambiguity can last for several minutes and is larger when the pre-exposure lasted longer. We suggest that the reported effects could be related to priming of the suppressed percept during pre-exposure. Alternatively, learning processes in the mutual inhibition between the possible perceptual interpretations may play a role. The effect was found for perceptual as well as binocular rivalry and was larger after ambiguous pre-stimulation than after unambiguous pre-stimulation. In all, our results are compatible with a mechanism that optimizes performance by learning from experience in the following manner: the nature of new sensory input is assessed quickly through the retention of past experience, while alternative interpretations are considered after continued evaluation of the information.

Chapter 4

Perceptual experience modulates cortical circuits involved in visual awareness

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4.1 Abstract

Successful interactions with the environment entail interpreting ambiguous sensory information. To address this challenge it has been suggested that the brain optimizes performance through experience. Here we used functional magnetic resonance imaging (fMRI) to investigate whether perceptual experience modulates the cortical circuits involved in visual awareness. Using ambiguous visual stimuli (binocular rivalry or ambiguous structure-from-motion) we were able to disentangle the co-occurring influences of stimulus repetition and perceptual repetition. For both types of ambiguous stimuli we observed that the mere repetition of the stimulus evoked an entirely different pattern of activity modulations than the repetition of a particular perceptual interpretation of the stimulus. Regarding stimulus repetition, decreased fMRI responses were evident during binocular rivalry but weaker during 3D-motion rivalry. Perceptual repetition, on the other hand, entailed increased activity in stimulus-specific visual brain regions: for binocular rivalry in the early visual regions and for ambiguous structure-from-motion in both early as well as higher visual regions. This indicates that the repeated activation of a visual network mediating a particular percept facilitated its later re-activation. Perceptual repetition was also associated with a response change in the parietal cortex that was similar for both types of ambiguous stimuli, possibly relating to the temporal integration of perceptual information. We suggest that perceptual repetition was associated with a facilitation of neural activity within and between percept-specific visual networks and parietal networks involved in the temporal integration of perceptual information, thereby enhancing the stability of previously experienced percepts.

4.2 Introduction

Sensory and perceptual experiences influence the way we interpret new sensory input (Gilbert et al., 2001; Karmarkar & Dan, 2006). In most paradigms prior sensory stimulation and prior perceptual experience are difficult to disentangled. Here, we discern these influences using ambiguous visual stimulation. In particular, we ask whether prior *perceptual* experience alters the neural processing of ambiguous signals in the brain. The dissociation from sensory stimulation is permitted by occasional alternations in the perceptual interpretation of an ambiguous stimulus, while the sensory stimulation remains unchanged (Blake & Logothetis, 2002).

When short presentations of an ambiguous stimulus are interleaved with blank intervals, one of the possible interpretations of the stimulus tends to be perceived repeatedly on consecutive presentations (Leopold et al., 2002; Orbach et al., 1963). As shown by psychophysical investigations, this stability in perception cannot be explained as a resistance to change (Brascamp et al., 2008/2009) or as repetition priming from one presentation to the next (Maier et al., 2003; Pearson & Brascamp, 2008). Rather, it reflects a form of perceptual memory that spans a timescale of at least several minutes and can be understood as a tendency to experience the perceptual interpretation that was most prevalent in the recent past (Pearson & Brascamp, 2008).

Repeated sensory stimulation is usually associated with a *decrease* in the amplitude of the neural response, which is ascribed to e.g. neural fatigue or more efficient encoding (Grill-Spector et al, 2006; Kohn, 2007; Krekelberg et al., 2006). Conversely, perceptual learning/memory can lead to an *increased* neural response, which is suggested to result from an increase in neural sensitivity (Miller et al., 1996; Kourtzi et al., 2005; Henson et al., 2000; Turk-Browne et al., 2007; Dolan et al., 1997; James and Gauthier, 2006). In line with this, we hypothesized that perceptual repetition during intermittent presentation of an ambiguous stimulus is associated with an increased neural response, while the mere repetition of the stimulus leads to a decreased neural response. These effects could be present in sensory regions specialized for the presented stimulus (Kourtzi et al., 2005;

Henson et al., 2000) and/or in frontal and parietal regions involved in the attentional and mnemonic processing of sensory information (Miller et al., 1996; Pasternak & Greenlee, 2005; Corbetta et al., 2002; Rees et al., 2002).

To test our hypotheses, we used two different ambiguous stimuli: binocular rivalry and ambiguous structure-from-motion, also referred to as three-dimensional (3D-) motion rivalry (Figure 4-1). During binocular rivalry the proposed modulation of sensory neurons may be primarily observed in the early visual cortex (V1-V3; Haynes & Rees, 2005; Lee et al., 2005; Gail et al., 2004), while during 3D-motion rivalry these effects could be present in ventral visual regions implicated in 3D-shape processing (V4, LO; Neri, 2005; Hinkle & Connor, 2005; Kourtzi et al., 2003; Preston et al., 2008) or dorsal and parietal regions implicated in global motion in depth (hMT+, V3A, V7, POIPS; Paradis et al., 2000; Orban et al., 2006; Brouwer & van Ee, 2007; Brascamp et al., 2010; Above abbreviations are explained in the legend of Figure 4-2A).

4.3 Materials and Methods

Participants

Six observers (5 male, 1 female) participated in the '3D-motion rivalry'-experiment. A subset from these and one additional male observer participated in the 'binocular rivalry'-experiment (total: 4 male, 1 female). All participants had normal or corrected to normal vision and gave written informed consent prior to participation. The study was approved by the ethics committee at the University of Birmingham, United Kingdom, and conforms to The Code of Ethics of the World Medical Association (Declaration of Helsinki).

Stimuli and Procedure

Stimuli were created using Mathematica (Wolfram Research) and Matlab (MathWorks Inc) and were presented in the center of a gray computer-screen (60 Hz, 1280x1040 pixels, gamma-linearized). For binocular rivalry we used two orthogonal sine wave black-and-white gratings, each presented to one of the eyes, on a mid-grey background (Figure 4-1A). The gratings subtended a circular patch of 2.9° in diameter and contained

1.38 cycles per degree (phase was chosen randomly at every presentation). The gratings were titled 45 degrees from vertical to either the left or right. Per experimental run the orientations were assigned randomly to one of the eyes. During binocular rivalry the perceptual conflict between the eyes results in the alternating dominance of either the left or right eye grating (Levelt, 1966;1967).

For 3D-motion rivalry we used an ambiguous structure-from-motion stimulus that consisted of 175 leftward and 175 rightward moving dots (each 0.064° in diameter, depicted either in black or in white, on a mid-grey background) representing random points on the surface of a virtual globe (2.9° in diameter). The sinusoidal speed profile of the dots (fastest near the vertical meridian) created the percept of a globe revolving around its vertical axis with a period of 6.7 seconds. The three-dimensional interpretation of the stimulus, and thereby its direction of rotation, was ambiguous, because no depth cues differentiated the rightward moving surface from the leftward moving surface. Either of the two surfaces could thus be perceived in front of the other (Figure 4-1A).

At every stimulus presentation the participants reported their percept by pressing one of two corresponding buttons, and pressed no button when they could not differentiate the two percepts (for example, when they had a mixed percept or a transition between percepts within one presentation of the stimulus). Participants were instructed to maintain strict fixation on a centrally presented, static fixation dot subtending 0.19° in diameter (globe: green dot; gratings: red dot with grey circular surround of 0.38°). An experimental run consisted of 24 blocks. A block started with intermittent presentation of the stimulus (for 18 seconds) followed by a blank screen (for 16 seconds; Figure 4-1). The period with intermittent presentation contained 12 presentations (lasting 900 milliseconds each) interleaved with short blanks (lasting 600 milliseconds each). Each run started and ended with an additional rest period (blank screen lasting 16 seconds). During the rest periods the fixation dot remained visible. Each participant completed 4 runs per experiment (except 2 participants in the 'binocular rivalry'-experiment who completed 5 runs). Blocks with less than 8 (out of 12) button responses were excluded from the analyses (=3.3% of blocks).

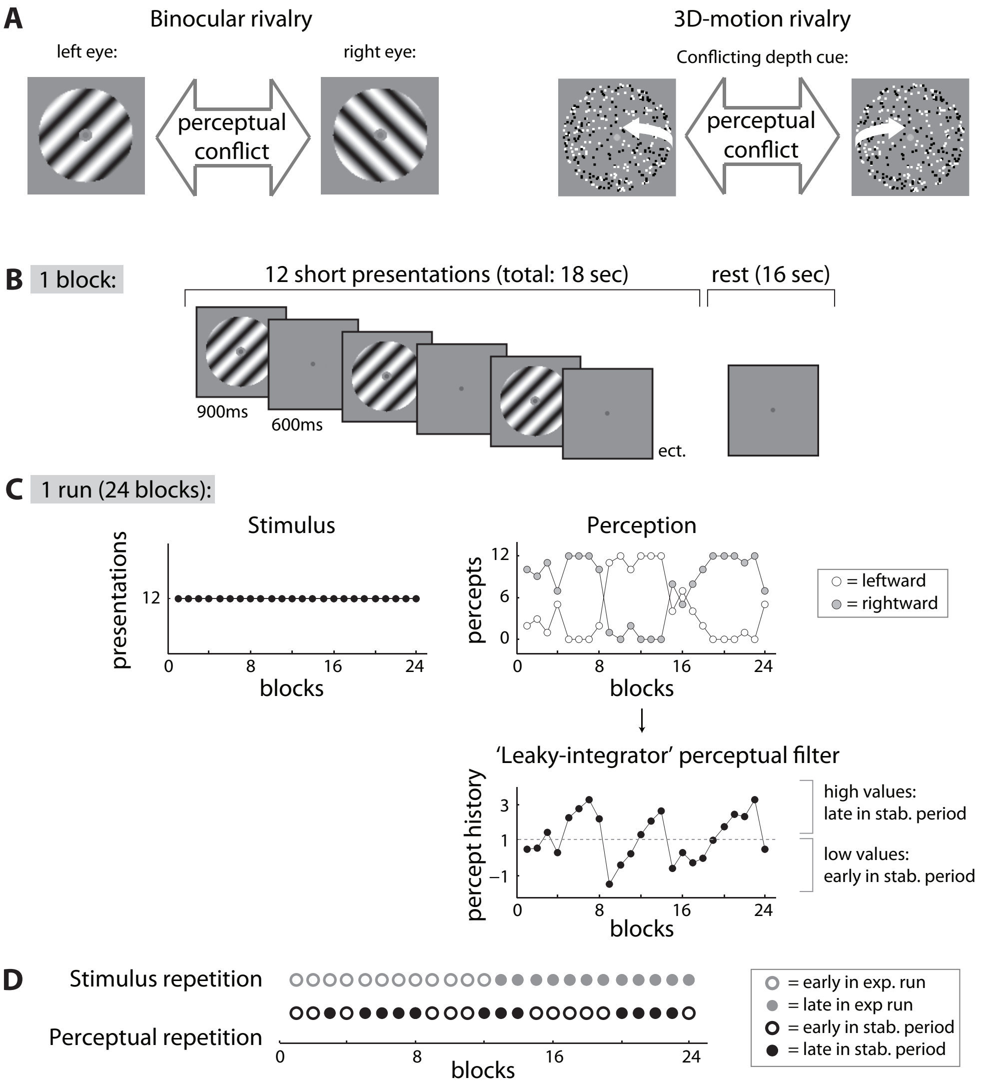


Figure 4-1. Stimuli and paradigm.

A) We used either of two ambiguous stimuli. During binocular rivalry a perceptual conflict arises because the images presented to the left and right eye are incompatible. During 3D-motion rivalry (structure-from-motion without stereoscopic disparity) there is a conflicting depth-cue in the image. Via button presses the participants indicated which of the two possible percepts they perceived at any given time (leftward or rightward tilt during binocular rivalry; leftward or rightward rotation direction during 3D-motion rivalry). The changes in perception that occur when ambiguous visual input is presented enabled us to dissociate the neural effects of *stimulus* repetition from those of *perceptual* repetition (see D).

B) Sequence of events during a block. A block consisted of an 18 seconds intermittent stimulation epoch (including 12 stimulus presentations) followed by a 16 seconds rest period.

C) Sequence of events during an experimental run. One experimental run lasted 14 minutes and consisted of 24 blocks. Participants completed at least 4 runs per experiment. The ambiguous stimulus was the same throughout the run (left graph), but perceptual experience changed in an oscillatory fashion with periods of largely stable perception that lasted several minutes (middle graph). We used a 'leaky integrator' filter of the perceptual timecourses as a straightforward and validated tool to identify the early and late phases of these periods of stabilized perception (see methods).
D) We hypothesized that the neural response, as measured with functional magnetic resonance imaging (fMRI), is concurrently modified by stimulus repetition as well as perceptual repetition. To investigate the influence of stimulus repetition we compared the first and second part of each experimental run (abbreviated: 'exp. run'). The influence of perceptual repetition was studied by comparing early and late stages of perceptually stable periods (abbreviated: 'stab. period'). Each block belonged to either one of the levels of stimulus repetition (early/late in exp. run, shown in open/filled grey circles) and either one of the levels of perceptual repetition (early/late in stab. period, shown in open/filled black circles). In this way, the effects of one measure were averaged out when the levels of the other measure were compared.

Perceptual History and Design of Analysis

We investigated the influence of perceptual repetition as well as stimulus repetition on functional magnetic resonance imaging (fMRI) responses. Stimulus repetition was studied by comparing blocks early in each experimental run (the first half) with later blocks in that run (the second half), reasoning that effects of stimulus repetition may accumulate during a run. While the stimulus remained the same across a run, perception changed occasionally. Observers tended to experience the same percept for prolonged periods of time, a 'perceptually stable period', after which perception would switch and the other percept would be experienced during the next period. Perceptual repetition, i.e. repeatedly seeing the same perceptual interpretation, was studied by comparing blocks early in a perceptually stable period (after few repeats) with blocks late in a perceptually stable period (after many repeats). This approach was based on the idea that memory for the perceptual interpretation accumulates during such periods (Figures 4-1C and 4-1D), given previous findings that the tendency to experience the same percept across repetitions of an ambiguous stimulus grows as the same percept is seen over and over (Brascamp et al., 2008), i.e. it is a self-reinforcing tendency.

Whereas it was evidently easy to divide each experimental run into two halves to investigate the effects of stimulus repetition (first 12 and last 12 blocks), it was not possible to simply divide the perceptually stable periods into two halves, as these depended on the individual perceptual timecourses of the participants. The perception-based periods could differ in duration and did not always have an instantaneous beginning or ending (Figure 4-1C). We used a low-pass perceptual filter from Brascamp et al. (2009) as a tool to identify perceptually stable periods in an objective and validated way. The only assumption of this simple perceptual filter is that perceptual experience with a certain percept accumulates over time when the percept is seen, and slowly decays when the percept is not seen. The final measure of perceptual experience (memory) is the difference in experience between the dominant and the suppressed percept. Brascamp et al. (2009) have shown that this low-pass filter of perceptual timecourses accurately describes the long-term dynamics of perceptual stabilization during intermittent ambiguous perception. Its slow dynamics seem appropriate in relation to the sluggishness of the blood oxygen level–dependent (BOLD) response (note that the filter does not involve the fast dynamics of the model mentioned in Brascamp et al., 2009).

Specifically, the accumulated experience (E) of a given percept was calculated per block by 'leaky' integration of the proportion of presentations that percept was experienced (P) during that block: $E = Eprev + P - (0.2*Eprev)$. Eprev refers to the E of the previous block. This measure of perceptual experience, E, was calculated separately for each of the two percepts (i.e. a given rotation-direction for the rotating globe; a given tilt-direction for the orthogonal gratings). This method takes into account recent percepts (P) as well as percepts longer ago (reflected in Eprev). Following Brascamp et al. (2009), we used the difference between the E value associated with the dominant percept and the E value associated with the suppressed percept as the final measure of perceptual experience E_{final}. Late in a perceptually stable period, when the current percept was also frequently seen in the past, E_{final} has a high value. Alternatively, early in a perceptually stable period, when the current percept was seen just a few times or when the opposite percept was seen frequently, E_{final} is small or negative.

We compared blocks early in a perceptually stable period with blocks late in a perceptually stable period (low vs. high values of E, overall median split; Figures 4-1C and 4-1D). We used a median-split, because this is a straightforward method that is free of assumptions regarding the shape of the relation between the BOLD signal change and the value of E and we had no a priori assumption regarding the detailed shape of this relation. Also, a median-split approach is not affected by possible serial correlations in the time series data and it is less sensitive to outliers than, for example, a linear regression analysis (a similar split method was used by Brascamp et al., 2009). When the values of E are distributed equally throughout the experimental run the differences related to stimulus repetition (i.e. the difference between the first and second half of an experimental run) are averaged out when the effects of perceptual repetition (i.e. low vs. high values of E) are investigated. Also, with an equal distribution the effects of perceptual repetition are averaged out when the effects of stimulus repetition are investigated. Given that several changes in perception occurred during an experimental run, the distribution of the blocks is likely to be fairly equal. To verify this we compared the number of blocks in which both tested variables (i.e. perceptual repetition and stimulus repetition) had the same value (i.e. both early or both late) with the number of blocks in which the tested variables had different values (early for one, late for the other). The resulting 'relatedness index' ((same – different) / (same + different)) is zero with equal distribution and positive or negative when the tested variables are positively or negatively related, respectively.

fMRI Data Acquisition and Analysis

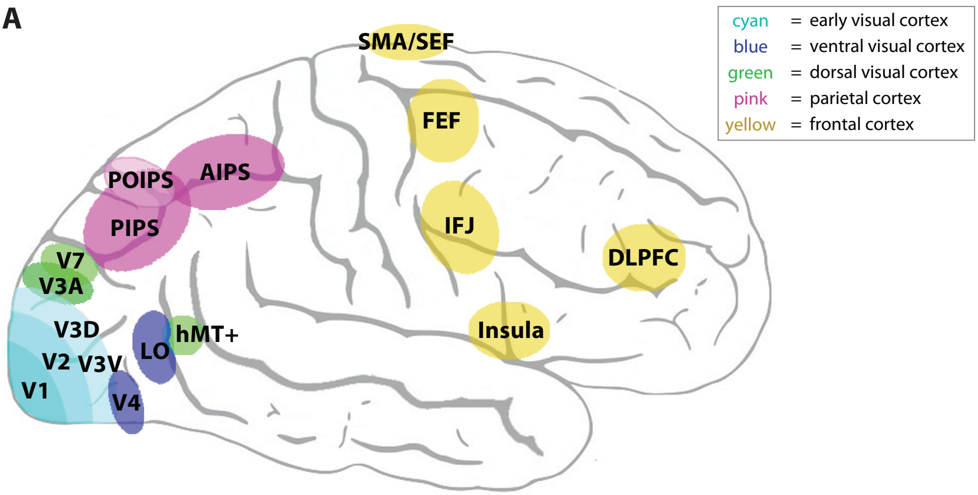
A 3-Tesla Philips Achieva scanner at the Birmingham University Imaging Centre was used. T2*-weighted functional (2.5x2.5x3 mm resolution) and T1-weighted anatomical (1x1x1 mm resolution) data were collected with an eight-channel SENSE head coil. Echo planar imaging data (EPI, gradient echo-pulse sequences) with occipital, parietal and frontal coverage were acquired (repetition time = 2,000 milliseconds; echo time = 35 milliseconds). The number of slices was 32 for the binocular rivalry experiment and 32 (3 subjects) or 29 (3 subjects) for the 3D-motion rivalry experiment.

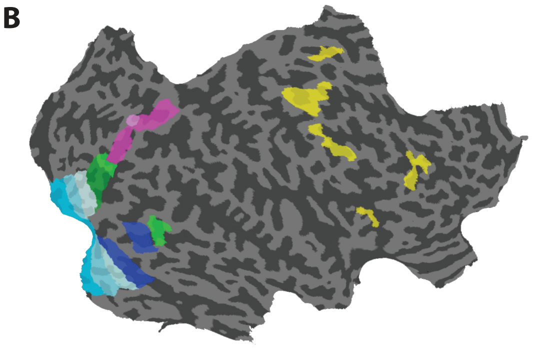
Preprocessing of functional data was performed using Brain Voyager QX (Brain Innovations BV) and included slice scan-time correction (cubic spline, ascending interleaved), head movement detection (trilinear) and correction (trilinear for 3D-motion rivalry experiment, trilinear/sinc for binocular rivalry experiment) and temporal high-pass filtering (2 cycles). No spatial smoothing was performed. For each participant, the functional imaging data between runs were co-aligned automatically and then manually aligned to anatomical data. All data were transformed to Talairach space and anatomical data were used for 3D cortical reconstruction, inflation and flattening. Matlab (MathWorks Inc) was used for further analysis of the averaged MRI timecourses per region-of-interest (ROI).

Regions-of-interest

We identified retinotopic visual areas V1, V2, V3V, V3D, V3A, V7 and V4 using standard rotating-wedge mapping procedures and in accordance with known anatomical structures (DeYoe et al., 1996; Engel et al., 1994; Sereno et al., 1995; Abbreviated ROI-names are explained in the legend of Figure 4-2A). V7 was defined as a region anterior and dorsal to V3A (Press et al., 2001; Tootell et al., 1998; Tyler et al., 2005; Figure 4-2A). Three additional functional localizers were performed, all using a conventional block design. Motion sensitive medial temporal area (hMT+, also known as V5) was defined as the set of voxels in the temporal cortex that responded significantly higher ($p<10^{-4}$) to a coherently moving array of dots than to a static array of dots (Tootell et al., 1995; Zeki et al., 1991). The lateral occipital area (LO) was defined as the set of voxels in lateral occipito-temporal cortex which responded more strongly ($p<10^{-4}$) to intact than scrambled images of objects (Kourtzi and Kanwisher, 2000). Region 'POIPS', named according to its anatomical location in the parieto-occipital intraparietal sulcus (Figure 4-2A; Vanduffel et al., 2002; Orban et al., 2006), was defined as the set of voxels in the superior parietal lobule that responded more strongly ($p<10^{-4}$) to structure-from-motion (SFM) than to motion without perceived depth. The stimuli used were moving random-dot patterns that either did or did not contain SFM cues. The stimuli had no stereoscopic depth and consisted of black and white dots on a mid-grey background. The participants completed two scanning runs, which lasted nearly 6 minutes each. During each run eight 18 s blocks with SFM, eight 18 s blocks without SFM and four 12 s blank fixation blocks were presented in pseudo-random order. The task of the participants was to report changes in the luminance of the fixation dot in the center of the stimulus, which occasionally changed from black to white or vice versa.

Based on previous studies (Rees et al., 2002; Grefkes & Fink, 2005; Corbetta et al., 2002; Lumer et al. 1998; Kleinschmidt et al., 1998; Zanto et al., 2010; Asplund et al., 2010; Sterzer & Kleinschmidt, 2010; Pasternak & Greenlee, 2005; Constantinidis et al., 2001) we may expect that memory for perceptual history also involves frontal and parietal regions involved in attentional and mnemonic processing of sensory information, particularly the anterior and posterior intraparietal sulcus (AIPS and PIPS), the supplementary eye-fields / supplementary motor area (SMA/SEF), the frontal eye-fields (FEF), the inferior frontal junction (IFJ), the dorso-lateral prefrontal cortex (DLPFC) and the insula (see Figure 4-2A). In accordance with the anatomical locations described in these previous studies, we defined each of these regions as the set of voxels, near the known anatomical location, that responded significantly stronger to visual stimulation vs. fixation ($p < 0.05$, bonferroni corrected for total number of voxels; see table with talairach coordinates in Figure 4-2C). In the binocular rivalry experiment we used the data from the 3D-motion rivalry experiment as a localizer of voxels with significantly





C

	Right			Left		
	x	y	z	x	y	z
LO	40	-72	-9	-40	-73	-3
hMT+	43	-64	-1	-45	-67	1
POIPS	20	-66	46	-22	-64	45
PIPS	25	-69	36	-22	-69	36
AIPS	32	-55	44	-33	-52	42
SMA/SEF	7	1	53	-5	-5	57
FEF	34	-9	51	-32	-11	52
IFJ	47	0	33	-44	0	31
Insula	33	20	7	-31	17	10
DLPFC	38	33	28	-35	40	26

Figure 4-2. Regions-of-interest.

A) Schematic drawing of the locations of the regions-of-interest. Colors indicate different cortical regions. V1= visual area 1, V2= visual area 2, V3V= ventral part of visual area 3, V3D= dorsal part of visual area 3, V4= ventral visual area 4, LO= lateral occipital area, hMT+= motion-selective medio-temporal area, V3A= visual area 3A (anterior to V3), V7= visual area 7, PIPS= posterior intraparietal sulcus, AIPS= anterior intraparietal sulcus, POIPS= parieto-occipital intraparietal sulcus (structure-from-motion sensitive parietal region), SMA/SEF= supplementary motor area / supplementary eye-fields, FEF= frontal eye-fields, IFJ= inferior frontal junction, DLPFC= dorsolateral prefrontal cortex.

B) An example (right) hemisphere showing the delineation of the regions-of-interest.

C) Table presenting talairach coordinates averaged over participants.

stronger responses to visual stimuli vs. fixation. Analogously, we used the data from the binocular rivalry experiment as a visual localizer for the 3D-motion rivalry experiment. By using independent datasets for localizing regions of interest, we ensured statistical independence of the selection of the ROIs and the hypothesis testing per experiment. With the same method we also selected visually responsive voxels within each of the other ROIs (the retinotopic visual areas, hMT+, LO and POIPS) and included only those voxels in the data analysis.

There were two participants that only performed the 3D-motion rivalry experiment and not the binocular rivalry experiment. For these participants the data of the SFM functional mapping experiment served as an independent localizer of visually responsive voxels (stimuli with SFM and without SFM were collapsed; $p<10^{-4}$). This independent localizer was also utilized to define hMT+ in one of these participants and LO in both of them, because the corresponding localizers were not completed. In accordance with the average talairach-coordinates of hMT+ and LO in the remaining subjects, the regions were defined as the set of voxels, near the target anatomical location, that responded significantly stronger to stimuli vs. fixation. One other participant performed only the binocular rivalry experiment and not the 3D-motion rivalry experiment. This participant completed an extra (5th) run, which we utilized as an independent visual localizer ($p< 0.05$, bonferroni corrected for total number of voxels) for hypothesis testing based on the remaining 4 runs.

BOLD Amplitude and Statistical Analysis

For each of the two levels (early and late) of perceptual repetition and stimulus repetition the event-related BOLD responses were calculated and referenced to the 2 image volumes preceding block-onset ((data–baseline) / baseline). We used this method, which is free of assumptions regarding the shape of the response, because we did not have a standard hemodynamic response to use as a model for the observed saddle-shape of the responses (see Figures 4-3B, 4-3D and 4-4B). Also, this method eliminates possible low-frequency fluctuations, because the activation is measured relative to the baseline activation just before block onset. The magnitude of the event-related responses was quantified as the integrated BOLD response (i.e. the area under the BOLD curve). The relative response change between the early and the late level ((late-early) / (late+early)) was statistically analyzed for perceptual and stimulus repetition using PASW Statistics 18 (formerly SPSS Statistics). For statistical analysis the regions-of-interest were grouped into 5 cortical regions: early visual (V1, V2, V3V, V3D), ventral occipital (V4, LO), dorsal occipital (V3A, V7, hMT+), parietal (POIPS, PIPS, AIPS) and frontal (SMA, FEF, IFJ, Insula, DLPFC) cortex. We performed a repeated-measures analysis of variance (ANOVA) over regions-of-interest, with *type of rivalry* (binocular/3D-motion rivalry) and *repetition modality* (stimulus/perceptual repetition) as within factors and *cortical region* (early visual, ventral visual, dorsal visual, parietal and frontal) as a between factor (unless indicated otherwise). An α of 0.05 was adopted and a Greenhouse-Geisser correction was applied to all tests to correct for possible violations of sphericity.

Eye position recording and analysis

Eye positions were recorded for four participants during fMRI scanning of the 3D-motion rivalry experiment using a ASL 6000 Eye-tracker (Applied Science Laboratories) with a sample frequency of 60 Hz. Preprocessing was performed using the Eyenal software package (Applied Science Laboratories) and further analysis was performed using custom Matlab (Mathworks) software. We computed the number of blinks and saccades and the horizontal and vertical eye position during each block of intermittent stimulation. Because we wanted to compare the eye movement data to the event-related BOLD responses per block, we included blinks and saccades during the entire block, i.e. the short presentations within a block as well as the interleaved short blanks. Blinks were defined as periods in which no gaze position was recorded (no recognition of pupil or no coronal reflection) that lasted 100-400 milliseconds. Saccades were defined as periods with a rapid change of gaze position (velocities between 25-500 °/s) that lasted >2 sample points. The eye position during fixations was calculated over periods when the stimulus was present and no blink or saccade was detected. Eye positions were referenced per stimulus presentation to the mean over the 100-ms preceding stimulus onset (to remove drift).

4.4 Results

Behavioral results

Short presentations of ambiguous stimuli were interleaved with blank periods and participants were asked to indicate their percept at every presentation (Figures 4-1A and 4-1B). It is known that in such an intermittent paradigm perception tends to stabilize across repetitions of the stimulus. The participants indeed reported robust perceptual stabilization for prolonged periods of time, referred to as 'perceptually stable periods', at the end of which perception switched and the other percept was experienced during the next period. The percentage of same percepts seen within a block was on average 81.2% (± 3.0% SEM, standard error of the mean) during the binocular rivalry experiment and 88.4% (± 2.9% SEM) during the 3D-motion rivalry experiment, respectively. Here, a 'block' refers to a sequence of 12 short presentations followed by a 16 seconds rest (Figure 4-1B). Perceptual stabilization across the rest periods separating the blocks, i.e. when the first percept of a given block is the same as the last percept of the previous block, was on average 69.0% (± 1.9% SEM) and 78.3% (± 5.8% SEM) for the binocular and 3D-motion rivalry experiments, respectively. The participants refrained from responding upon presentations where they could not differentiate the two percepts, for example because they experienced a mixed percept or a transition between percepts within one presentation of the stimulus. This occurred in 1.6% (± 0.7% SEM) and 3.0% (± 1.5% SEM) of the presentations for the binocular and 3D-motion rivalry experiments, respectively.

We had anticipated that the distinct and consecutive periods of perceptual stabilization for one or the other percept would result in a temporal de-correlation of stimulus repetition and perceptual repetition (Figure 4-1C). Indeed the number of a block, relative to the start of the run, was not correlated with the output value of the perceptual filter for that block (see next paragraph and methods; binocular rivalry: -0.032 ± 0.030 SEM, $t_{(4)}$= -1.1, p= 0.3; 3D-motion rivalry: 0.003 ± 0.034 SEM, $t_{(5)}$= 0.1, p= 0.9, slope of repeated-measures regression; Figure 4-5A). Stimulus repetition and perceptual repetition were thus not correlated in time, allowing separate investigations of these co-occurring phenomena.

We reasoned that effects of stimulus repetition might accumulate during the experimental run. Therefore, we studied the effects of stimulus repetition by comparing blocks early and late in a run (first half vs. second half). Following a similar reasoning, we studied perceptual repetition by comparing the early and late stages of perceptually stable periods, as identified using a 'leaky integrator' perceptual filter (Figure 4-1C). The early and late stages of perceptually stable periods did not differ in the percentage of presentations where participants refrained from responding, indicating no difference in the occurrence of blended/mixed percepts (binocular rivalry: $t_{(4)}= 0.2$, $p= 0.8$; 3D-motion rivalry: $t_{(5)}= 1.3$, $p= 0.2$). Also, the number of blinks and saccades was similar (blinks: $t_{(3)}= -1.1$, $p= 0.4$; saccades: $t_{(3)}= 0.7$, $p= 0.5$), as was the eye position during fixation on the stimulus (horizontal: $t_{(3)}= 1.1$, $p= 0.4$; vertical: $t_{(3)}= 1.0$, $p= 0.4$; measured during the 3D-motion rivalry experiment; Figure 4-5D). The blocks in the early and late stages of perceptual repetition were equally distributed between the first and second halves of the runs, ensuring that effects of stimulus repetition were averaged out when the levels of perceptual repetition were compared, and the other way around (relatedness index: binocular rivalry: -0.08, $t_{(4)}= -1.0$, $p= 0.4$; 3D-motion rivalry: -0.06, $t_{(5)}= -0.8$, $p= 0.4$; see methods for calculation of relatedness index; Figure 4-5B).

Magnetic resonance imaging (MRI) results

We were interested in changes in the magnitude of the BOLD response under conditions of repeated perception of - and stimulation with - the same ambiguous stimulus. We hypothesized that the integrated BOLD response (reflecting the area under the BOLD curve) would be larger during the late than early stages of perceptual repetition (i.e. repetition enhancement). In contrast, for stimulus repetition we hypothesized an adaptation-like decrease of the integrated BOLD response in the late compared with the early part of the experimental runs (i.e. repetition suppression). On average the relative signal change ((late-early) / (late+early)) was indeed positive for perceptual repetition and negative for stimulus repetition (0.04 and -0.08, respectively; Figure 4-3), in line with these predictions. There were marked differences between binocular and 3D-motion rivalry, which will be described below.

Response changes during binocular rivalry

During binocular rivalry the influences of perceptual repetition and stimulus repetition clearly differed ($F_{(1,12)}= 212.4$, $p< 10^{-8}$, effect of repetition modality) and the difference

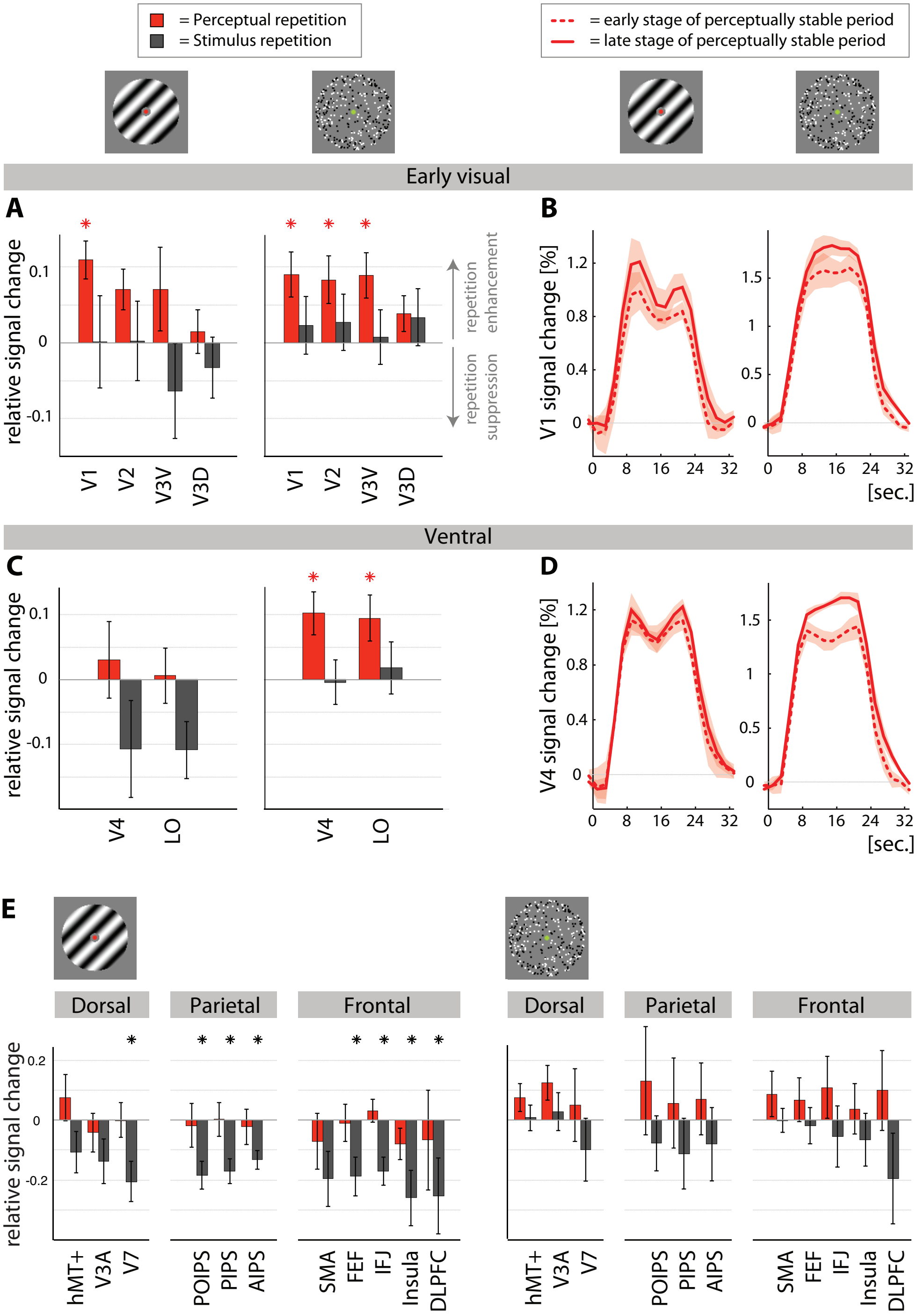

🟥 = Perceptual repetition
■ = Stimulus repetition
= early stage of perceptually stable period
= late stage of perceptually stable period
Early visual
A
relative signal change
0.1
0
-0.1
V1
V2
V3V
V3D
repetition enhancement
repetition suppression
B
V1 signal change [%]
1.2
0.8
0.4
0
1.5
1
0.5
0
8
16
24
32
[sec.]
Ventral
C
V4
LO
D
V4 signal change [%]
E
Dorsal
Parietal
Frontal
0.2
-0.2
hMT+
V3A
V7
POIPS
PIPS
AIPS
SMA
FEF
IFJ
Insula
DLPFC

Figure 4-3. Stimulus repetition suppression and perceptual repetition enhancement.
A) Modulations of the magnitude of the BOLD response related to stimulus repetition (black bars) and perceptual repetition (red bars) during binocular rivalry (left graph) and 3D-motion rivalry (right graph; ±SEM) in the early visual regions. Upward bars indicate repetition enhancement; downward bars indicate repetition suppression. In both experiments perceptual repetition was reflected in an enhancement of the BOLD response in early visual regions. Asterisk (*) indicates statistical significance ($p< 0.05$) in t-test across participants (depicted in red for perceptual repetition and in grey for stimulus repetition). Abbreviations as in Figure 4-2A.
B) Event-related BOLD responses for early visual region V1 during binocular (left graph) and 3D-motion rivalry (right graph), averaged over blocks in the early (= after a few repeats; dashed lines) and late (= after many repeats; solid lines) stage of a perceptually stable period (±SEM). In the early visual cortex there was perceptual repetition enhancement during binocular as well as 3D-motion rivalry.
C) Repetition-related modulations of the magnitude of the BOLD response in the ventral visual regions (layout and colors as in A). In the ventral visual cortex perceptual repetition enhancement was only observed during 3D-motion rivalry and not during binocular rivalry.
D) Event-related BOLD responses for ventral visual region V4, averaged over blocks in the early and late stage of a perceptually stable period (layout and colors as in B). Perceptual repetition enhancement was only observed during 3D-motion rivalry.
E) Repetition-related modulations of the magnitude of the BOLD response in the dorsal visual, parietal and frontal regions (layout and colors as in A). While perceptual repetition was reflected in an enhancement of the BOLD response in stimulus-specific visual regions (see A-D), stimulus repetition resulted in an adaptation-like suppression of the BOLD response in higher-order regions, particularly during binocular rivalry.

was similar in magnitude across the cortical regions ($F_{(4,12)}= 3.2$, $p= 0.06$, no interaction between repetition modality and cortical region). However, the response changes in the early visual cortex were different from those in the other cortical regions ($F_{(4,12)}= 10.8$, $p< 0.001$, effect of cortical region). Perceptual repetition enhancement was present only in the early visual cortex and not in any of the other cortical regions (early visual: $t_{(3)}= 3.4$, $p< 0.05$; other cortical regions: all $p\geq 0.1$), while stimulus repetition suppression was present in all but the early visual cortex (early visual: $t_{(3)}= 1.5$, $p= 0.2$; other cortical regions: all $p< 0.05$; t-tests over regions-of-interest per cortical region; Figure 4-3).

Response changes during 3D-motion rivalry

During 3D-motion rivalry the difference between the repetition modalities was also highly significant ($F_{(1,12)}= 60.4$, $p< 10^{-5}$, effect of repetition modality) and there were no differences between the cortical regions ($F_{(4,12)}= 1.9$, $p= 0.2$, no effect of cortical region; $F_{(4,12)}= 2.5$, $p= 0.1$, no interaction between repetition modality and cortical region). Perceptual repetition enhancement was robust ($t_{(4)}= 21.3$, $p< 10^{-4}$), but the relative signal change related to stimulus repetition was not significant ($t_{(4)}= = 1.4$, $p= 0.2$, t-test over cortical regions; Figure 4-3). This indicates that during 3D-motion rivalry the magnitude of the perceptual repetition enhancement was similar across the cortical regions. This

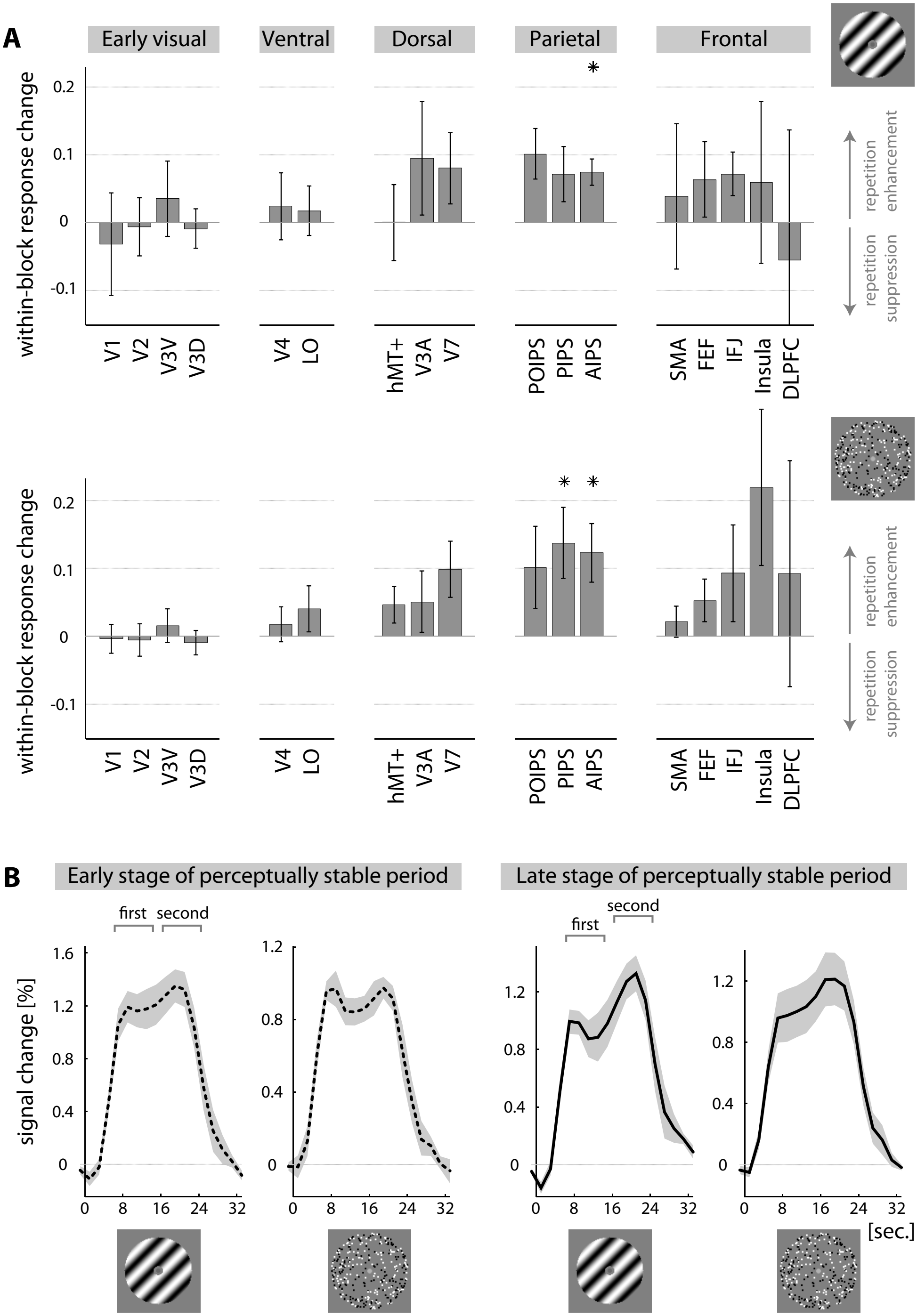

A
Early visual
Ventral
Dorsal
Parietal
Frontal
within-block response change
0.2
0.1
0
-0.1
*
repetition enhancement
repetition suppression
V1
V2
V3V
V3D
V4
LO
hMT+
V3A
V7
POIPS
PIPS
AIPS
SMA
FEF
IFJ
Insula
DLPFC
within-block response change
0.2
0.1
0
-0.1
* *
repetition enhancement
repetition suppression
B
Early stage of perceptually stable period
Late stage of perceptually stable period
first
second
signal change [%]
1.6
1.2
0.8
0.4
0
0
8
16
24
32
[sec.]

Figure 4-4. Perceptual repetition enhancement of the within-block response.
A) Within-block changes in the shape of the BOLD response (±SEM) as reflected in the difference in amplitude between the first and second part of the response. Upward bars indicate that the second part of the response was relatively enhanced in the late compared with the early stage of a perceptually stable period; downward bars indicate suppression of the second part of the response. Perceptual repetition enhancement of the within-block response change was found in the parietal cortex, suggesting additional neural processing when there is memory of stable perceptual history. Asterisk (*) indicates statistical significance in t-test across participants ($p< 0.05$). Abbreviations as in Figure 4-2A.
B) Event-related BOLD responses for the anterior intraparietal sulcus (region AIPS) during binocular and 3D-motion rivalry (graphs are labeled with an icon of the corresponding stimulus), averaged over blocks in the early (= after a few repeats; dashed lines) and late (= after many repeats; solid lines) stage of a perceptually stable period (±SEM). For both types of rivalry, the first and second part of the within-block response had similar amplitudes in the early phase of a perceptually stable period, whereas in the late stage of a perceptually stable period the second part was larger in amplitude than the first part.

was in contrast to binocular rivalry, during which perceptual repetition enhancement was observed only in the early visual cortex (see above). As hypothesized, the perceptual repetition enhancement was thus more widespread during 3D-motion rivalry than during binocular rivalry (direct statistical comparison: $F_{(1,12)}= 38.6$, $p< 10^{-4}$, effect of type of rivalry). Perceptual repetition enhancement was indeed reliable in the ventral visual regions V4 and LO as well as the early visual regions V1, V2 and V3V (all $t_{(5)}\geq 2.7$, all $p< 0.05$), while in the other regions-of-interest there was no real consistency across participants (all $t_{(5)}\leq 2.1$, all $p\geq 0.09$; t-tests over participants per region-of-interest; Figure 4-3). The perceptual repetition enhancement during 3D-motion rivalry was thus most robust in early visual and ventral visual cortex.

Response changes in the parietal cortex

In both experiments the event-related BOLD responses exhibited a characteristic ‘saddle-shape’, with a dip in activity around 15 seconds after stimulus onset (see BOLD curves in Figures 4-3 and 4-4). The amplitude of the response just before and just after this dip in activity could differ quite substantially, suggesting that activity levels changed not only across blocks, but also within blocks (see Figure 4-1B for definition of ‘block’). With regard to perceptual repetition the first and second part of the response (measured 6-14 and 16-24 seconds after block onset, respectively) had similar amplitudes in the early stages of perceptual stabilization, whereas in the late stages of perceptual stabilization the second part of the response was enhanced relative to the first part ((second – first) / (second + first); difference divided by sum to correct for differences in the overall magnitude of the response). This suggests that activity in the later stage of the block was enhanced (Figure 4-4B).

Interestingly, during both experiments this effect was observed in the parietal cortex (both $t_{2)} \geq 8.7$, both $p < 0.05$), particularly the anterior intraparietal sulcus (AIPS, both $p < 0.05$, t-tests over participants per experiment), rather than the sensory cortical regions (early, ventral and dorsal visual; all $p \geq 0.06$; t-tests over regions-of-interest per cortical region per experiment; $F_{(4, 12)} = 5.1$, $p < 0.05$, effect of cortical region across both experiments). During both experiments similar responses were also observed in the frontal cortical region, but they appeared more variable between participants. Importantly, there were no differences between binocular and 3D-motion rivalry in the localization of the within-block response enhancement (direct statistical comparison: $F_{(4, 12)} = 0.8$, $p = 0.5$, no interaction between type of rivalry and cortical region; Figure 4-4A). Further, for stimulus repetition we did not observe any consistency in the within-block modulation of the response across participants (all $p > 0.07$, t-tests over participants per region-of-interest per experiment; $F_{(1, 12)} = 55.1$, $p < 10^{-5}$, effect of repetition modality across both experiments).

The influence of within-block perceptual stabilization

We observed a modest repetition suppression in the parietal and frontal cortical regions in relation to within-block perceptual stabilization, i.e. the percentage of same percepts within a block (Figure 4-5C; binocular rivalry: $F_{(4, 16)} = 17.1$, $p < 10^{-4}$; 3D-motion rivalry: $F_{(4, 12)} = 5.4$, $p < 0.05$, effect of cortical region). A median-split procedure was used in the same way as for the other analyses described above. Regarding the individual ROIs the effect of within-block perceptual stabilization was significant in AIPS, SMA, IFJ and Insula during binocular rivalry only. This pattern of results may remotely resemble the results for stimulus repetition (see Figure 4-3). However, there was no correlation in time between these variables, ensuring that the effects of within-block perceptual stabilization were averaged out when the effects of stimulus repetition were investigated (relatedness index: binocular rivalry: -0.01, $t_{(4)} = -0.2$, $p = 0.8$; 3D-motion rivalry: -0.05, $t_{(5)} = -1.3$, $p = 0.3$; see methods for calculation of relatedness index; Figure 4-5B).

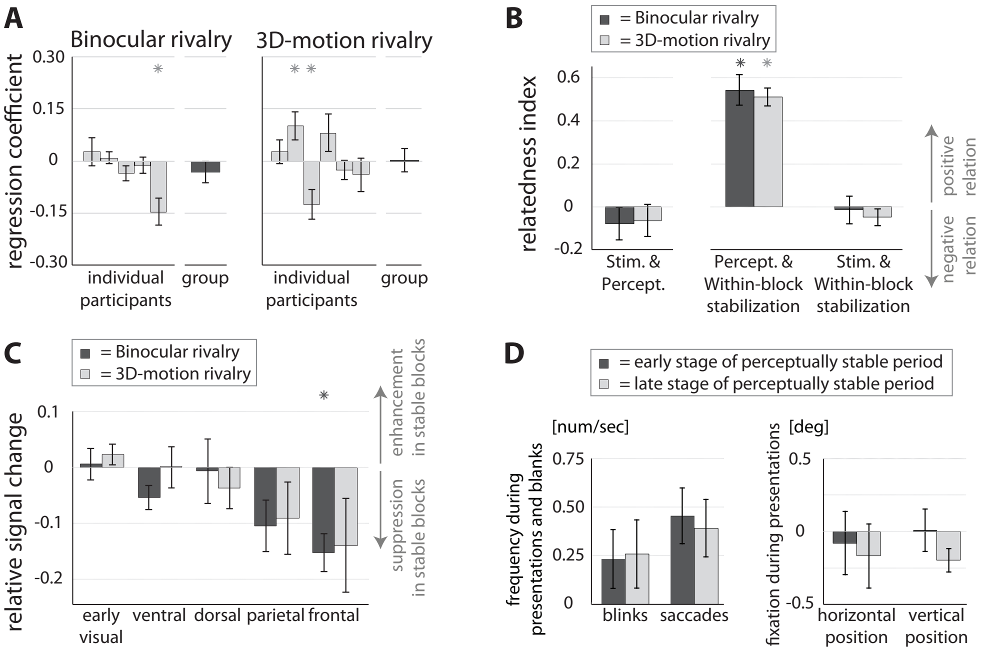


Figure 4-5. Perceptual repetition and its psychophysical (behavioral) relation with stimulus repetition, within-block perceptual stabilization and eye movements.

A) Slopes (±SEM) of the regression between stimulus repetition, i.e. the number of a block relative to the start of the run, and perceptual repetition, i.e. the output value of the perceptual filter (see Figure 4-1C), for the individual participants (light grey bars) and the group of participants per experiment (dark grey bars, repeated measures regression). The results did not exhibit a consistent temporal relation between stimulus repetition and perceptual repetition on the group level, allowing separate investigations of these co-occurring phenomena (as explained in Figure 4-1D and performed in Figure 4-3). Asterisk (*) indicates significant difference from zero.

B) The relation in time between stimulus repetition (Stim.), perceptual repetition (Percept.) and within-block perceptual stabilization, i.e. the percentage of same percepts within a block, for binocular rivalry (dark grey bars) and 3D-motion rivalry (light grey bars), as reflected in the relatedness index (see methods; ±SEM). In both experiments perceptual repetition is positively related in time with the within-block perceptual stabilization (bars in the middle). Stimulus repetition is neither related with perceptual repetition (bars on the left; in line with A), nor with the within-block perceptual stabilization (bars on the right). Asterisk (*) indicates significant difference from zero.

C) Modulations of the magnitude of the BOLD response (±SEM) related to within-block perceptual stabilization, per cortical region, for binocular rivalry (dark grey bars) and 3D-motion rivalry (light grey bars). There was a modest suppression of the BOLD response in perceptually stable compared with unstable blocks, particularly in the frontal cortical region during binocular rivalry. Within-block perceptual stabilization was related in time with long-term perceptual repetition (see B), but the associated modulations of the BOLD response were markedly different (compare with Figure 4-3). Asterisk (*) indicates significant difference from zero.

D) Eye movements (left graph) and fixations (right graph) in the early (dark grey bars) and late (light grey bars) stages of perceptually stable periods (±SEM). The left graph presents the average number of blinks and saccades per second during the intermittent presentation blocks (during stimulus presentations and short blanks). The right graph presents the horizontal and vertical eye position in degrees of visual angle (relative to baseline) during fixation on the stimulus. The early and late stages of a perceptually stable period did not differ in the frequency of eye movements or the eye position during fixation.

The percentage of same percepts within a block was generally smaller in the early than in the late stages of a perceptually stable period (relatedness index: binocular rivalry: 0.54, $t_{(4)}= 7.7$, $p< 0.01$; 3D-motion rivalry: 0.51, $t_{(5)}= 12.2$, $p< 10^{-4}$; Figure 4-5B). Although long-term perceptual repetition was thus related in time with the within-block perceptual stabilization, the associated modulations of the BOLD response were markedly different (see Figure 4-3). Also, the within-block response enhancement observed in the anterior intraparietal sulcus in relation with perceptual repetition (Figure 4-4) was not observed in relation with within-block perceptual stabilization (binocular rivalry: -0.03, $t_{(4)}= -1.0$, $p=0.4$; 3D-motion rivalry: 0.09, $t_{(5)}= 2.2$, $p= 0.08$, t-test over participants).

Overview of results

Minutes-long periods of largely stabilized perception were reported during passive viewing of either a binocular rivalry or 3D-motion rivalry stimulus. While stimulus repetition per se was associated with a decreased BOLD response, these involuntarily/automatically occurring perceptually stable periods were associated with an increased BOLD response in visual brain regions specific for the type of rivalry. More specifically, perceptual repetition enhancement was observed in early visual cortex during binocular rivalry, whereas it was present in both the early visual and the ventral visual cortex during 3D-motion rivalry (Figure 4-3). Perceptually stable periods were also characterized by a within-block response enhancement in the parietal cortex. This parietal effect of perceptual experience was similar for both types of rivalry and was not observed in any of the visual regions (Figure 4-4).

4.5 Discussion

We investigated how perceptual experience modifies neural processing in sensory and cognitive brain regions. It is inherently difficult to separate the influence of prior perceptual experience from that of prior sensory stimulation. In contrast to previous studies, we discerned these two influences using ambiguous stimuli. Passive viewing of intermittent presentations of an ambiguous stimulus is known to elicit distinct and consecutive periods of stabilized perception that can last several minutes (Figure 4-1;

Leopold et al., 2002; Orbach et al., 1963). We repeatedly presented either a binocular rivalry or a 3D-motion rivalry stimulus, interleaved with short blank intervals, and observed that the mere repetition of the stimulus evoked an entirely different pattern of activity modulations than the repetition of a particular perceptual interpretation of the stimulus. Perceptual repetition was associated with an enhanced response in stimulus-specific visual brain regions (Figure 4-3) as well as a response change in the parietal cortex that was similar for both types of stimuli used and was not observed in any of the visual regions (Figure 4-4). Stimulus repetition, on the other hand, resulted in an attenuated response in higher-level regions, particularly during the binocular rivalry experiment (Figure 4-3). Below we will discuss these results in further detail.

Perceptual repetition enhancement in stimulus-specific visual brain regions

During a period of repeated experience of the same *binocular rivalry* percept we found an enhanced BOLD response in early visual regions. These low-level regions process basic stimulus features and modulate their activity in response to changes in binocular rivalry perception (Haynes & Rees, 2005; Lee et al., 2005; Gail et al., 2004). When the same *3D-motion rivalry* percept was repeatedly experienced the enhanced BOLD response was not only present in early visual regions, but also in ventral visual regions (Figure 4-3). The additional involvement of ventral visual regions is consistent with their role in processing relative disparity (Neri, 2005; Hinkle & Connor, 2005; Preston et al., 2008) and 3D-shape (Kourtzi et al., 2003).

Previous studies have also reported experience-dependent increases of fMRI responses in early visual regions (Furmanski et al., 2004; Schwartz et al., 2002) and ventral visual regions (Turk-Browne et al., 2007; Kourtzi et al., 2005; James & Gauthier, 2006; Dolan et al., 1997). Since the BOLD signal is an indirect measure of the combined activity of many sensory neurons (Logothetis & Wandell, 2004), it does not provide information regarding the physiological mechanisms underlying these effects. The stimulus-specific localization of the observed perceptual repetition enhancement is an indication that neurons tuned to the features of the stimulus were involved (Kourtzi et al., 2005; Krekelberg et al., 2006; Grill-Spector et al., 2006).

It is unlikely that the observed increased response is confounded by eye movements or difficulty of recognition of the percepts (recognition hypothesis proposed by Henson et al., 2000), as there was no difference between the early and late stages of a perceptually stable period in the number of eye movements, the eye position during fixation or the frequency of blended/mixed percepts (Figure 4-5). For 3D-motion rivalry we had anticipated an additional role of motion-sensitive dorsal and parietal brain regions (Paradis et al., 2000; Orban et al., 2006; Brouwer & van Ee, 2007; Preston et al., 2009; Brascamp et al., 2010); however, this was found only in a subset of the participants. Possibly, the involvement of these regions was determined by the extent to which the task-strategy of the participant employed spatial attention (Corbetta et al., 2002; Shulman et al., 1999) and/or the processing of coarse depth-judgments and absolute disparity (as contrasted to the processing of detailed depth-perception and relative disparity in ventral regions; Neri, 2005; Preston et al., 2008; Anzai & DeAngelis, 2010).

Possible mechanisms underlying perceptual repetition enhancement

There are some tentative explanations for the observed perceptual repetition enhancement based on previous neurophysiological and neuroimaging findings and, most likely, multiple of these physiological mechanisms play a role (Karmarkar & Dan, 2006; Holtmaat & Svoboda, 2009). Firstly, the number of activated neurons may have increased (Gilbert et al., 2001). For example, an increase in the number of neurons responsive to the features of the dominant percept can occur when the tuning curves of individual neurons shifted toward these features (Kohn & Movshon, 2004; Ghisovan et al., 2009). Also, additional neural processing may have been recruited, such as activity specific to perceptual stability (Sterzer & Rees, 2008; Pitts & Britz, 2011; Rees et al., 2002) or the perception of ambiguous stimuli (Sterzer et al., 2009; see also degraded stimuli: Kourtzi et al., 2005; Rainer et al., 2004; James & Gauthier, 2006). An increase in activity, or disinhibition, of the neurons associated with the suppressed percept may also contribute (Hock et al., 1996; Klink et al., 2010; de Jong et al., 2012a), similar to the phenomenon of motion opponency (Petersen et al., 1985; Krekelberg et al., 2006).

It could also be that the sensitivity/excitability of the activated neurons increased during a perceptually stable period, rather than the number (Frenkel et al., 2006; Grill-Spector et al., 2006). An increased excitability of percept-specific neurons at the moment of the perceptual choice could bias the competition between the possible percepts in favor of the most experienced percept, thereby favoring re-occurrence of this percept (Noest et al., 2007; Heekeren et al., 2008; Wilson, 2007). During further processing of the stimulus the initial increase in excitability may ultimately lead to an increase in the amplitude of the BOLD response (in a fashion similar to the accumulation hypothesis proposed by James & Gauthier, 2006). There is a variety of physiological changes that can lead to an increase in neural excitability, such as experience-dependent connectivity changes, local recurrent excitation, a reduction in neural noise, an increase in sub-threshold activity or a change in local field potentials (Holtmaat & Svoboda, 2009; Klink et al., 2012; Rainer et al., 2004; Hock et al., 1996; Noest et al., 2007; Schwartz et al., 2002; Crist et al., 2001).

In future electrophysiology studies the above-proposed increase in excitability can presumably be measured upon activation of the involved neurons, soon after the onset of the stimulus (Heekeren et al., 2008). Yet, its presence might be measurable during the blank periods in between the stimulus presentations as well (Britz et al., 2011; Hsieh et al., 2012; Ehm et al., 2011), as is also seen during the delay period in working memory tasks (Naya et al., 2003; Miller et al., 1996). The idea of increased activity during the blank periods fits with the observed effects, as this would eventually contribute to the BOLD response measured for the entire block of intermittent stimulation. A previous fMRI study reported that percept-specific activations lingered on during the first few seconds after removal of an ambiguous stimulus (Sterzer et al., 2008). If the duration of this 'lingering on' of activity is modulated by perceptual repetition, increased activity during the blank periods can also result from an increase in the duration of the activations to each individual stimulus presentation.

In all, we provided several possible mechanisms underlying the observed perceptual repetition enhancement, namely an increase in the number of activated neurons, an increase in the excitability of percept-specific neurons or an increase in activity during the blank periods. Future studies are needed to investigate these speculations, as they cannot be distinguished with the present fMRI data. Regardless of the underlying mechanism, the present data suggest that the repeated activation of the visual networks biased toward the dominant percept facilitated later re-activation of these networks.

Perceptual repetition reflected in parietal regions

In contrast to the stimulus-specific activations in the visual cortex, we observed a change in the 'saddle shape' of the hemodynamic response in the parietal cortex that was similar during binocular and 3D-motion rivalry (see Figure 4-4B). Saddle-shaped responses have been observed previously with unambiguous sensory stimuli, particularly when the stimulation blocks were long-lasting (> 16 seconds; e.g. Soltysik et al., 2004; Boynton et al., 1996; Friston et al., 1998). In the present study we observed that, over the course of a perceptually stable period, the second part of the hemodynamic response became larger relative to the first part of the response (Figure 4-4A). A previous study also found an enhancement of the later part of the response when the first and second presentations of an unfamiliar visual stimulus were compared (Martens & Gruber, 2012).

The second peak in the response occurred too early to be an offset effect. Also, the effect could not be attributed to within-block perceptual stabilization (Figure 4-5). Given that it was observed for both types of rivalry it probably relates to aspects of perception that are independent of specific percepts or stimuli. The early visual cortex is necessary for conscious perception, but not sufficient (Tong, 2003; Rees et al., 2002), and parietal regions could have an additional interpretive or evaluative involvement in perceptual experience (Gilbert et al., 2001; Sterzer et al., 2009; Dolan et al., 1997). Particularly the intraparietal sulcus has been implicated in monitoring ambiguous perception over time in paradigms that investigated perceptual switches during continuous stimulus presentation (Kanai et al., 2011; Rees et al., 2002) or the repetition of the most recent percept across a single interruption of the stimulus (trial-to-trial perceptual stabilization; Sterzer & Rees, 2008; Britz et al., 2011).

The perceptual stabilization in the present study did not require conscious effort or active mnemonic processing (Pearson & Brascamp, 2008) and cannot be explained as repetition priming of the most recent percept (Long & Toppino, 2004; Pearson & Brascamp, 2008). Perhaps the repeated co-activation of parietal networks involved in the integration of perceptual information over time and visual networks dedicated to the dominant percept strengthened the connections between them. When the parietal networks are associated with the dominant rather than the suppressed percept, the stability of the dominant percept could be further enhanced. Also, parietal regions could provide stimulus-specific feedback to visual cortex, for example to counteract the above-proposed disinhibition of neurons associated with the suppressed percept (Kanai et al., 2011). However, these and other speculations need further investigation.

Stimulus repetition suppression

Experience with the *stimulus* per se evoked an entirely different pattern of results than the perceptual repetition enhancement described above. While the perceptual experience of the stimulus changed occasionally, the stimulus itself was the same throughout an experimental run. Over the course of an experimental run the repeated presentation of the binocular rivalry stimulus resulted in a widespread suppression of the BOLD response, possibly due to neural fatigue and/or more efficient or sparser encoding (Kohn, 2007; Krekelberg et al., 2006; Grill-Spector et al, 2006). In line with earlier reports that repetition suppression is often confined to higher visual regions this effect was not present in early visual regions (Krekelberg et al. 2006). The repeated presentation of 3D-motion rivalry was not associated with suppression of the BOLD response, perhaps because the small moving dots that constituted the 3D-motion stimulus resulted in less luminance adaptation than the stationary black and white bars that constituted the binocular gratings (Figure 4-1A).

Conclusions

Experience-driven modulation of neural processing in the adult brain is likely to be important for adapting our behavior to dynamic environments. The present results indicate that the repeated activation of visual networks mediating a particular percept enhanced later re-activation when compatible visual input is presented. Possible physiological mechanisms might be an increase in the number of activated neurons, an increase in the excitability of the percept-specific neurons, and an increase in activity during the blank periods, but these speculations need further investigation. In contrast, the parietal cortex contributed to perceptual stability in a manner that was similar for both of the ambiguous stimuli tested. We speculate that perceptual experience is associated with a facilitated neural response within and between percept-specific visual networks and parietal networks involved in the temporal integration of perceptual information. The parietal regions may modulate percept-specific processing in visual areas. Future human and animal electrophysiology investigations into the temporal dynamics underlying these effects may advance our understanding of the experience-dependent activity in these cortical circuits. We conclude that the visual and parietal cortices play dissociable and complementary roles in the interpretation of ambiguous sensory information based on previous experience.

Chapter 5

Implicit perceptual memory modulates early visual processing of ambiguous images

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5.1 Abstract

The way we perceive the present visual environment is influenced by past visual experiences. Here we investigated the neural basis of such experience-dependency. We repeatedly presented human observers with an ambiguous visual stimulus (structure-from-motion) that can give rise to two distinct perceptual interpretations. Past visual experience is known to influence the perception of such stimuli. We recorded fast dynamics of neural activity shortly after stimulus onset using event-related electro-encephalography. The number of previous occurrences of a certain percept modulated early posterior brain activity starting as early as 50 ms after stimulus onset. This modulation developed across hundreds of percept repetitions, reflecting several minutes of accumulating perceptual experience. Importantly, there was no such modulation when the mere number of previous stimulus presentations was considered regardless of how they were perceived. This indicates that the effect depended on prior perception rather than prior visual input. The short latency and posterior scalp location of the effect suggest that perceptual history modified bottom-up stimulus processing in early visual cortex. We propose that bottom-up neural responses to a given visual presentation are shaped, in part, by feedback modulation that occurred during previous presentations, thus allowing these responses to be biased in light of prior perceptual decisions.

5.2 Introduction

An essential attribute of our sensory systems is that past neural processing affects present neural activity. In the adult brain the response properties of sensory neurons are continually tuned to the current sensory environment (Clifford et al. 2007; Chopin & Mamassian 2012; Thompson & Burr 2009). Previous visual input and its associated perception can both influence later perception (Leopold et al., 2002; Maier et al., 2003; Pearson & Brascamp 2008) and neural processing (Kornmeier and Bach, 2006; De Jong et al., 2012b; Pitts and Britz, 2011). To study the neural effects of prior perception specifically, we here measured electroencephalograms (EEG) while participants viewed an ambiguous visual stimulus. Because ambiguous stimuli can be perceived in multiple ways while visual stimulation remains constant, they allow a partial dissociation between stimulation and perception (Figure 5-1A).

How an ambiguous stimulus is perceived, depends strongly on prior perception of that stimulus (Leopold et al., 2002; Orbach et al., 1963; Maier et al., 2003; Pearson & Brascamp, 2008). This dependence includes both a short-term effect of the latest percept experienced just before the current one, but also a longer-term effect of perception during the past minutes (Pearson & Brascamp, 2008; de Jong et al., 2012a; Pastukhov & Braun, 2008; Brascamp et al., 2009). Existing EEG studies have focused on the short-term influence of the latest presentation (Kornmeier and Bach, 2004; 2005; 2006; Pitts and Britz, 2011). These studies generally compared cases where two consecutive stimulus presentations yield identical perception to cases where they yield different perception, revealing differential EEG activity starting from 130 ms after stimulus onset. Here we specifically investigate the neural mechanism by which a minutes-long perceptual history can influence current perception.

Behaviorally, the effect of long-term perceptual history tends to be facilitatory, leading to reoccurrence of the percept that was experienced most in the recent past (Pearson and Brascamp, 2008). In contrast, the aftereffect of prior stimulation is usually suppressive, causing a perceptual bias away from the features of prior stimulation (Long & Toppino, 2004; Thompson & Burr 2009; Pearson & Clifford 2005). We studied cortical activity associated with stimulus history as well as percept history, the latter being our main interest.

We analyzed event-related brain potentials (ERPs) derived from the EEG while the participants viewed short presentations of an ambiguous visual stimulus interleaved with short blank periods (fig 1B). At our stimulus settings this paradigm elicits minutes-long sequences during which the same perceptual interpretation is experienced repeatedly, interspersed with occasional changes in perception (Figure 5-1C; Leopold et al. 2002; de Jong et al. 2012b; Pearson & Brascamp 2008; perceptual changes can occur more frequently at other settings: Kornmeier & Bach, 2004; Noest et al, 2007). Because of these perceptual changes, stimulus repetitions were not always coupled with percept repetitions, allowing investigation of their separate influences on neural processing. We observed that minutes-long sequences of perceptual repetitions were associated with a modulation of posterior activity present as early as 50-140 ms after stimulus onset, suggesting that long-term perceptual history modified bottom-up stimulus processing.

5.3 Materials and Methods

Participants

There were 21 participants (13 female, 8 male) who all gave written informed consent prior to participation and who had normal or corrected to normal vision and no neurological history. Four participants (1 female, 3 male) were excluded because their perceptual time courses were not sufficiently stable for our analysis (see criteria in following sections). All experiments were carried out in accordance with the ethical guidelines in the Declaration of Helsinki (World Medical Association 2000).

Stimulus

An ambiguous structure-from-motion stimulus that consisted of 350 dots (each 0.077° in diameter) was presented in the center of a computer-screen (75 Hz refresh rate) on a grey background. The dots were either black or white, had unlimited lifetime and represented random points on the surface of a virtual globe (5.0° in diameter; viewing distance was 107 cm; Figure 5-1A). The dots moved leftward or rightward and their speed on the screen was fastest in the middle of the stimulus and slowest near the left and right edges (at the edges the motion direction reversed). The sinusoidal speed profile of the dots created the percept of a globe revolving around its vertical axis every 7.8 seconds. The three-dimensional interpretation of the stimulus, and thereby its direction of rotation, was ambiguous, because no depth cues differentiated the rightward moving surface from the leftward moving surface.

An experimental session consisted of 600-ms presentations of the rotating globe interleaved with blank intervals with a duration that was randomly selected out of 10 evenly-spaced fixed values between 480 and 720 ms (duration was 600 ms on average; Figure 5-1B). During the stimulus presentations as well as the blank intervals a centrally presented green fixation dot remained visible that subtended 0.18° degrees of visual angle. Presentation durations were sufficiently brief to minimize the occurrence of changes in perceived rotation direction within one presentation epoch. The stimuli were created using Mathematica (Wolfram Research) and Presentation (Neurobehavioral Systems Inc.).

Procedure

Participants were instructed to maintain strict fixation on the fixation dot throughout the experimental session. At every stimulus presentation the participants indicated the direction of motion of the surface that was perceived to be in front by pressing one of two corresponding buttons using their corresponding hand. They refrained from responding when they could not differentiate the front from the back surface.

While the stimulus was the same on every presentation, the perceptual interpretation changed occasionally. The participants reported minutes-long periods of repeated perception of one rotation direction of the globe after which perception would switch and the other rotation direction would be experienced for the next period (Figure 5-1C). This is consistent with existing findings (Orbach et al. 1963; Leopold et al. 2002). An experimental session was terminated when 3 perceptually stable periods were completed (see below for our definition of a stable period). These 3 consecutive periods are hereafter referred to as period A, B and C. Most participants completed 3 experimental sessions. Two of the participants completed only 1 session and two others completed only 2 sessions, because of technical and practical limitations. During the

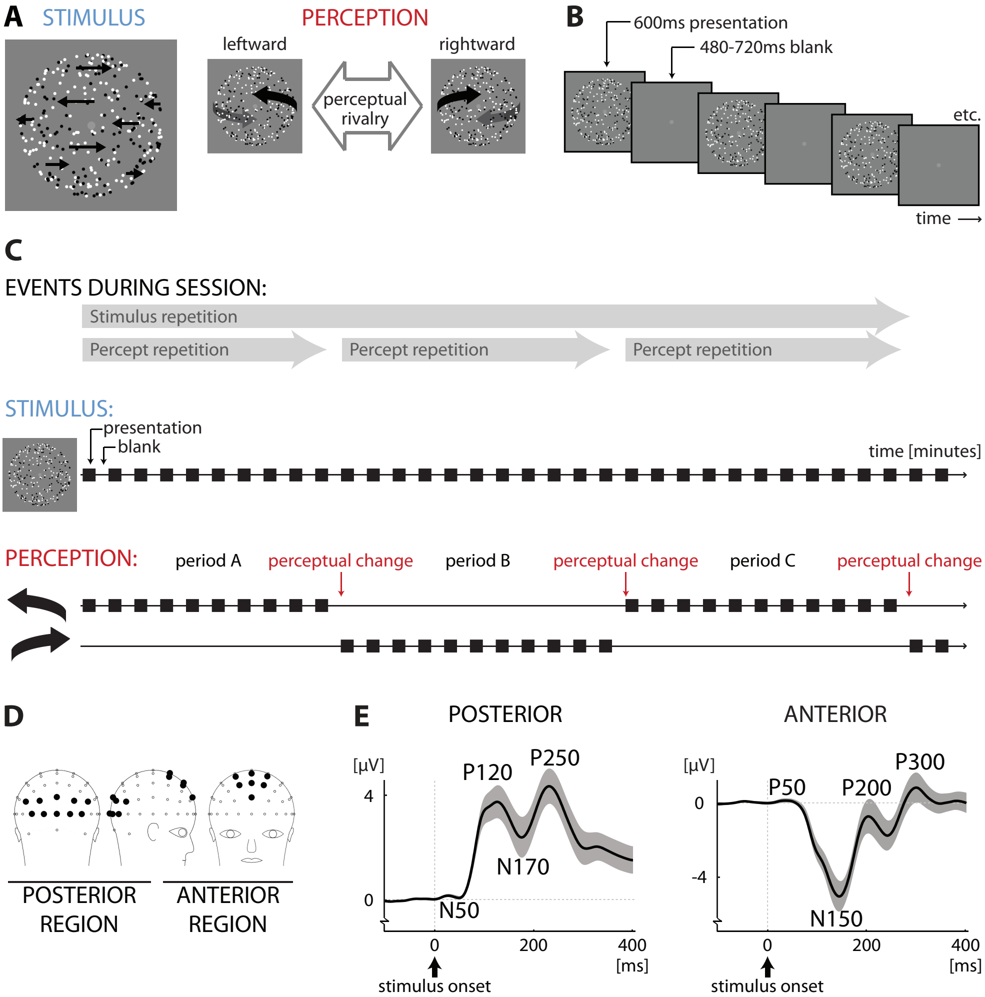


Figure 5-1: Stimuli and paradigm.

A) The ambiguous 3D-motion stimulus. The horizontal speed of the dots was faster near the vertical meridian than near the left and right edges (indicated by the length of the black arrows). This provided an ambiguous depth-cue (structure-from-motion without stereoscopic disparity): either the leftward or the rightward moving dots were perceived as the front surface of a rotating globe. The occurrence of different perceptual interpretations of the same stimulus enabled us to dissociate the neural effects of *stimulus* repetition from those of *percept repetition*.

B) The intermittent presentation paradigm. Each presentation consisted of a 600 ms presentation of the stimulus followed by a blank period lasting 480-720 ms. Observers tend to experience the same percept consecutively for many presentations when such short-lasting presentations of an ambiguous stimulus are interleaved with blank intervals. In the present study a change in perception occurred occasionally (ones every several minutes), which then indicated the end of the current perceptually stable period and the start of the next period, during which the other percept was experienced.

C) Schematic drawing of the events during an experimental session. The ambiguous stimulus was the same throughout the session, but the conscious perception of the stimulus changed from one perceptually stable period to the next. For illustration purposes a limited amount of stimulus presentations is drawn in each period. The actual number of presentations amounted

on average up to 229 per period (lasting 4.6 minutes), but could vary between periods and participants as it was determined by the reported perceptual time course. An experimental session consisted of repeated presentation of the ambiguous rotating globe and lasted until 3 consecutive perceptually stable periods were completed (referred to as periods A, B and C, respectively). For our data analysis we divided each period into four quartiles that each contained 25% of the presentations of that period. We hypothesized that the neural response, as measured with electro-encephalography (EEG), is concurrently modified by stimulus repetition (across periods) as well as percept repetition (within periods; across quartiles). These effects are presented in blue and red colors, respectively, in the figures throughout this manuscript.
D) Topographical map of the scalp locations of the electrodes in the posterior (on the left) and anterior (on the right) region of interest (see filled circles, other electrodes are shown as open circles).
E) Grand mean waveform of event-related potentials (ERPs) derived from electro-encephalograms (EEG) over the posterior (on the left) and anterior (on the right) region of interest (n= 17; shading indicates ± 1 SEM). Peaks in the ERPs are named according to their polarity and timing: P and N indicate positive and negative deflections, respectively, and the number indicates the approximate stimulus-onset-to-peak latency in milliseconds. In the literature the posterior N50, P120 and N170 are often referred to as the visually evoked ‘C1’, ‘P1’ and ‘N1’, respectively.

break between sessions the participants were free to rest and/or walk around. The break lasted at least as long as the previous experimental block and was intended for recovery from adaptation/mnemonic traces that were built-up during the previous session (sessions lasted 14 minutes on average).

Analysis of perceptual stabilization

The perceptual time courses of the individual participants were analyzed using Matlab (MathWorks Inc). For each stimulus presentation manual responses occurring between 133 (8 screen refresh intervals) and 1000 ms after stimulus onset were recorded. Presentations to which no response was recorded were excluded from further analysis (5.6% of presentations were excluded on average across participants). We also excluded the first 30 seconds of each session, to ensure that initial adaptation processes present in this period would not influence the results (see Van Ee, 2009). For each experimental session the perceptually stable periods, i.e. periods of consecutive reoccurrence of the same percept, were identified as follows: The first of a train of at least 10 consecutive reports of the same percept was considered the start of the first perceptually stable period. After that, a perceptually stable period was considered terminated as soon as the opposite, non-stabilized percept was reported on 10 consecutive presentations, marking the start of a new stabilized period for this opposite percept. This definition allows the non-stabilized percept to occur occasionally (<10 times consecutively) within a stabilized period of the other percept, in line with the known perceptual dynamics of the rotating globe and other bistable stimuli (Brascamp et al., 2009; de Jong et al., 2012b; Leopold et al, 2002). The limit of 10 repetitions was considered reasonable based on previous studies (Brascamp et al., 2009; de Jong et al., 2012b; Leopold et al, 2002), but we repeated our analyses using more extreme limits of either 5 or 60 repetitions and found equivalent results (data not shown).

In our analysis we discarded all presentations in which the non-stabilized percept was reported. Furthermore, we discarded all perceptual alternations, i.e. presentations in which perception had changed relative to the preceding presentation. Together these two categories amounted to 3.9% of the presentations on average across participants. We chose this strategy because perceptual alternations from one presentation to the next may evoke additional neural processes (Kornmeier and Bach 2004; 2005; 2006; Pitts et al. 2007; 2009). These processes are outside of our present scope, because we focus on long-term history effects rather than those that act from one presentation to the next. To make sure our specific manner of discarding presentation-to-presentation perceptual alternations did not critically affect our results we repeated our analyses while discarding not one presentation following each non-stabilized percept, but instead discarding the entire period if it was not perfectly stable. This yielded equivalent results (see Results; Figure 5-2C).

EEG data recording and preprocessing

The participants were seated in an electronically and acoustically shielded room. Electroencephalography (EEG) was sampled at 2048 Hz and recorded with 64 silver/silver-chloride (Ag/AgCl) flat type active electrodes (Active Two system, Biosemi) positioned at standard locations on an elastic cap (Quickcap, Neuromedical supplies of Neurosoft inc.) and referenced to an additional active electrode (Common Mode Sense) during recording. Two of the electrodes in the cap provided an active ground. An additional electrode was placed at the right mastoid and horizontal and vertical electro-oculograms (EOG) were measured.

Preprocessing of the EEG data was performed using BrainVision Analyzer 2.0 (Brainproducts GmbH) and included a 0.1-20 Hz band-pass filter, a 50 Hz Notch filter and referencing to the right mastoid for all electrodes. Epochs time-locked to the onset of the stimulus were extracted from the continuous data. Artifacts due to eye movements were removed (algorithm by Gratton et al. 1983). Epochs containing EEG amplitudes >

±50 µV or within-epoch amplitude differences >75 µV were removed from the analysis. We also checked for recording failure by excluding epochs with <0.5 µV amplitude differences within a 200ms window (abnormally low activity) and epochs with amplitude steps per sample point >50 µV (abnormal recording gradient), although this seldom occurred. Baseline correction was performed relative to a 100ms pre-stimulus interval.

Selection of regions of interest

Activity changes in *sensory* brain regions have been related to stimulus repetition (Krekelberg et al. 2006), percept repetition (de Jong et al., 2012b), perceptual learning/memory (Henson et al. 2000; Kourtzi et al. 2005; Furmanski et al. 2004; Schwartz et al. 2002) and presentation-to-presentation perceptual alternations during ambiguous visual stimulation (Kornmeier et al., 2004; Pitts et al., 2009; Sterzer et al., 2009). On the other hand, activity in *frontal and parietal* brain regions has also been associated with presentation-to-presentation perceptual alternations (Sterzer et al., 2009; Pitts et al. 2009; Pitts & Britz 2011), as well as attention/mnemonic processing of sensory information (Desimone 1996; Pasternak & Greenlee 2005). Interestingly, ERPs derived from scalp EEG measured during ambiguous perception are also modulated at anterior as well as posterior electrodes (Kornmeier and Bach 2004; 2005; 2006; Pitts et al. 2007; 2008; 2009; Khoe et al. 2008). This is in line with the involvement of posterior as well as anterior regions in perceptual processing, although the inverse problem makes it hard to justify conclusions about which brain regions these scalp ERP modulations originate from.

Across the above-mentioned ERP investigations into ambiguous perception there is a remarkable consistency regarding the electrodes that responded to ambiguous stimuli per se as well as to manipulations of ambiguous perception. Using different stimuli (e.g. binocular as well as perceptual rivalry) and different types of perceptual manipulations (bottom-up as well as top-down, stimulus driven as well as attentional in nature) the same electrodes were repeatedly reported to show affected ERPs. Given this consistency in the reported electrode sites of interest across ambiguous stimuli and across perceptual manipulations, we expected that these same electrodes would also reflect the long-term perceptual manipulations investigated in the present study. We therefore selected a posterior region and an anterior region of interest for further analysis of the

ERPs (Figure 5-1D; choice of electrodes based on: Kornmeier and Bach 2004; 2005; 2006; Pitts et al. 2007; 2008; 2009; Khoe et al. 2008). For the posterior region of interest we averaged the signals of electrodes O1, O2, Oz, P5, P6, PO3, PO4, PO7, PO8 and POz, and for the anterior region of interest we averaged the signals of electrodes AFz, F1, F2, FC1, FC2, FCz and Fz. We did not consider the individual electrodes, but analyzed the averaged signal in the pre-defined regions of interest, thereby limiting the number of analyzed spatial locations to two (limitation of multiple comparisons problem). As a further precaution against any false positive results making their way into our data, we repeated our analyses of the posterior activity using a more assumption-free method of selecting the region of interest. Specifically, we found similar results when we replaced our posterior region of interest with one that comprised the entire back-half of the scalp, i.e. the averaged signal of all electrodes posterior to Cz.

In the above-mentioned existing literature the latencies of the ERPs that reflected perceptual manipulations were relatively early. Considering the present study, the behavioral definition of longer-term perceptual stability also points to a critical contribution of short-latency neural processing. Perceptual stability influences current perception (see Introduction) and this can be effectively done only when processes that lead up to, i.e. precede, the perceptual decision are changed. Given these considerations we were mainly interested in – and restricted our analyses to – short-latency ERPs. Irrespective of stimulus/percept history, the time-locked epochs in the posterior region typically showed 3 short-latency peaks: the P120, N170 and P250 peak (Figure 5-1E, left graph). In the anterior region the N150, P200 and P300 peaks were present in the typical ERP (Figure 5-1E, right graph). Peak names were chosen such that N and P indicate negative and positive deflections, respectively, and the number indicates the approximate across-participant latency of the peak relative to stimulus onset.

We used these peaks to guide further analyses and searched for their session-specific latencies within the following intervals after stimulus onset (intervals based on visual data inspection): 95-170 ms, 150-225 ms and 210-285 ms for the posterior P120, N170 and P250 peaks, respectively, and 120-195 ms, 160-235 ms and 265-340 ms for the anterior N150, P200 and P300 peaks, respectively. Within each of these intervals the session-specific peak latency was defined as the time point at which the maximum (minimum for N peaks) voltage occurred in the session-averaged ERP. When the outcome of this automated definition did not reflected a true peak/extremum we manually selected a local extremum instead (if present; this occurred only for the anterior P200 peak in 2 participants). Based on additional observations of the data (see results) we furthermore analyzed the posterior N50 and anterior P50 components (Figure 5-1E), applying the same method as described above. We used a 30-80 ms interval after stimulus onset for these components. A local extremum was manually selected for 6 participants (in 1 or 2 of their sessions) regarding the N50 and for 4 participants (in 1 of their sessions) regarding the P50 component. A control analysis in which we excluded, per peak, all sessions with an unclear or manually adjusted peak value yielded equivalent results (data not shown), indicating that the used method of manual peak selection did not critically influence our results.

Further processing of EEG data

Further analysis was performed using Matlab (MathWorks Inc.). The critical idea underlying our approach was to compare ERPs across presentations of the stimulus *within* as well as *across* perceptually stable periods. The effects of stimulus repetition can accumulate during a session, across perceptually stable periods, because perceptual changes are irrelevant with regard to stimulus repetition. The effects of percept repetition, on the other hand, can accumulate within a perceptually stable period, but not across perceptually stable periods that are separated by a change in perception. To test changes in the EEG data within as well as across perceptually stable periods we identified the three perceptually stable periods A, B and C as described above. We discarded experimental sessions where one or more of these periods did not last long enough to provide enough repetitions (<60) for calculation of meaningful ERPs (for 5 participants 1 session was excluded, for 3 participants 2 sessions were excluded, leaving 2.0 sessions on average per participant).

To implement our analysis we split each period into four quartiles that each contained 25% of the presentations of that period. Depending on the length of the period the quartiles of different periods could thus contain varying absolute numbers of stimulus presentations. Our procedure yielded 4 consecutive time bins in each period, which could be compared to investigate percept repetition, and 12 consecutive time bins across the three periods that together spanned the entire experimental session (3 periods x 4 quartiles = 12 time bins). The consecutive periods could be compared to investigate stimulus repetition. The 12 consecutive time bins will be referred to as A1, A2, A3, A4, B1, B2, B3, B4, C1, C2, C3 and C4, respectively, and ERPs recorded within each time bin were averaged.

For each of the 12 time bins separately, we calculated the amplitude of each of the above-defined ERP components (represented in Figure 5-1E) by determining the mean voltage in a 30ms time window that was centered on the session-wide latency defined previously for that component (see above). We also determined the peak-latency of each component for each time bin by searching for the maximum or minimum voltage within this 30ms window. The data were then averaged across all sessions of a given participant and, on average, reflected the recordings of 95.8 stimulus presentations per time bin (after discarding data).

Statistical analysis was performed using PASW Statistics 18. Unless indicated otherwise, we performed a repeated-measures analysis of variance (ANOVA) over participants, with *perceptually stable period* (period A, B or C) and *quartile of perceptually stable period* (quartile 1, 2, 3 or 4) as within factors ($\alpha = 0.05$). A Greenhouse-Geisser correction was applied. Since we expected the effects of stimulus repetition to accumulate during a session, across the perceptually stable periods, a main effect of *period* would indicate an effect of stimulus repetition. The effects of percept repetition were expected to accumulate within a perceptually stable period, across the repeated occurrences of the stabilized percept, and might thus be reflected in a main effect of *quartile* but not of *period*. In addition, we performed a Pearson correlation analysis in some instances to get a better understanding of effect sizes. These cases are clearly indicated in the text.

5.4 Results

The present study investigated modulations of the neural response in a posterior and an anterior region of interest (Figure 5-1D) under conditions of repeated perception of - and stimulation with - the same ambiguous stimulus. Our protocol was designed to elicit 3 distinct and consecutive periods of stable perception across repetitions of the same ambiguous stimulus, referred to as period A, B and C (Figure 5-1C). The behavioral and EEG data in each perceptually stable period were binned per quartile, each quartile containing 25% of the presentations of that period. We investigated changes across the stable periods, which may reflect the influence of stimulus repetition, and changes within the stable periods, across the quartiles, which may reflect the influence of percept repetition (*period x quartile* ANOVA, see methods).

Behavioral results

All participants experienced prolonged periods of perceptual stability that lasted on average 4.6 minutes (±0.3 SEM; equivalent to 229 presentations). Periods A, B and C did not differ in average duration ($F_{(1.9, 28.4)}$= 1.6, p= 0.2, effect of duration in repeated-measures ANOVA over participants). The non-stabilized perceptual interpretation was on average seen in 2.5% of the presentations (±0.9% SEM; these presentations were excluded from the analysis, see methods). The percentage of non-stabilized percepts did not differ between periods A, B and C ($F_{(1.7, 27.8)}$= 0.6, p= 0.5, main effect of period), but within the periods a higher proportion of non-stabilized percepts was reported in the fourth quartile compared with the other three quartiles (1.5%, 1.2%, 1.6% and 6.1% in quartiles 1 to 4, respectively; $F_{(1.6, 25.9)}$= 7.8, p= 0.004, main effect of quartile; all $F_{(1, 16)}$> 9.1, all p≤ 0.008, per quartile tests of difference from fourth quartile).

Stimulus repetition: Modulation of late perceptual processing

Stimulus repetition influenced the amplitudes and latencies of ERP components around 200 ms after stimulus onset, as is illustrated by the modulation of the posterior P250 peak (Figure 5-2A). The P250 peak showed a gradually decreasing amplitude during an experimental session (0.7 µV average difference between period A and C; $F_{(1.4, 22.5)}$= 8.7, p= 0.004). Note that this change occurred slowly over the course of several minutes, as an experimental session lasted on average almost 14 minutes (see above).

The effect of stimulus repetition on the P250 peak is nicely illustrated by the difference wave between the posterior ERPs of stable periods A and C, which shows a clear deviation around the timing of the posterior P250 peak (Figure 5-3C, blue line). There were additional effects of stimulus repetition, which are summarized in table form in Figure 5-4C. In general, increased latencies over stimulus repetitions were found somewhat earlier than the P250, in both the posterior and anterior region of interest (posterior N170 peak: 3.2 ms delay, $F_{(1.4, 23.1)}$= 6.7, p= 0.01, effect of period; anterior P200

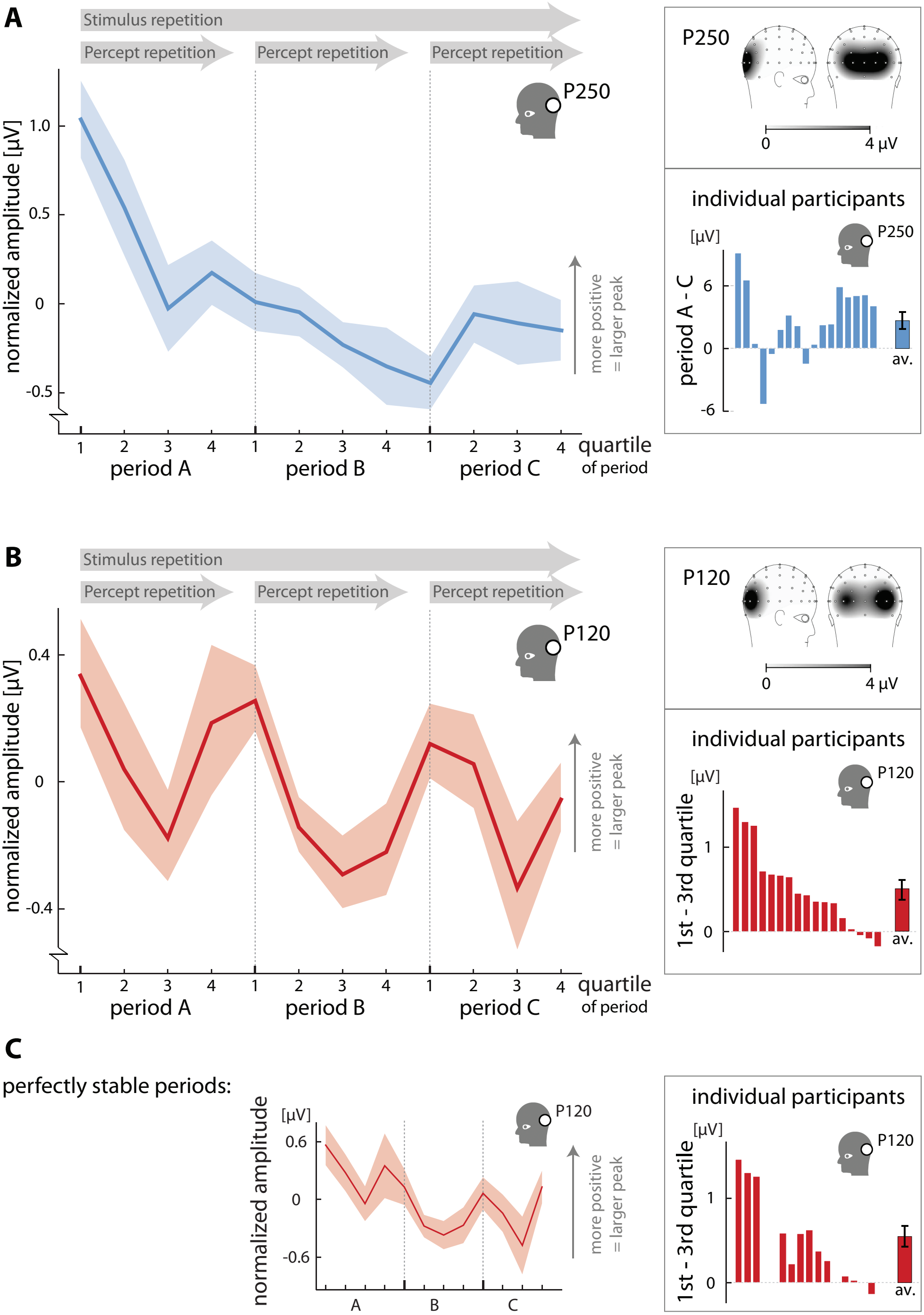

A
Stimulus repetition
Percept repetition
Percept repetition
Percept repetition
P250
normalized amplitude [µV]
1.0
0.5
0
-0.5
more positive = larger peak
1 2 3 4 1 2 3 4 1 2 3 4
period A
period B
period C
quartile of period
P250
0
4 µV
individual participants
[µV]
P250
period A - C
6
0
-6
av.
B
Stimulus repetition
Percept repetition
Percept repetition
Percept repetition
P120
normalized amplitude [µV]
0.4
0
-0.4
more positive = larger peak
1 2 3 4 1 2 3 4 1 2 3 4
period A
period B
period C
quartile of period
P120
0
4 µV
individual participants
[µV]
P120
1st - 3rd quartile
1
0
av.
C
perfectly stable periods:
normalized amplitude
[µV]
0.6
0
-0.6
A
B
C
P120
more positive = larger peak
individual participants
[µV]
P120
1st - 3rd quartile
1
0
av.

Figure 5-2: The influence of stimulus repetition and percept repetition on peak values in the posterior region of interest.
A) The influence of stimulus repetition on the amplitude of the posterior P250 peak. During an experimental session the amplitude gradually decreased over time, regardless of the experienced percept (i.e. regardless of the changes in perception between the 3 perceptually stable periods that constituted a session; see Figure 5-1C; n= 17; shading indicates ± 1 SEM). The right top inset shows the topographical map of the P250 peak (EEG signal measured over the scalp between 200-250 ms after stimulus onset; darker shades indicate more positive amplitude; n= 17). The bottom inset shows the difference in P250 amplitude between period A and period C (averaged across quartiles) for individual participants.
B) The influence of percept repetition on the amplitude of the posterior P120 peak. Within each perceptually stable period the amplitude decreased from the first to the third quartile and slightly recovered from the third to the fourth quartile (n= 17; shading indicates ± 1 SEM). This fall-and-rise pattern of the P120 amplitude was present within each period and resulted in an oscillating pattern across periods. Since this modulation developed within rather than across periods, we contribute it to percept repetition and not to stimulus repetition. The data thus reflect an early peak in the ERP, occurring about 120 ms after stimulus onset, whose amplitude is modulated across many stimulus presentations, constituting an oscillatory pattern over the course of many minutes. Importantly, this oscillatory pattern developed relative to the perceptual time course rather than relative to real time or the absolute amount of stimulus presentations, given that the perceptually stable periods (and thus the quartiles) contained varying absolute numbers of stimulus presentations. The right top inset shows the topographical map of the P120 peak (EEG signal measured over the scalp between 100-150 ms after stimulus onset; darker shades indicate more positive amplitude; n= 17). The bottom inset shows the difference in P120 amplitude between the first and third quartile for individual participants, averaged across periods A, B and C. The order in which the participants are depicted is the same as in the bottom inset of Figure 5-2A.
C) The influence of percept repetition on the amplitude of the posterior P120 peak, when the analysis included the perfectly stable periods only (zero reports of the non-stabilized percept; n= 12; shading indicates ± 1 SEM). A fall-and-rise pattern occurred within each period, similar to the graph presented in panel B, suggesting that the recovery in P120 amplitude from the third to the fourth quartile was not related to the sporadic occurrence of the non-stabilized percept in quartile 4. The inset on the right shows the difference in P120 amplitude between the first and third quartile for individual participants, averaged across periods A, B and C (perfectly stable periods only; same order of participants as the bottom insets of panels A and B).

peak: 5.2 ms delay, $F_{(1.9, 29.8)}$= 10.9, p= 0.0004, effect of period). A further amplitude modulation followed later in the anterior ROI (the P300 peak: 1.4 µV increase, $F_{(1.8, 28.9)}$= 8.2, p= 0.002, effect of period). Interestingly, the amplitude was gradually increased in the anterior region (P300 peak), while it was decreased in the posterior region (P250 peak). A period x quartile interaction ($F_{(3.8, 60.9)}$= 4.7, p= 0.003) indicated that the amplitude of the posterior P250 peak was extra large in the very first time bin (quartile 1 of period A) compared with all other time bins (Figure 5-2A; the effect of quartile was only significant in period A). To test this directly we performed a post hoc alternative ANOVA in which we treated the 12 consecutive time bins that constituted an experimental session as one factor (i.e. repeated-measures ANOVA over participants with *time bin* as the only within factor, α= 0.05, a Greenhouse-Geisser correction was applied). The 12 time bins indeed differed from each other ($F_{(3.8, 61.3)}$= 5.1, p= 0.002) and partial testing revealed that the first time bin differed from all but the second time bin (second time bin: $F_{(1, 16)}$= 3.2, p= 0.09, other time bins: all $F_{(1, 16)} \geq$ 6.7, all p≤ 0. 02). The extra large P250 amplitude in the first time bin suggests that initial adaptation was greater than later adaptation in the posterior region.

Percept repetition: Modulation of early perceptual processing

In comparison with stimulus repetition, the modulations related to *percept* repetition occurred markedly early in the ERP (compare Figure 5-4D and Figure 5-4C; see Figure 5-3C). One of the earliest effects of percept repetition occurred on the posterior P120 peak (Figure 5-2B). The P120 component is common in visual ERPs. It usually occurs between 100-150 ms after stimulus onset and is thought to reflect basic perceptual processing. Across the four quartiles of each perceptually stable period the P120 showed a systematic amplitude change, which repeated during each consecutive stable period, and was manifested in a significant effect of quartile ($F_{(2.5, 40.7)}$= 4.3, p= 0.01). However, rather than there being a monotonic effect of quartile, we observed a decrease in the amplitude of the P120 peak from the first to the third quartile of a perceptually stable period ($F_{(1, 16)}$= 18.1, p< 0.001, partial test between first and third quartile; 0.50 μV ±0.12 SEM average amplitude difference), followed by a slight increase in each fourth quartile (0.24 μV relative to third quartile). The fourth quartile differed neither from the first quartile ($F_{(1, 16)}$= 2.5, p= 0.1), nor from the third quartile ($F_{(1, 16)}$= 2.5, p= 0.1). Below a further analysis is presented to help characterize this fall-and-rise pattern, and it is discussed further in the Discussion section. First, however, note that the pattern was present within each perceptually stable period, creating the oscillating curve seen in Figure 5-2B, and that the difference in P120 amplitude between the first and the third quartile was very robust across participants (see bottom inset in Figure 5-2B).

The difference in P120 amplitude between the first and the third quartile was not stronger in longer-lasting or more stable periods, as it did not correlate with the duration of the perceptually stable periods (R= -0.1 averaged across participants, $t_{(16)}$= -0.5, p= 0.6) nor with the general prevalence of the non-stabilized percept (R= 0.0 averaged across participants, $t_{(16)}$= 0.0, p= 1.0; t-test across participants). The increase in P120 amplitude from the third to the fourth quartile might be related to the higher proportion of non-stabilized percepts reported in the fourth quartile compared with the other three quartiles (see above). However, an analysis of only the perfectly stable periods (i.e. periods in which the non-stabilized percept was never reported) provided no support for this idea. Instead, this analysis revealed the same fall-and-rise pattern as obtained when including all data (Figure 5-2C; $F_{(2.2,\ 23.7)}= 2.6$, $p= 0.095$, effect of quartile; $F_{(1,\ 11)}= 12.8$, $p= 0.004$, partial test between first and third quartile; fourth quartile differed neither from the first quartile, nor from the third quartile, both $F_{(1,\ 16)}< 2.4$, both $p\geq 0.2$).

Additional effects of percept repetitions beyond the P120 peak are summarized in table form in Figure 5-4D, and illustrated for the posterior region of interest in Figure 5-3B and 3C by a comparison between the average ERP waveforms for the first and third quartiles, respectively (averaged across perceptually stable periods). In the posterior region we did not observe amplitude modulations on any peaks later than the P120 (Figure 5-3B). There was a fall-and-rise latency modulation on the posterior N170 peak, meaning that the latency decreased from the first to the third quartile and increased again in the fourth quartile ($F_{(2.6,\ 41.5)}= 4.0$, $p< 0.05$, effect of quartile; normalized latencies for quartiles 1-4 averaged across periods: 0.48, -1.56, -0.90 and 1.22 ms; Figure 5-4D). Combined with the latency effect of stimulus repetition reported above for the N170 (Figure 5-4C), this peak thus showed a superposition of both these effects. In the anterior region an effect of percept repetition did not appear until well after the posterior effects, namely only on the P200 peak around 200 ms after stimulus onset. The amplitude of the anterior P200 peak was larger in the first quartile of each period than in the following quartiles (the first quartile differed from all others: all $F_{(1,\ 16)}> 8.4$, all $p\leq 0.01$; $F_{(2.1,\ 33.7)}= 6.1$, $p= 0.005$, effect of quartile). The pattern of results within each period was thus L-shaped rather than U-shaped (normalized amplitudes for quartiles 1-4 averaged across periods: 0.59, -0.50, -0.28 and -0.41 ms; Figure 5-4D).

Percept repetition: Modulation of N50 peak

Above we reported that the amplitude of the posterior P120 peak increased from the first to the third quartile of every stable period (Figures 5-2B and 5-3B). The difference between the posterior ERP waveforms from the first and third quartile (averaged across periods) indeed shows a deviation from zero coinciding with the timing of the P120 peak (Figure 5-3C, red line). However, inspection of Figures 5-3B and 5-3C suggests that this difference already existed earlier on in the ERP, around the latency of the negative deflection preceding the P120. Hereafter, we will refer to this deflection as the N50 peak. When we analyzed the amplitude and latency of the N50 we found a fall-and-rise amplitude modulation similar to that of the P120 (Figure 5-4A; $F_{(2.1,\ 33.9)}= 4.4$, $p= 0.02$,

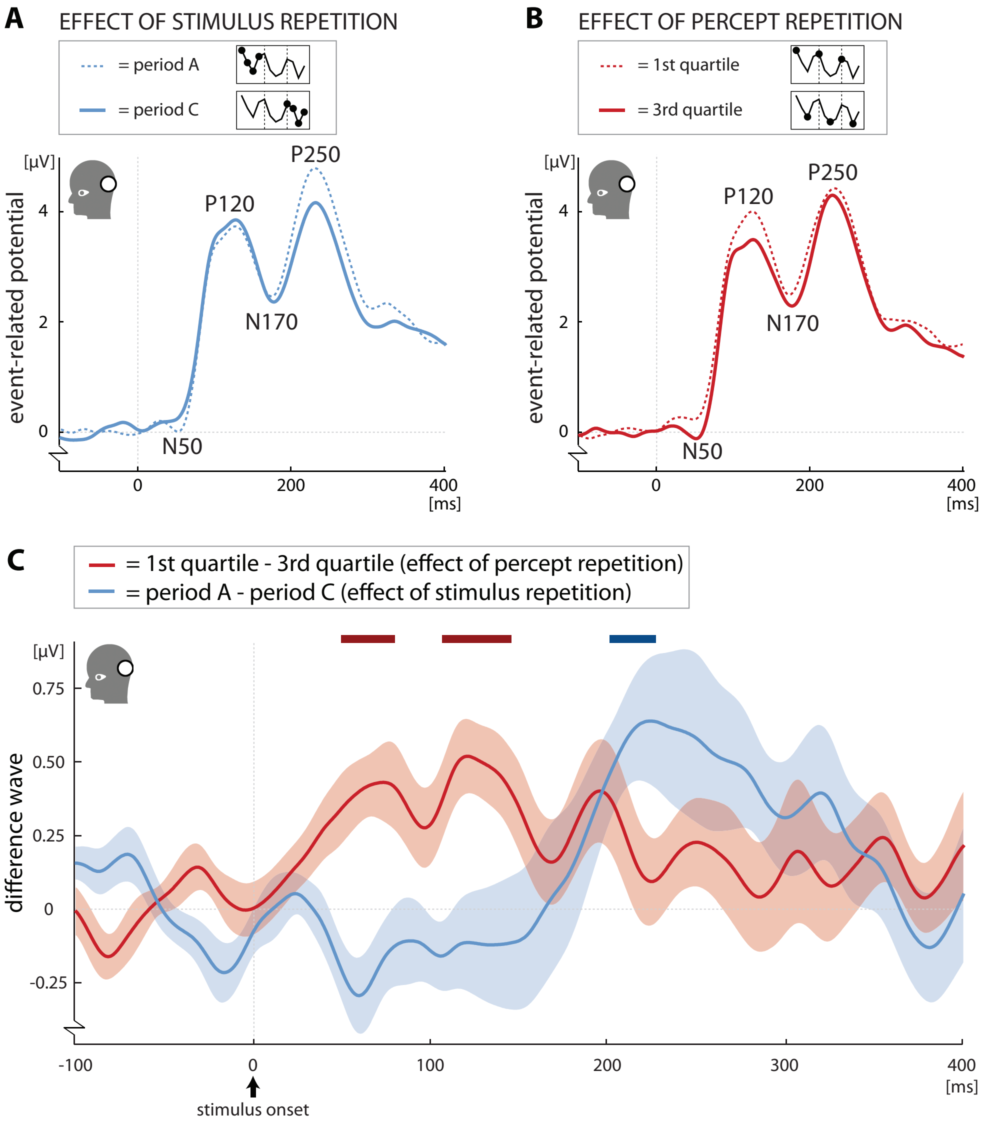


Figure 5-3: The influence of stimulus repetition and percept repetition on the waveform of the posterior event-related potential.

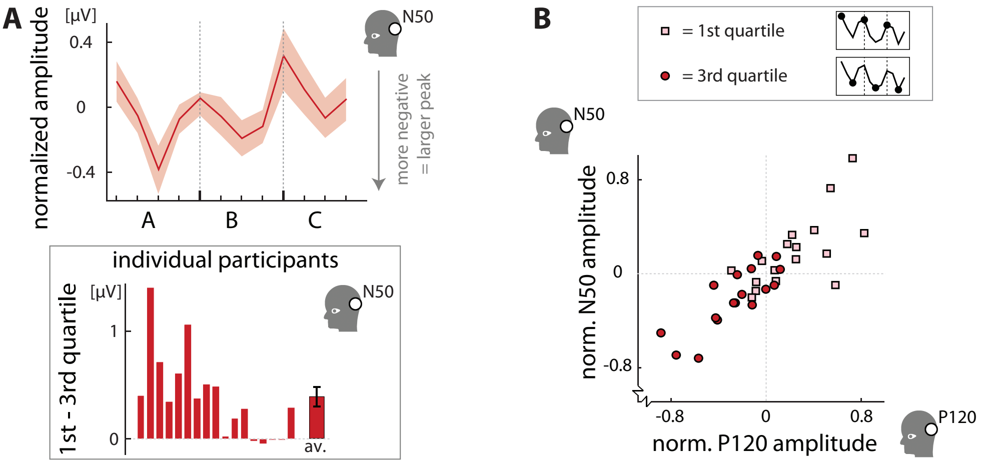
A) Waveform of ERPs measured in the posterior region of interest in the first period (period A; dashed line) and the last period (period C; solid line), showing the influence of stimulus repetition on the posterior P250 peak. Both waveforms are averaged across the four quartiles of the respective period (as indicated by the cartoon in the legend; n= 17).

B) Waveform of ERPs measured in the posterior region of interest in the first (dashed line) and third quartile (solid line), showing the modulation of the posterior N50 and P120 peaks. Both waveforms are averaged across the periods A, B and C (as indicated by the cartoon in the legend; n= 17).

C) Difference wave illustrating that in the posterior region of interest the effect of percept repetition occurred shortly after stimulus onset (red line) and the effect stimulus repetition occurred later in the ERP (blue line; n= 17; shading indicates ± 1 SEM). These effects are in line with the peak amplitude analyses reported in Figure 5-2 and 5-4, which indicated that the N50 and P120 peaks are affected by percept repetition and the P250 peak is affected by stimulus repetition. Specifically, the red line here represents the difference between the ERPs measured in the first and third quartile (see B; 1st quartile – 3rd quartile; averaged across periods A, B and C) and the blue line represents the difference between the ERPs measured in the first and last period (see A; period A - period C; averaged across the four quartiles of each period). Statistical analysis of continuous waves like these is not straightforward, because there is a strong temporal correlation between successive time-points. For illustration purposes only, we performed t-tests on each time-point of these difference waves using a conservative alpha of 0.01. The horizontal bars at the top of the graph represent the time-points where the t-tests indicated a difference from zero for the effects of percept repetition (dark red bars) and stimulus repetition (dark blue bar).

effect of quartile; $F_{(1, 16)}$= 16.3, p= 0.001, partial test between first and third quartile; fourth quartile differed neither from the first quartile, nor from the third quartile, both $F_{(1, 16)}$< 3.0, both p> 0.1). As was the case for the P120 peak, the difference in N50 amplitude between the first and third quartile was very robust across participants (inset in Figure 5-4A), and it averaged to 0.39 µV ±0.10 SEM.

Thus, the observed effects of *percept* repetition on the posterior ERP started to arise as early as 50 ms following stimulus onset. The effects of *stimulus* repetition, in comparison, occurred much later, starting around 200 ms after stimulus onset (Figures 5-3A, 5-3C and 5-4C). To ensure that this early effect of percept repetition could not be attributed to fluctuations during the baseline interval, we analyzed activity during the 100ms baseline interval preceding stimulus onset. For this additional analysis we placed our 30ms analysis window in either the early (-100 to -70 ms), middle (-65 to -35 ms) and late (-30 to 0 ms) part of the baseline interval and performed baseline correction on the remainder of the original baseline interval (which spanned -100 to 0 ms relative to stimulus onset). The results show that the effect of percept repetition was absent prior to stimulus onset, as there was no amplitude effect of percept repetition in either of these segments of the baseline interval (all F< 1.3, all p> 0.3, effect of quartile; all $F_{(1, 16)}$< 2.7, all p> 0.1, partial test between first and third quartile). Moreover, with these alternative baseline corrections the amplitude modulations of the N50 and P120 were still present (all F≥ 3.0, all p≤ 0.06, effect of quartile; all $F_{(1, 16)}$> 12.0, all p≤ 0.003, partial test between first and third quartile). Thus, the reported early posterior effect of percept repetition arose after stimulus onset and could not be attributed to fluctuations during the baseline interval.



C

STIMULUS REPETITION	P50	N50	P120	N150	N170	P200	P250	P300
ERP amplitude	-	-	-	-	-	-	✱d	✱i
ERP latency	-	-	-	-	✱i	✱i	-	-

D

PERCEPT REPETITION	P50	N50	P120	N150	N170	P200	P250	P300
ERP amplitude	-	✱u	✱u	-	-	✱L	-	-
ERP latency	-	-	-	-	✱u	-	-	-

Figure 5-4: The influence of percept repetition on the posterior N50 peak and an overview of the influences of stimulus repetition and percept repetition on event-related potentials.

A) The influence of percept repetition on the amplitude of the posterior N50 peak, showing a fall-and-rise pattern within each period similar to the modulation of the P120 peak (see Figure 5-2B; n= 17; shading indicates ± 1 SEM). Note that the N50 is a negative deflection, meaning that smaller amplitudes (voltages) actually indicate a larger (more negative) peak and a lower starting point of the upstroke in activity leading to the P120 peak. The inset on the right shows the difference in N50 amplitude between the first and third quartile for individual participants, averaged across periods A, B and C (same order of participants as the bottom insets of Figures 5-2A, 5-2B and 5-2C)

B) The amplitudes of the posterior N50 (vertical axis) and P120 (horizontal axis) peaks for the first (pink squares) and third (red circles) quartile separately, averaged across periods. For both peaks the amplitudes were relatively high (i.e. above average) in the first quartile and relatively small (i.e. below average) in the third quartile. Also, participants with a high P120 amplitude tended to have a high N50 amplitude as well. The difference between the first and third quartile in the amplitude of early

posterior peaks reflects the influence of percept repetition. Participants with a large effect size for the P120 also tended to have a large effect size for the N50 (compare the bottom insets in Figures 5-2B and 5-4A). Note that the N50 is a negative deflection, meaning that smaller peak amplitudes (voltages) actually indicate a larger (more negative) peak, whereas for the P120 peak, being a positive deflection, smaller amplitudes indicate a smaller (less positive) peak.
C) Overview of the effects of stimulus repetition on ERP peak values in both the posterior (white background) and the anterior (grey background) region of interest (open circle in cartoons indicate the appropriate region; see Figure 5-1D). From left to right the peaks are chronologically ordered relative to stimulus onset. Peaks that were significantly influenced by stimulus repetition are indicated with an asterisk (*). In both the anterior and posterior region there was a late latency modulation (around 200 ms after stimulus onset), followed by a late amplitude modulation ('i' and 'd' indicate gradual increases and decreases over the course of a session, respectively). See Figure 5-2A and 5-3A.
D) Overview of the effects of percept repetition on ERP peak values in the posterior (white background) and the anterior (grey background) region of interest (layout and symbols as in panel C). There was an early posterior amplitude modulation related to percept repetition that emerged around 50 ms after stimulus onset (see Figures 5-3B and 5-3C) and influenced the N50 and P120 peak (see Figure 5-2B and 5-4A, respectively). The amplitude of the early posterior N50 and P120 peaks decreased from the first quartile to the third quartile of each perceptually stable period, and partially recovered during the fourth quartile (Figure 5-2B). Such fall-and-rise effects are indicated with 'u' in the table, whereas 'L' indicates a fall without the rise in the fourth quartile.

The magnitudes of the effect of percept repetition (i.e. the difference between the first and the third quartile) for the N50 and P120 peaks correlated across participants ($R= 0.70$, $t_{(15)}= 3.7$, $p= 0.002$), meaning that participants with a large effect size for the P120 also tended to have a large effect size for the N50 (compare the insets in Figure 5-2B and 5-4A showing the effect sizes of the individual participants). This association between the P120 and the N50 was also present when the peak amplitudes in first and third quartile were considered separately (Figure 5-4B). In the first quartile participants with a high P120 amplitude also tended to have a high N50 amplitude ($R= 0.67$, $t_{(15)}= 3.5$, $p= 0.003$), although the amplitudes of both peaks were relatively high (above average) for all participants. In the third quartile the peak amplitudes were generally small (below average) and across participants the smaller P120 amplitudes were associated with the smaller N50 amplitudes ($R= 0.82$, $t_{(15)}= 5.6$, $p= 0.0001$; see Figure 5-4B for the data of individual participants). Note that the N50 is a negative deflection, meaning that smaller peak amplitudes (voltages) actually indicate a larger (more negative) peak, whereas for the P120 peak, being a positive deflection, smaller amplitudes indicate a smaller (less positive) peak. Since the N50 peak precedes the P120 peak, smaller N50 amplitudes might constitute a lower starting point of the upstroke in activity leading to the P120 peak. The positive correlation between the two peaks is consistent with this idea.

Using a post hoc paired t-test we compared the magnitude of the effect of percept repetition in the first and second experimental session per participant. For both the N50 and the P120 peak the effect sizes did not differ between the two sessions (N50 peak: $t_{(10)}$= 1.1, p= 0.3; P120 peak: $t_{(10)}$= 0.6, p= 0.6, paired t-tests across participants). Finally, to assess the spatial specificity of the effect of percept repetition around 50 ms after stimulus onset, we analyzed the anterior P50 peak, which coincides in time with the posterior N50 peak. Contrary to the posterior N50, the anterior P50 was not influenced by percept repetition (Figure 5-4D; P50 amplitude: $F_{(2.7, 43.5)}$= 1.0, p= 0.4, effect of quartile; $F_{(1, 16)}$= 2.8, p> 0.1, partial test between first and third quartile).

Overview of results

The participants viewed an ambiguous structure-from-motion stimulus, which was presented intermittently, and reported seeing the same perceptual interpretation for several minutes at a time (Figure 5-1A to 5-1C). Within such a minutes-long perceptually stable period the amplitude of the P120 peak, which is known to reflect early perceptual processing, decreased from the first to the third quartile of each period and slightly increased again from the third to the fourth quartile (Figure 5-2B). This fall-and-rise amplitude modulation associated with percept repetition emerged shortly after stimulus onset in the posterior region of interest (50 ms, posterior N50 peak; Figure 5-3B and 5-4A, overview in Figure 5-4D). The influences of stimulus repetition emerged later in the ERP (200 ms; Figures 5-3A and 5-3C) in both the posterior and anterior region of interest (overview in Figure 5-4C) and consisted of gradual changes in peak latencies and amplitudes over the course of an entire experimental session, across the perceptually stable periods (see P250 peak, Figure 5-2A).

5.5 Discussion

We investigated modulations in cortical activity while participants viewed an intermittently presented ambiguous stimulus. In our experimental design minutes-long sequences of perceptual repetitions were interspersed with occasional changes in perception, while the stimulus itself remained unchanged (Figure 5-1A to 5-1C). These changes in perception allowed us to dissociate the co-occurring aftereffects of prior stimulation and prior perception, as the former accumulated throughout the session and the latter only within the perceptually stable periods.

Stimulus repetition

During the experimental sessions, which lasted about 14 minutes, a gradual delay arose of late ERP components (150-250 ms after stimulus onset; Figures 5-2A and 5-3A). This modulation did not depend on perceived interpretation of the stimulus, as it occurred across, rather than within, the perceptually stable periods. It may reflect a reduction in processing speed, either due to a gradual build-up of neuronal adaptation for the stimulus or a gradual increase in the attention required to maintain focus on the task.

Stimulus repetition was also accompanied by a gradual amplitude increase in the anterior scalp region (P300 peak), perhaps reflecting an increase in attention (Khoe et al. 2008; Luck et al., 2000) or in familiarity of object representations (Guo et al. 2007, Henson et al. 2004).

Previous research has described a positive deflection with similar latency, present only when a stimulus is consciously perceived (the P3b, see Dehaene & Changeux, 2011). We did not find percept-dependent effects on the P300. However, in our experiment the stimulus was always consciously perceived and, accordingly, the P300 was always present. In contrast to the *increased* amplitude of the anterior P300 across stimulus repetitions, the posterior scalp region showed a progressive, apparently saturating, *decrease* in amplitude (P250 peak; Figure 5-2A), possibly reflecting adaptation or fatigue (Kovacs et al. 2006; Heinrich 2007).

We focused on effects accumulating across several minutes. It is possible that different effects are present on shorter timescales, for example between two consecutive stimulus presentations. These short-term effects may be saturated on the long timescale investigated here and, therefore, invisible in our analysis.

Percept repetition

The most notable influence of percept repetition was present on the posterior N50 and P120 peaks (50-140 ms after stimulus onset, Figures 5-2B, 5-3B and 5-4A), thus preceding the above-discussed influences of stimulus repetition (Figure 5-3C). The modulation was absent in the anterior region (Figure 5-4D). A control analysis argued against an explanation in terms of changes in the baseline interval. The early posterior N50 and P120 peaks reflect perceptual processing and are modulated by basic stimulus features like spatial frequency (Pitts et al. 2010), luminance (Wijers et al. 1997) and contrast (Musselwhite & Jeffreys 1982).

The P120 peak is thought to originate from extrastriate and ventral occipito-temporal cortex (Di Rosso et al., 2002). Its amplitude showed a striking fall-and-rise pattern during perceptually stable periods, involving a gradual decrease from the first to the third quartile (75%) of the period and a slight increase during the last quartile (25%). This U-shaped effect repeated in each perceptually stable period, creating an oscillatory pattern across periods (Figure 5-2B). Note that this pattern developed relative to the perceptual time course rather than relative to real time, given that the perceptually stable periods varied in duration.

The observed fall-and-rise pattern may reflect varying stability of the dominant percept. Previous studies have indicated that perceptual stability gradually accumulates over the course of a stabilized period (like a perceptual 'memory'), but is reduced again near the end of the period, shortly before stabilization of the opposite percept begins (Brascamp et al. 2008; 2009). The gradual P120 amplitude decrease we observed from the first to the third quartile (Figure 5-2B) may be related to the initial increase in stability and possibly associated with sparser encoding and/or neural adaptation (Krekelberg et al. 2006). In turn, the slight increase in P120 amplitude in the fourth quartile (Figure 5-2B) could be related to the eventual destabilization. Similar to the mechanism of motion opponency (Petersen et al. 1985; Krekelberg et al. 2006), this increase in amplitude could be associated with weakened inhibition onto – and increased responses in - neurons that prefer the opposite, suppressed, percept (Hock et al. 1996; Klink et al. 2010; de Jong et al. 2012a). Using the metaphor of a (noisy) two-attractors model (Braun & Mattia, 2010; Kornmeier & Bach, 2012), the attractor for the stabilized percept initially becomes increasingly more stable/favorable, while near the end of a period the favorability of the other attractor starts increasing.

The N50 peak showed a similar amplitude modulation as the P120 peak (Figure 5-4A). Whereas the P120 peak is affected by attention and probably by short-term (presentation-to-presentation) perceptual history, the N50 peak is not (attention: Luck et al. 2000; Wijers et al. 1997; Martinez et al., 1999; 2001; short-term history: Kornmeier & Bach, 2005; 2006; Pitts et al., 2007; 2011). The N50 peak is believed to reflect bottom-up processing (Foxe & Simpson, 2002; Arroyo et al. 1997). The anatomical source of scalp EEG activity is indeterminate, but based on previous literature we see two plausible anatomical sources of the N50 modulation: 1) early activation of the motion sensitive medio-temporal area (human MT+/visual area 5; Inui & Kakigi, 2006; see also Brascamp et al., 2010) and/or 2) the striate visual cortex (V1), which is a substantial contributor to EEG activity at this early latency (Clark et al., 1995; Martinez et al., 1999). One way to dissociate these options is to compare upper and lower visual field stimulation, because early ERP deflections can change polarity between upper and lower visual field stimulation when they originate in striate visual cortex, but not when they originate in MT (Clark et al., 1995; Pitzalis et al., 2012). Additionally, it would be interesting to compare moving ambiguous figures, like the one used here, with nonmoving ambiguous figures, for example binocular rivalry of orthogonal gratings, as the latter is likely to activate MT less strongly and V1 more strongly than the former. Note that the temporal coincidence of the stimulus-driven early posterior peaks (N50 and P120) with the perception-driven modulations discussed here does not necessarily mean that the same neural generators underlie both (see Kornmeier et al., 2011). Still, the early onset of the modulations (50 ms after stimulus onset) suggests a change in the stimulus-driven, bottom up response.

Possible mechanisms

Three timescales are important in understanding our results. The first is whether modulations occur early or late in the ERP (relative to stimulus onset), which may be related to early or late in the processing hierarchy, and to bottom-up versus top-down processing. Generally, we found that percept repetition modulated early ERP components (at 50-140 ms), while stimulus repetition modulated late ERP components (at 150-300 ms).

The second timescale concerns perceptual history over several seconds, for example between successive presentations. We equated the immediate perceptual history (from one presentation to the next) by analyzing only perceptual repetitions. Previous studies have compared presentation-to-presentation alternations with repetitions and reported modulations starting from 130 ms after stimulus onset or much later (Kornmeier & Bach

2004, 2005, 2006; Pitts et al. 2007, 2008, 2009; O'Donnell et al. 1988). Some reported a P120 modulation, potentially related to changes in spatial attention (Pitts et al., 2007), but none reported a modulation of the N50 peak. By design there were few perceptual alternations in our data, precluding replication of these findings.

The third timescale concerns the minutes-long perceptually stable periods, whose occurrence cannot be explained exclusively by presentation-to-presentation priming, but depends on an accumulation of percept history across minutes (Brascamp et al, 2008; 2009; Pearson & Brascamp 2008). We report the above-discussed fall-and-rise modulation of early posterior ERPs within such perceptually stable periods (Figure 5-2B). This modulation developed relative to the perceptual time course, rather than relative to real time or the amount of stimulus repetitions. By distinguishing these three timescales we can see that 1) the present study investigated long-term perceptual history (third timescale) rather than short-term history (second timescale); and 2) the effects of this long-term perceptual history (third timescale) occur strikingly early in the ERP (first timescale; 50-140 ms after stimulus onset).

Logically, perceptual history can only influence later perception if it is implemented in neural processing that precedes or constitutes the perceptual decision. Considering the early latency and posterior scalp location of our effects we tentatively propose the following interpretation of our results. When perceiving an ambiguous stimulus, a perceptual 'mnemonic trace' is left in the bottom-up response properties of neurons in early visual areas that differentiate between the possible interpretations of the stimulus (see possible neuronal mechanisms in Crist et al. 2001; Karmarkar & Dan 2006). For our stimulus these could include neurons selective for motion direction and depth (Pastukhov et al., 2013; Pastukhov and Braun, 2013). These altered bottom-up responses then lead to modulations of early ERP components during later stimulus presentations, explaining why this modulation appears soon after stimulus onset. In this view perceptual stability accumulating across many presentations leaves a 'mnemonic trace' that affects future perceptual decisions.

Although we propose a mnemonic trace that takes effect in a bottom-up way, we do not exclude the possibility that further, potentially top-down, processing contributes to the buildup of the mnemonic trace across presentations, for example indirectly by shaping the observer's perceptual experience. Indeed, perception of our stimulus plausibly involves feedback activity (Blake & Logothetis, 2002) and profound late activations of early visual regions could reflect such feedback activity (150-400 ms after stimulus onset; Pitts and Brits, 2011; Pitzalis et al., 2012; Martinez et al., 2001). Higher-order visual, parietal and frontal regions implicated in perceptual stabilization (de Jong et al., 2012b) and perceptual reversals (Kanai et al., 2011; Sterzer et al., 2009) could be involved. Regardless of the extent to which bottom-up or top-down factors determined perceptual decisions on preceding encounters with the stimulus, we suggest that the mnemonic trace left by preceding perceptual decisions affects current processing in a bottom-up way, thereby constituting an early bias in perceptual decision-making toward the currently prevailing percept.

We focused on modulations soon after stimulus onset and regarded an ERP analysis most suitable considering its temporal precision, sensitivity to stimulus-evoked responses and high signal-to-noise ratio. However, ERPs have the limitation of focusing on stimulus-locked effects. In future studies a time-frequency analysis of similar data may reveal important additional information, especially regarding long-term trends and feedback signals that may not be phase-locked to stimulus onset. Induced gamma oscillations, although they are too slow to influence the perceptual decision process (typically occurring 200-300 ms after stimulus onset), could be crucial for the proposed feedback activations. Additionally, it should be mentioned that the present study is explorative in nature, without much prior constraint on the data patterns of interest. This has allowed us to identify results not observed previously, but it also means that these results call for replication in studies constrained by our findings.

Conclusion

We found that very early posterior activity starting around 50 ms after stimulus onset was associated with percept repetition, suggesting that the information gained through previous perceptual experience is incorporated in the perceptual decision process via modification of the bottom-up visual response. We propose that, while viewing an ambiguous stimulus, feedback projections to early visual regions can modulate the response properties of these regions such that the perceptual decision process is biased in favor of the stabilized percept on future encounters with this stimulus.

Chapter 6

Discussion

6.1 Summary

The studies described in this thesis investigated how the human brain processes visual information. To this end participants were presented with ambiguous images that elicit two mutually exclusive perceptual interpretations while the image remains unchanged, thereby enabling the study of perceptual processes separately from processes related to mere visual stimulation. The studies focused on two phenomena reflecting temporal modulation of the perception of ambiguous images: 1) spontaneous changes in perception while the stimulus is constant and 2) perceptual memory for one of the interpretations of the stimulus. Some researchers have argued that both these phenomena mainly involve cognitive brain regions. Conversely, here we find strong indications that they originate within the occipital cortex, a sensory part of the brain specialized for processing visual information. The involvement of the occipital cortex was tested using a variety of techniques and the results all point in the same direction: complex temporal modulations of perception, such as spontaneous perceptual changes and perceptual memory, reside within visual brain regions. The findings are discussed in more detail below.

6.2 Spontaneous changes in visual awareness

Spontaneous changes in perception occur during continued observation of an ambiguous stimulus, even though the stimulus is constant (Figure 1-1). As there is no concomitant change in the visual input, these changes originate within the mind of the observer. Most previous neuro-imaging studies into the perception of ambiguous images have searched for sustained activations reflecting the perceptual state and found an involvement of visual (sensory) but not cognitive brain regions. In contrast, transient activations associated with spontaneous perceptual changes were found in cognitive rather than visual regions (chapter 1). Accordingly, it has been suggested that the maintenance of a perceptual state involves the visual cortex, while a spontaneous perceptual change, lacking a concomitant stimulus change, originates outside the visual cortex (Lumer et al., 1998; Leopold & Logothetis, 1999; Sterzer & Kleinschmidt, 2007; Sterzer et al., 2009).

In chapter 2 we describe intracranial recordings of activity in the human occipital lobe. Contrary to most existing studies that measured neural activity with conventional neuro-imaging techniques, we observed transient occipital activity changes associated with spontaneous perceptual changes using this intracranial recording technique. Specifically, we found indications that the initiation of spontaneous perceptual changes occurs locally within the occipital cortex, after which the change is distributed to other parts of the occipital cortex, arguably to mediate the maintenance of the perceptual state. Our results thus point to a source in visual cortex for spontaneous perceptual changes, compatible with the idea of reciprocal inhibition between sensory neuron pools described in the introduction of this thesis (chapter 1). Previously reported transient activations in cognitive brain regions may reflect additional processing associated with spontaneous changes in perception, like attention, introspection or perceptual uncertainty, but not their initiation (Frassle et al., 2014; Knapen et al., 2011; de Graaf et al., 2011; Raemaekers et al, 2009).

6.3 Memory for one of the percepts

As argued in the introduction of this thesis (chapter 1), our sensory systems do not process stimuli in a pre-defined manner regardless of the temporal context. The influence of past on present neural activity is an essential attribute of the processing of sensory brain regions. In chapter 3 we introduced the phenomenon of perceptual memory, evident when intermittent presentation of an ambiguous stimulus results in minutes-long sequences of the same percept reoccurring at every presentation (Leopold et al., 2002; Orbach et al., 1963). It has recently been shown that this phenomenon develops involuntarily (Klink et al., 2008) and reflects perceptual history at the scale of minutes rather than seconds (Brascamp et al. 2009; Pearson & Brascamp, 2008). We had two research goals regarding perceptual memory, as described below.

Firstly, we wanted to find out whether perception during continued viewing of an ambiguous stimulus is influenced by perceptual memory built up during intermittent viewing of the stimulus (chapter 3). Intermittent viewing can be regarded as the repeated instigation of perceptual choices at the onset of an ambiguous stimulus, which are believed to be caused by neural processes distinguishable from those underlying spontaneous perceptual changes during continued viewing of a constant stimulus (Figure 1-3). While the influence of prior perception and prior stimulation on perceptual choices has been thoroughly studied, generally showing facilitative and suppressive aftereffects, respectively, the influence during continued viewing had never been systematically investigated.

A series of psychophysical tests described in chapter 3 revealed that perceptual memory influenced perception during continued viewing in a qualitatively opposite way compared with perception at the onset of the stimulus. At stimulus onset the memorized percept was facilitated, while during continued viewing of the same stimulus there was facilitation of the alternative percept. Interestingly, durations of the memorized percept were not much affected during continued viewing, while durations of the alternative percept were increased. Facilitation of the alternative percept lasted approximately equally long as the preceding period during which perceptual memory was built up, which could be several minutes in our experiments. Within the concept of a regulated balance between stability and adjustability in neural systems (the stability-plasticity dilemma), these findings indicate that neural systems involved in competition between percepts initially favor stability of currently prevailing percepts, but, following the initial interpretation, are biased toward new interpretations of the stimulus. We speculate on possible underlying neural mechanisms in the next section.

Our second research goal regarding perceptual memory was to investigate modulations in neural activity associated with building up perceptual memory (chapters 4 and 5). To this end we compared early and late stages of perceptually stable periods during intermittent viewing of an ambiguous stimulus. The perceptually stable periods lasted several minutes and contained many (up to hundreds) repetitions of the same percept. Because the same ambiguous stimulus can elicit perceptual stabilization of either one of two possible perceptual interpretations, stimulus repetitions were not always coupled with percept repetitions and their separate influences on neural processing could be dissociated. In a functional magnetic resonance imaging (fMRI) study described in chapter 4 we found that percept repetition was associated with an increase in the response measured in stimulus-specific visual regions, whereas this effect was not observed in association with the mere repetition of the stimulus.

Using scalp electro-encephalograms (EEG) as described in chapter 5, we investigated the temporal dynamics of neural activity associated with perceptual memory. Previous scalp EEG studies have suggested that the perceptual interpretation of an ambiguous stimulus is completed around 130-160 ms after stimulus onset, because modulations reflecting the perceptual state arise at this latency (Pitts & Britz, 2011). Strikingly, we found that perceptual memory modulated the amplitude of responses at posterior electrodes occurring as early as 50 ms after stimulus onset. Interestingly, using the same scalp recording technique, effects of short-term perceptual memory for the last-perceived percept were not found until 130 ms after stimulus onset and later (Kornmeier & Bach, 2012), thus occurring later than our effect of long-term perceptual memory. While in the fMRI study amplitudes were increased (chapter 4), in the scalp EEG study (chapter 5) a negative deflection was increased in amplitude (more negative) and a subsequent positive deflection was decreased in amplitude. Considering the early latency of the observed amplitude modulation, we conclude that perceptual memory affects neural processing that precedes the completion of the perceptual interpretation, thereby effectuating its influence on the percept experienced at the onset of the stimulus.

In the final stage of a perceptually stable period amplitude modulations in the scalp EEG study attenuated and reversed a little, which we argued to be related to dis-inhibition of the alternative percept. Correspondingly, it has been shown that perceptual stability gradually increases over the course of a stabilized period, but is reduced again near the end of the period, shortly before stabilization of the opposite percept begins (Brascamp, 2008; Brascamp et al., 2009). This final stage of perceptual stabilization was probably less apparent in the fMRI study, as the perceptual stabilization experienced by the participants was generally longer lasting and more stable in the scalp EEG study than in the fMRI study, most likely due to the occasional long blank periods (of 16 seconds) inserted in the fMRI study. In the next section we will discuss possible neural mechanisms underlying increased perceptual stability during intermittent stimulus presentation as well as the effect of perceptual memory during continued viewing.

6.4 Neural mechanisms of perceptual memory

Summarizing our results, we found that spontaneous perceptual changes were associated with oscillatory activity in a high frequency range that is thought to reflect the processing of stimulus features (chapter 2) and that perceptual memory was associated with amplitude increases in stimulus-specific visual brain regions (chapter 4) as well as occipital activity modulations occurring as early as 50 ms after stimulus onset (chapter 5). Considering these results, we suggest that spontaneous perceptual changes as well as perceptual memory for perceptual choices originate within the visual cortex, both in the same visual networks specialized for the features of the used stimulus. Although we do not exclude the possibility that cognitive brain regions have a contributing role, we favor the parsimonious view that interactions within visual regions underlie our results. During binocular rivalry perceptual memory influenced the perceived pattern, but there was no influence of which eye was presented with this pattern, corroborating involvement of feature-selective neurons (chapter 3). An overlap in visual networks involved in spontaneous perceptual changes and perceptual memory for perceptual choices is suggested by our finding that the perceptual memory influenced later perception during continued viewing of the stimulus (chapter 3).

In the introduction (chapter 1) we described a minimal model of reciprocal inhibition between two sensory neuron pools, proposed as a metaphor for the neural mechanisms underlying the perception of ambiguous images. While there is extensive psychophysical support for this minimal model, existing neuro-imaging and neurophysiological investigations failed to provide consistent evidence (chapter 1). The involvement of feature-selective visual networks proposed to underlie the present neuro-imaging findings is largely compatible with the model, as the model implements interactions within and between visual neural networks preferentially involved in either of the two percepts. Regarding mechanisms underlying spontaneous perceptual changes, previous literature has proposed a cardinal influence of neural adaptation/fatigue and neural noise on the neural interactions implemented in the model (see chapter 1), which we will not discuss further here. Below, we will use the minimal model as a starting point for speculating about the neural mechanisms involved in perceptual memory.

Contrary to the proposed role of neural fatigue in perceptual changes (chapter 1), we argue that neural fatigue is not involved in perceptual memory. Firstly, fatigue is generally associated with decreased amplitudes of neural responses (Krekelberg et al., 2006), whereas we found increased amplitudes in association with perceptual memory (chapter 4). Secondly, fatigue associated with the memorized percept would presumably lead to decreased durations of this percept during continued viewing, which we did not observe (chapter 3). Interestingly, the first occurrence of the memorized percept lasted relatively short after continuous but not after intermittent prior stimulation (chapter 3, Figure 3-4C), possibly indicating that neuronal fatigue recovered during the blank intervals in the intermittent stimulation protocol.

Our findings point to a distinction between neural responses at stimulus onset, facilitating the memorized percept, and sustained neural activity during continued viewing of the stimulus, facilitating the alternative percept (chapter 3). It has been suggested that activity in the neuron pool involved in the suppressed percept is not completely silenced by the proposed inhibitory interactions (chapter 1), thus suggesting that sub-threshold activity associated with the alternative percept was present while the memorized percept was experienced during intermittent viewing. It could be that sub-threshold activation facilitated later sustained above-threshold activity in the neuron pool involved in the alternative percept, thereby contributing to the observed increased durations of the alternative percept during continued viewing. The alternative percept was prolonged more after ambiguous pre-exposure than after unambiguous pre-exposure (chapter 3), suggesting that ambiguous stimulation elicits more sub-threshold activation associated with the alternative percept than unambiguous stimulation.

Regarding facilitation of the memorized percept at stimulus onset, it is unlikely that lingering on of activity from the previous stimulus presentation plays a role, because the facilitation is effective over multiple minutes and is not overwritten by interleaved presentations of other stimuli (Pearson & Brascamp, 2008). It has been proposed that perceptual memory results in a faster upstroke of the neural response associated with the memorized percept compared with the alternative percept, favoring the memorized percept specifically at stimulus onset and not during continued viewing (Noest et al., 2007; Brascamp, 2008; Brascamp et al., 2009). However, arguing against this idea, we found that perceptual memory was associated with modulations of amplitude and not latency of the neural response (chapters 4 and 5).

We suggest that the repeated experience of the memorized percept could have led to experience-dependent changes in the response properties of the involved visual neurons (Karmarkar & Dan, 2006; Clifford et al., 2007). For example, experience-dependent shifts in the tuning curves of neurons may have recruited additional neural populations for this percept (Kohn & Movshon, 2004; Karmarkar & Dan, 2006; Ghisovan et al., 2009), contributing to the increased amplitudes of responses observed in later stages of a perceptually stable period (chapter 4). Alternatively or additionally, perceptual memory could be associated with decreased neural noise (Klink et al, 2012). In line with our findings, at stimulus onset coordinated activation of the neuron pool involved in the memorized percept could benefit from decreased noise levels, while during continued viewing decreased noise levels could result in less random terminations as well as initiations of the memorized percept, thus giving no net effect.

As mentioned above, we do not reject a contributing role of cognitive regions, which could be implemented in feedback connections to visual regions from frontal or parietal regions involved in monitoring and evaluating perceptual processing (see parietal modulation reported in chapter 4; Sterzer et al., 2009; Kanai et al., 2011). However, we suggest that perceptual memory is effectuated in visual cortex and that cognitive regions may contribute to - but are not essential for - its formation. Although much remains elusive regarding the neural mechanisms underlying perceptual memory, the proposed involvement of visual networks suggests that neural traces formed in visual neurons by previous perceptual processing influence neural processing leading up to later perceptual interpretations of visual input. Following the proposed involvement of visual networks in both spontaneous changes in visual awareness and minutes-long perceptual memory, the results presented in this thesis illustrate that complex temporal modulations of perception reside within the visual cortex. It should be noted that the described studies were explorative in nature, allowing us to identify modulations not observed previously, yet also calling for replication of our results in follow-up investigations.

Chapter 7

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Appendix I

Samenvatting in het Nederlands (in Dutch)

Neurale mechanismen die ten grondslag liggen aan temporele modulatie van visuele perceptie

Hoe ons brein visuele beelden verwerkt tot een waarneming van de wereld om ons heen en hoe deze waarneming van tijd tot tijd kan verschillen.

I.1 Introductie

Gelooft u uw ogen altijd? Soms kunnen uw ogen u voor de gek houden. Dit wordt treffend geïllustreerd door afbeeldingen die op twee verschillende manieren zijn waar te nemen, zoals de afbeelding in Figuur 1-1. Ziet u in deze afbeelding een zwarte vaas of twee rode gezichten? We noemen een dergelijke afbeelding “ambigu”. Wanneer de visuele informatie die via onze ogen ons brein binnenkomt ambigu is, wordt in het brein slechts één van de mogelijke interpretaties van de informatie tot een waarneming verwerkt. In het geval van Figuur 1-1 zult u ofwel de zwarte vaas zien, ofwel de rode gezichten. Uw waarneming kan ook wisselen, waardoor u op het ene moment de zwarte vaas ziet en op het andere moment de rode gezichten. U zult echter nooit deze twee interpretaties tegelijkertijd waarnemen. Op ieder moment wordt de waargenomen interpretatie beleefd als ware het de enige interpretatie van de afbeelding die mogelijk is. Wisselingen in de waarneming worden beleefd alsof de afbeelding is veranderd, terwijl de afbeelding ongewijzigd is gebleven en uw eigen brein de interpretatie van de afbeelding heeft veranderd. Hoe zeker wij ons ook wanen van onze waarneming van de wereld om ons heen, het kijken naar een ambigue afbeelding doet ons beseffen dat er geen één-op-één relatie is tussen de visuele informatie die onze ogen bereikt en de visuele waarneming die wij ervaren. Een ander woord voor waarneming is “perceptie”. Dit proefschrift gaat over deze relatie tussen de afbeelding waarnaar iemand kijkt, de visuele stimulatie, en de waarneming die daarbij ervaren wordt, de visuele perceptie.

Waarom komt onze waarneming van een afbeelding zo betrouwbaar op ons over, zelfs als de afbeelding ambigu is? Met andere woorden: waarom ervaren wij de relatie tussen visuele stimulatie en visuele perceptie als een één-op-één relatie, terwijl deze dat niet is. Het kan zijn dat het niet erg nuttig is om ambiguïteit waar te nemen, omdat visuele stimulatie altijd ambiguïteit bevat. Op de netvliezen in de ogen worden namelijk platte (tweedimensionale) reflecties van de buitenwereld geregistreerd, terwijl de buitenwereld ruimtelijk (driedimensionaal) is. In het brein worden deze platte reflecties als het ware ‘vertaald’ naar de meest waarschijnlijke ruimtelijke situatie in de buitenwereld. Er kan in het brein geen zekerheid zijn over de juistheid van de ruimtelijke vertaling, omdat deze moet worden afgeleid uit platte beelden. Bovendien berust de werking van ons brein op elektrische en chemische activiteit in zenuwcellen. Deze zogenoemde “neurale signalen” bevatten ruis en volgen een kansverdeling (waarschijnlijkheid) en zijn daardoor altijd enigszins ambigu. Het bestuderen van de waarneming van ambigue afbeeldingen, zoals Figuur 1-1, is daarom niet alleen interessant omdat we de perceptie van deze afbeeldingen willen begrijpen, maar ook omdat we via deze weg meer leren over hoe ons brein visuele stimulatie interpreteert.

De afbeelding in figuur 1-1 laat ons ook zien dat visuele waarneming meer is dan een registratie van de wereld om ons heen. De drie homogeen gekleurde vlakken waaruit de afbeelding bestaat worden door het brein geïnterpreteerd als zijnde een vaas of twee gezichten. Dat is een belangrijk gegeven: het brein construeert een betekenisvol beeld van de buitenwereld. Een manier om de inhoud van ons visuele bewustzijn betekenisvol te maken is “contextuele modulatie”. Dit wil zeggen dat de context waarin iets wordt gezien mede bepaalt hoe het wordt waargenomen. In Figuur 1-2A is te zien hoe de waargenomen grijswaarde van een vlak af kan hangen van naburige grijswaarden, een duidelijk voorbeeld van de invloed van ruimtelijke (spatiële) context. De halve ring in Figuur 1-2A lijkt lichter op een donkere achtergrond dan op een lichte achtergrond. Hoe iets wordt waargenomen wordt ook beïnvloed door de context in de tijd (temporele context), oftewel: door eerdere waarneming. In termen van neurale activiteit zeggen we dat de huidige activiteit in het brein is beïnvloed door activiteit die daaraan voorafging. Als u tien seconden strak naar het midden van de afbeelding in Figuur 1-1 staart en vervolgens uw ogen op een stuk wit papier richt kunt u een voorbeeld ervaren van de invloed van temporele context. Op het witte papier zult u een nabeeld van Figuur 1-1 zien dat bestaat uit een witte vaas en twee cyaan gekleurde gezichten. Dit nabeeld is niet op het papier aanwezig, maar vormt zich in uw brein.

In bovenstaand voorbeeld van temporele contextuele modulatie is het nabeeld een negatief van de afbeelding waarnaar u vlak daarvoor keek. De zwarte vaas is wit in het nabeeld en de rode gezichten zijn cyaan. Een negatief nabeeld wordt ook wel aangeduid als een tegengesteld of inhiberend effect van eerdere waarneming, wat wil zeggen dat hetgeen dat eerder werd waargenomen vervolgens juist niet waargenomen wordt. Eerdere waarneming kan ook een positief of faciliterend effect hebben op huidige waarneming, als hetgeen dat eerder werd waargenomen wederom waargenomen wordt. De eerdere waarneming wordt als het ware gebruikt als een aanname in de interpretatie van latere visuele informatie. Een voorbeeld hiervan is te zien in Figuur 1-2B, waarin zes platte cirkels staan afgebeeld die diepte lijken te hebben. De waargenomen diepte ontstaat doordat de ruimtelijke interpretatie van schaduwen mede bepaald wordt door de aanname dat licht van boven komt. De zes platte cirkels in Figuur 1-2B worden hierdoor waargenomen als vijf bulten en één gat. De aanname dat licht van boven komt zit bij iedereen ingebakken in het brein, maar veel faciliterende effecten van eerdere waarneming zijn verschillend van persoon tot persoon, omdat iedereen andere waarnemingen heeft gehad. Recente perceptuele ervaringen kunnen bijvoorbeeld een sterke invloed hebben op hoe u ambigue afbeeldingen waarneemt. Als er een ambigue afbeelding in uw gezichtsveld verschijnt is de kans groot dat u de interpretatie zult waarnemen die het meest lijkt op andere objecten die u vaak heeft gezien. Als u deze ambigue afbeelding al vaker heeft gezien, dan zult u de interpretatie waarnemen die u recent het vaakst heeft gezien. Bij gevolg kan het gebeuren dat u steeds dezelfde interpretatie waarneemt wanneer een ambigue afbeelding herhaaldelijk kort getoond wordt, ondanks het feit dat de afbeelding op twee verschillende manieren is waar te nemen. We noemen dit perceptueel geheugen. Het is een vorm van geheugen waar u niet bij nadenkt. Het ontstaat vanzelf en u bent zich daar niet van bewust. Uw visuele bewustzijn wordt dus niet alleen bepaald door de afbeelding waarnaar u kijkt, maar ook door factoren die zich in uw brein bevinden, zoals sporen van eerdere waarneming. Visuele waarneming is daarmee uw persoonlijke interpretatie van de wereld om u heen.

Dit proefschrift beschrijft een aantal studies naar hoe ambigue afbeeldingen in het brein worden verwerkt tot een waarneming en hoe dit proces wordt beïnvloed door eerdere waarneming. De focus ligt op twee aspecten van het waarnemen van ambigue afbeeldingen: 1) wisselingen in de waarneming die spontaan optreden terwijl gekeken wordt naar een ambigue afbeelding die niet verandert en 2) de wijze waarop waarneming van een ambigue afbeelding wordt beïnvloed als in het recente verleden de ene interpretatie van de afbeelding veel vaker is waargenomen dan de andere. Het interessante aan het bestuderen van het brein tijdens het zien van ambigue afbeeldingen is dat de waarneming kan wisselen terwijl de afbeelding onveranderd blijft. Hierdoor kan neurale activiteit betrokken bij het waarnemen (visuele perceptie) onderscheiden worden van neurale activiteit betrokken bij het registreren van de afbeelding (visuele stimulatie).

I.2 Bestaande kennis over het waarnemen van ambigue afbeeldingen

In het brein vertonen sommige zenuwcellen meer activiteit wanneer de ene interpretatie wordt waargenomen, terwijl andere zenuwcellen meer activiteit vertonen als de andere interpretatie wordt waargenomen. We zeggen dan dat een zenuwcel meer “gevoelig” is voor de ene of de andere interpretatie van de afbeelding. Zo een waargenomen interpretatie heet een “percept”. Alle zenuwcellen die gevoelig zijn voor een bepaald percept worden als groep aangeduid als de “neurale representatie” van het percept. Activiteit in de neurale representatie van een bepaald percept kan er toe leiden dat dit percept wordt waargenomen. Hoe dat precies werkt weten we echter niet. Hier is onderzoek naar gedaan met verschillende technieken, waaronder psychofysische en beeldvormende technieken. Hieronder zullen eerst de bestaande psychofysische onderzoeken beschreven worden en daarna de bestaande literatuur over beeldvormende technieken.

Psychofysica is de studie van de relatie tussen sensorische stimulatie, bijvoorbeeld het kijken naar een afbeelding, en perceptie, de waarneming van die afbeelding. Psychofysica heeft ons geleerd dat er drie karakteristieke verschijningsvormen zijn van de waarneming van ambigue afbeeldingen, welke mogelijk alle drie uitingen zijn van verschillende neurale processen in het brein. Ten eerste zijn er de perioden waarin één van de mogelijk interpretaties van de afbeelding wordt waargenomen (Figuur 1-3A). Deze perioden noemen we perceptuele toestand. De waarneming van de afbeelding (de perceptie) verandert tijdens deze perioden niet. Een perceptuele toestand duurt vaak een aantal seconden en wordt doorgaans vernoemd naar de interpretatie die op dat moment wordt waargenomen. Zo kan de afbeelding in Figuur 1-1 leiden tot een vaas-toestand en een gezichten-toestand. Er zijn ook twee verschijningsvormen die juist een veranderingen in de waarneming van een ambigue afbeelding betreffen. De eerste is de perceptuele wisseling, duidend op de wisselingen in de waarneming die ontstaan als men langer naar de ambigue afbeelding kijkt (Figuur 1-3A). De tweede is de perceptuele keuze. Hiermee wordt de eerste interpretatie van de afbeelding bedoeld nadat deze tijdelijk uit beeld is geweest of wanneer deze nog nooit eerder gezien is. Perceptuele keuzes worden sterk beïnvloed door perceptueel geheugen. Vandaar dat steeds dezelfde interpretatie wordt waargenomen wanneer een ambigue afbeelding herhaaldelijk kort getoond wordt, zoals eerder besproken. Telkens als de afbeelding verschijnt wordt een perceptuele keuze gemaakt voor de interpretatie die recent het vaakst gezien is, en perceptuele wisselingen komen niet voor. Perceptuele wisselingen ontstaan immers als men langer naar de ambigue afbeelding kijkt en daarvoor is de afbeelding steeds te kort in beeld.

Dit proefschrift kan bouwen op een stevige basis aan psychofysische kennis over het waarnemen van ambigue afbeeldingen, maar er is nog weinig bekend over de bijgaande neurale processen die zich in het brein afspelen. Het is aannemelijk dat bij het kijken naar een ambigue afbeelding in eerste aanleg de neurale representaties van beide percepten actief worden. Er is als het ware “bewijs” voor beide interpretaties van de afbeelding. Omdat uit psychofysisch onderzoek blijkt dat we maar één percept tegelijk hebben, moet er in het brein een keuzeproces plaatsvinden tussen de twee percepten. Vanuit de psychofysica zijn er aanwijzingen dat de neurale processen die ten grondslag liggen aan dit keuzeproces gezien kunnen worden als een competitieve race tussen de neurale representaties van de twee percepten. In het geval van een perceptuele keuze is de afbeelding pas net verschenen en beginnen beide neurale representaties vanaf de startlijn, waarna er uiteindelijk één aan kop zal gaan. In het geval van een perceptuele wisseling wordt er al langere tijd naar de afbeelding gekeken, dus zal de race in volle gang zijn. De perceptuele wisseling kan gezien worden als een overname van de koppositie van de ene door de andere neurale representatie. Een perceptuele toestand is een periode met een stabiele koppositie. Het idee dat er maar één neurale representatie aan kop kan gaan en dat beide representaties nooit samen vooraan gaan, wordt verklaard door “reciproke inhibitie” (wederkerige remming): activiteit van de ene neurale representatie onderdrukt activiteit van de andere neurale representatie, en vice versa. Een neurale representatie die op kop gaat is erg actief en daarmee is er sterke onderdrukking van activiteit in de andere representatie. Als gevolg daarvan is er extra weinig activiteit in die andere representatie en is de onderdrukking die deze representatie uitvoert op de eerste representatie erg klein. Zo wordt de koppositie van de eerste representatie uitvergroot, waardoor een stabiele perceptuele toestand ontstaat.

I.3 Bestaande kennis over de werking van het brein tijdens het waarnemen van ambigue afbeeldingen

Zoals gezegd is het niet duidelijk welke neurale processen in het brein zorg dragen voor de veronderstelde competitieve race tussen de beide neurale representaties. Dit kan worden onderzocht met beeldvormende technieken zoals fMRI (functionele beeldvorming met magnetische resonantie), waarbij als het ware een foto van het actieve brein wordt gemaakt, en EEG (elektro-encefalografie), waarbij electroden op het hoofd hersenactiviteit meten. Met deze technieken kan hersenactiviteit in beeld worden gebracht terwijl een proefpersoon naar een ambigue afbeelding kijkt. Grofweg zijn daarbij twee groepen hersengebieden interessant. Ten eerste zijn dat de gebieden waarvan we weten dat ze betrokken zijn bij het verwerken van de beelden die onze ogen bereiken. We noemen ze ‘sensorische’ hersengebieden en voor visuele waarneming liggen ze in de occipitaalkwab, het deel van het brein dat achterin de schedel ligt. De neurale representaties van de beide percepten huizen grotendeels in deze sensorische gebieden in de occipitaalkwab. Ten tweede zijn er gebieden die wat meer vooraan in de hersenen liggen, in de pariëtale en frontale kwab, en die betrokken zijn bij de cognitieve aspecten van visuele waarneming zoals aandacht en geheugen.

Bestaande onderzoeken met beeldvormende technieken hebben laten zien dat de sensorische gebieden in de occipitaalkwab betrokken zijn bij de waargenomen perceptuele toestand. Zo is het mogelijk om uit hersenactiviteit die hier gemeten is af te leiden welke interpretatie van de afbeelding wordt waargenomen. Daarentegen geven perceptuele wisselingen vooral activiteit in cognitieve hersengebieden en niet in de sensorische occipitaalkwab. Gecombineerd met het gegeven dat perceptuele wisselingen voorkomen zonder dat de afbeelding verandert, is hierdoor de hypothese ontstaan dat perceptuele wisselingen geïnitieerd worden in cognitieve hersengebieden, terwijl de perceptuele toestand wordt vertegenwoordigd in sensorische hersengebieden. Over neurale activatie in het brein bij perceptuele keuzes is nog weinig bekend. Tevens is niet duidelijk via welk neurale mechanisme perceptuele keuzes worden beïnvloed door perceptueel geheugen. Vaak wordt aangenomen dat cognitieve hersengebieden hierin een belangrijke rol spelen, omdat het gaat om een geheugenproces.

Zoals eerder genoemd ligt de focus van dit proefschrift op twee aspecten van het waarnemen van ambigue afbeeldingen: 1) perceptuele wisselingen die optreden terwijl de ambigue afbeelding niet verandert en 2) perceptueel geheugen dat een sterke invloed heeft op perceptuele keuzes. Voor beide verschijnselen is in bestaande literatuur een belangrijke rol van cognitieve hersengebieden verondersteld. De hypothese is dat sensorische hersengebieden in de occipitaalkwab verantwoordelijk zijn voor de verwerking van externe informatie, namelijk de afbeelding die geregistreerd wordt door de ogen, terwijl cognitieve hersengebieden verantwoordelijk zijn voor de invloed van factoren die zich enkel in het brein bevinden (interne factoren), zoals spontane perceptuele wisselingen en perceptueel geheugen. Deze hypothese gaat echter voorbij aan het feit dat verwerking uitsluitend op basis van externe factoren vrijwel niet bestaat in het brein. Neurale processen zijn altijd een mengeling van de eigenschappen van de input en de eigenschappen van het neurale systeem. Bovendien zou het voordelig kunnen zijn om voor interne factoren, zoals perceptueel geheugen, dezelfde neurale representaties te gebruiken als die hierboven beschreven zijn en die hoofdzakelijk huizen in de sensorische occipitaalkwab.

In dit proefschrift onderzoeken we daarom een alternatieve hypothese: perceptuele wisselingen en perceptueel geheugen ontstaan in sensorische hersengebieden en cognitieve hersengebieden zijn daarvoor niet noodzakelijk. Om deze hypothese te toetsen gebruiken we zowel psychofysische (hoofdstuk 3) als verschillende beeldvormende (hoofdstuk 2, 4 en 5) technieken. We hebben ambigue afbeeldingen gebruikt, omdat deze uitermate geschikt zijn om neurale activiteit geassocieerd met het waarnemen (visuele perceptie) te kunnen onderscheiden van neurale activiteit geassocieerd met het registreren van de afbeelding (visuele stimulatie).

I.4 Onze bevindingen over perceptuele wisselingen

Zoals reeds genoemd wordt in bestaande literatuur verondersteld dat perceptuele wisselingen ontstaan in cognitieve hersengebieden. Het eerste onderzoeksdoel van dit proefschrift is om een alternatieve hypothese te toetsen, namelijk dat perceptuele wisselingen ontstaan in sensorische gebieden in de occipitaalkwab. Hiertoe hebben we activiteit gemeten in de occipitaalkwab op het moment dat een proefpersoon een perceptuele wisseling waarneemt zonder dat de afbeelding verandert (hoofdstuk 2). We hebben een bijzondere meetmethode gebruikt: intracraniële EEG. Dat wil zeggen dat we binnen de schedel EEG hebben gemeten. De electroden waarmee hersenactiviteit gemeten werd waren niet op de hoofdhuid bevestigd, zoals gewoonlijk, maar onder de schedel direct op de hersenen. De proefpersonen die hieraan deelnamen waren patiënten die deze electroden tijdelijk geïmplanteerd kregen, omdat ze aan een ernstige vorm van epilepsie leden. Met behulp van de electroden werd geprobeerd in kaart te brengen waar in het brein de bron van de epileptische activiteit was, om eventueel deze bron chirurgisch te verwijderen. Het was medisch noodzakelijk om de electroden onder de schedel te plaatsen, omdat het EEG dan veel nauwkeuriger gemeten kan worden. Deze patiënten hebben vrijwillig meegedaan aan ons onderzoek en ons daarmee de kans gegeven om unieke metingen te doen. Intracraniële metingen zijn heel schaars, omdat er weinig patiënten zijn die hiervoor in aanmerking komen. Ze zijn tevens heel waardevol, omdat direct vanaf het oppervlak van het brein gemeten kan worden in een proefpersoon die leeft en wakker is.

In tegenstelling tot eerdere beeldvormende onderzoeken toonden onze intracraniële EEG metingen duidelijke activiteit in de sensorische gebieden van de occipitaalkwab op het moment dat een spontane perceptuele wisseling plaatsvond. Verdere analyse van het gemeten signaal suggereerde dat een perceptuele wisseling ergens in de sensorische occitpitaalkwab ontstaat en vervolgens naar andere delen van de occipitaalkwab wordt overgebracht. Wellicht duidt dit er op dat de wisseling ontstaat in de neurale representaties van de beide percepten (of in de interacties daartussen) en daarna als het ware wijdverspreid "bekendgemaakt" wordt, om het stabiliseren van de nieuwe perceptuele toestand te bevorderen. Onze interpretatie van deze gegevens is dat perceptuele wisselingen ontstaan in de neurale representaties van percepten die zich bevinden in de sensorische gebieden van de occipitaalkwab. Dit zou betekenen dat dit deel van het brein niet alleen externe informatie verwerkt, maar dat interne factoren hier ook hun oorsprong vinden. Het zou kunnen dat de eerder gevonden activiteit in cognitieve hersengebieden bijdraagt aan de beleving van een wisseling of de aandachtverschuiving die een wisseling oproept, maar niet noodzakelijk is voor het ontstaan van de wisseling.

I.5 Onze bevindingen over perceptueel geheugen

Zoals reeds beschreven hebben waarnemingen die men eerder heeft ervaren invloed op de huidige waarneming. Dit is goed merkbaar als een ambigue afbeelding herhaaldelijk kort getoond wordt. Elke korte presentatie vraagt om een perceptuele keuze in het brein en het is gebleken dat deze keuze meestal op het percept valt dat in het recente verleden het vaakst gezien is. Dit verschijnsel noemen we perceptueel geheugen. Het leidt er toe dat een ambigue afbeelding bij herhaalde korte presentaties steeds op dezelfde manier wordt waargenomen. Perceptueel geheugen heeft dus een zeer sterke invloed op perceptuele keuzes die gemaakt worden wanneer een ambigue afbeelding verschijnt. Het tweede onderzoeksdoel van dit proefschrift is om perceptueel geheugen beter te begrijpen en daartoe hebben we twee deelvragen opgesteld. Ten eerste wilden we weten of perceptueel geheugen naast perceptuele keuzes ook invloed heeft op perceptuele wisselingen die voorkomen tijdens langdurig kijken naar een ambigue afbeelding. Ten tweede wilden we in kaart brengen welke activiteit in het brein geassocieerd is met perceptueel geheugen, om zo te kunnen afleiden hoe perceptueel geheugen uit neurale processen ontstaat.

Tot nu toe was er geen effect bekend van perceptueel geheugen op perceptuele wisselingen, wat zou kunnen betekenen dat perceptuele keuzes en perceptuele wisselingen deels veroorzaakt worden door verschillende neurale processen in het brein. In lijn hiermee ontstaan perceptuele wisselingen spontaan in het brein, terwijl perceptuele keuzes samenhangen met het verschijnen van de afbeelding. Echter weten we uit ons onderzoek dat beschreven staat in hoofdstuk 2 dat perceptuele wisselingen toch geassocieerd zijn met activiteit in sensorische gebieden in de occipitaalkwab en vermoedelijk, evenals perceptuele keuzes, hun oorsprong vinden in aldaar gelegen neurale representaties van de twee percepten. We hebben een aantal psychofysische experimenten gedaan die direct toetsen of perceptueel geheugen invloed heeft op perceptuele wisselingen (hoofdstuk 3). In deze experimenten is perceptueel geheugen opgebouwd door een proefpersoon enkele minuten te laten kijken naar herhaalde korte presentaties van een ambigue afbeelding, waarbij de proefpersoon telkens dezelfde interpretatie van deze afbeelding waarnam. Vervolgens lieten we de proefpersoon enkele minuten onafgebroken naar de ambigue afbeelding kijken, zodat er perceptuele wisselingen werden waargenomen.

Uit onze experimenten bleek dat perceptuele wisselingen wel degelijk worden beïnvloed door perceptueel geheugen. Echter is deze invloed tegenovergesteld van aard in vergelijking met de invloed op perceptuele keuzes. Het percept dat herhaaldelijk werd waargenomen tijdens de korte presentaties wordt doorgaans wederom waargenomen op het moment van een volgende perceptuele keuze. Echter werd juist het andere percept langer waargenomen tijdens het onafgebroken kijken naar de afbeelding. De tijdsregeling van de perceptuele wisselingen was zo dat het percept dat vaak was waargenomen niet langer of korter duurde dan wanneer er geen perceptueel geheugen was, maar dat juist het alternatieve percept langer duurde. Dit suggereert dat het brein bij het verschijnen van een afbeelding of object aanvankelijk afgaat op percepten die recent vaak zijn voorgekomen, alsof deze gebruikt worden als een verwachting of aanname. Echter, als er meer tijd is om naar de afbeelding te kijken lijkt het brein te zoeken naar alternatieve interpretaties.

Onze tweede deelvraag aangaande perceptueel geheugen was welke activiteit in het brein geassocieerd is met perceptueel geheugen. Dit hebben we onderzocht met behulp van twee verschillende beeldvormende technieken, respectievelijke beschreven in hoofdstuk 4 en 5. We hebben proefpersonen wederom laten kijken naar een lange reeks herhaalde korte presentaties van een ambigue afbeelding en vervolgens de hersenactiviteit tijdens het eerste deel van de reeks te vergelijken met de hersenactiviteit tijdens het laatste deel van de reeks. In het begin van de reeks zal er nog niet veel perceptueel geheugen zijn geweest, terwijl tegen het eind van de reeks al veel perceptueel geheugen was opgebouwd voor het percept dat steeds opnieuw werd waargenomen.

In hoofdstuk 4 hebben we in een MRI scanner fMRI metingen gedaan, waarmee een gedetailleerde foto gemaakt kan worden van de activiteit in het brein van een proefpersoon. De opbouw van perceptueel geheugen bleek geassocieerd te zijn met een toename van activiteit in de occipitaalkwab. Dit suggereert dat perceptueel geheugen zijn oorsprong niet in cognitieve hersengebieden vindt, maar in sensorische hersengebieden. We hebben dit experiment met twee verschillende ambigue afbeeldingen gedaan en de toename in activiteit kwam voor deze twee afbeeldingen voor in verschillende delen van de occipitaalkwab, namelijk die delen waarvan bekend is dat juist daar, voor die afbeelding, de neurale representaties van de twee mogelijke percepten liggen. Dit is een sterke indicatie dat perceptueel geheugen huist in de neurale representaties in de occipitaalkwab. Voorheen werd gedacht dat deze representaties zich vooral bezig hielden met de verwerking van externe factoren (de informatie die de ogen registreren), maar onze vindingen laten zien dat interne factoren (die zich in het brein bevinden), zoals perceptueel geheugen, eveneens in deze representaties worden verwerkt.

Het onderzoek dat beschreven is in hoofdstuk 5 lijkt in opzet sterk op het fMRI onderzoek in hoofdstuk 4, alleen hebben we hier een andere beeldvormende techniek gebruikt, namelijk EEG. Met een fMRI meting is nauwkeurig in kaart te brengen waar in het brein gebieden actief zijn, maar het is niet zo nauwkeurig te zeggen wanneer die activiteit plaatsvindt. Met een EEG meting is dat andersom. Bij een EEG meting worden electroden tegen de hoofdhuid geplaatst en deze kunnen zeer nauwkeurig meten wat het tijdsverloop van hersenactiviteit is, maar geven weinig nauwkeurigheid over de locatie van de activiteit. Uit eerder onderzoek weten we dat de perceptuele toestand die een proefpersoon waarneemt is terug te vinden in het EEG signaal ongeveer 160 milliseconden nadat de afbeelding in beeld is gekomen. De interpretatie van de afbeelding is dus waarschijnlijk voltooid in 160 milliseconden.

Onze EEG metingen lieten een invloed van perceptueel geheugen zien op activiteit in het brein in de periode van 50 tot 150 milliseconden nadat de afbeelding in beeld kwam. Daarmee is het waarschijnlijk dat perceptueel geheugen invloed heeft op hersenactiviteit die vooraf gaat aan de voltooiing van de interpretatie van de afbeelding. Dit is in lijn met de psychofysische vinding dat perceptueel geheugen invloed heeft op hoe een afbeelding wordt waargenomen (hoofdstuk 3), want om daar invloed op te hebben zullen neurale processen voorafgaand aan de voltooiing van de interpretatie beïnvloed moeten worden. Bovendien was in onze metingen de invloed van perceptueel geheugen zichtbaar aan de achterkant van de schedel, dicht bij de plek waar de occipitaalkwab ligt. Uit eerder onderzoek weten we dat hersenactiviteit die zo snel na het verschijnen van de afbeelding plaatsvindt zijn oorsprong hoofdzakelijk vindt in de occipitaalkwab, waarschijnlijk in de neurale representaties van de percepten. Tot nu toe werd gedacht dat zulke “vroege” verwerking vooral gedreven wordt door externe factoren. Onze vinding laat zien dat ook een interne factor als perceptueel geheugen al zo kort na het verschijnen van de afbeelding de verwerking in het brein beïnvloedt.

Als we de fMRI en EEG resultaten uit, respectievelijk, hoofdstuk 4 en 5 samen beschouwen wijzen ze er op dat perceptueel geheugen ontstaat – en opgeslagen wordt – in de neurale representaties van de percepten die zich bevinden in de occipitaalkwab. Hoe dit precies werkt vraagt verder onderzoek. Het zou kunnen dat een neurale representatie die veel actief is (wanneer het percept dat het representeert veel wordt waargenomen) meer geneigd is om opnieuw actief te worden op het moment van een perceptuele keuze. Het trainen van een spier kan als metafoor dienen: een spier wordt sterker als hij vaak gebruikt wordt en kan dan meer kracht leveren op het moment dat hierom gevraagd wordt. Dit mechanisme kan echter niet verklaren waarom tijdens langdurig kijken naar een ambigue afbeelding juist het andere percept langer wordt waargenomen, terwijl het percept dat het meest gezien is niet beïnvloed wordt, zoals de psychofysica in hoofdstuk 3 liet zien. In de lijn van de metafoor van de spier zou het kunnen zijn dat de explosieve kracht van de spier is toegenomen, maar het uithoudingsvermogen niet. Vandaar dat er geen invloed is op de duur van het percept dat het meest gezien is. Daarnaast geven enkele details in onze metingen aanleiding om te veronderstellen dat tijdens de korte presentaties van de afbeelding de herhaaldelijke deelname van het andere percept aan de eerder besproken competitieve race tussen de twee percepten als het ware het “uithoudingsvermogen” van het andere percept doet toenemen. Dit percept wordt weliswaar niet waargenomen tijdens de kort presentaties, maar de bijbehorende neurale representatie wordt wel steeds een klein beetje geactiveerd. Ook andere verklaringen zijn zeer wel mogelijk. Het exploratieve karakter van de onderzoeken die in dit proefschrift beschreven staan heeft geleid tot bevindingen die nog niet eerder gedaan zijn, echter vervolgonderzoek en replicatie van onze resultaten is van groot belang.

I.6 Samenvatting en conclusie

In dit proefschrift is onderzocht hoe beelden die uw ogen registreren in het brein worden verwerkt tot een waarneming van de wereld om ons heen. Om dit goed te kunnen doen hebben we ambigue afbeeldingen gebruikt die op twee manieren zijn waar te nemen. Met behulp van deze afbeeldingen is het mogelijk om neurale processen die te maken hebben met het waarnemen (perceptie) te onderscheiden van neurale processen die te maken hebben met het kijken met de ogen (stimulatie). De focus ligt in dit proefschrift op twee aspecten van visueel waarnemen die in het brein ontstaan (interne factoren) en dus niet direct zijn te herleiden tot het kijken naar de afbeelding (externe factoren), namelijk: 1) wisselingen in de waarneming die spontaan optreden terwijl de afbeelding niet verandert en 2) de wijze waarop perceptueel geheugen de waarneming van een ambigue afbeelding beïnvloedt. Van beide verschijnselen is in bestaande literatuur verondersteld dat ze hun oorsprong vinden in cognitieve hersengebieden. De bevindingen die beschreven staan in dit proefschrift geven echter sterke aanwijzingen dat beide ontstaan in sensorische hersengebieden gelegen in de occipitaalkwab en niet in cognitieve hersengebieden. We hebben de betrokkenheid van de occipitaalkwab met verschillende technieken onderzocht en de resultaten wijzen alle in dezelfde richting: interne invloeden op onze waarneming huizen in neurale representaties in de occipitaalkwab die bij het zien van een afbeelding ook de eigenschappen van die afbeelding verwerken. Het verwerken van externe factoren (de afbeelding waarnaar gekeken wordt) blijkt dus in dezelfde hersengebieden plaats te vinden als de verwerking van interne factoren (die alleen in het brein bestaan), zoals perceptueel geheugen en perceptuele wisselingen. Als externe en interne factoren in dezelfde delen van het brein worden verwerkt en daarmee onlosmakelijk met elkaar verbonden zijn kan waarneming onmogelijk een exacte weergave van de buitenwereld zijn. Aan u de keus of u voortaan nog uw ogen gelooft.

Appendix II

Publications

II.1 Journal publications

de Jong MC, Hendriks RJM, Vansteensel MJ, Raemaekers M, Verstraten FAJ, Ramsey NF, Erkelens CJ, Leijten FSS, van Ee R (submitted) Intracranial recordings of occipital cortex responses to illusory visual events.

de Jong MC, Brascamp JW, Kemner C, van Ee R, Verstraten FA (2014) Implicit perceptual memory modulates early visual processing of ambiguous images. Journal of Neuroscience 34/30: 9970-81.

de Jong MC, Kourtzi Z, van Ee R (2012) Perceptual experience modulates cortical circuits involved in visual awareness. European Journal of Neuroscience 36/12: 3718-3731.

de Jong MC, Knapen T, van Ee R (2012) Opposite influence of perceptual memory on initial and prolonged perception of sensory ambiguity. PLoS ONE 7/1: e30595.

de Graaf TA, de Jong MC, Goebel R, van Ee R, Sack AT (2011) On the functional relevance of frontal cortex in bistable vision and voluntary control. Cerebral Cortex 21/10: 2322-31.

de Jong MC, Boersma CH (2010) Device-guided breathing as a possible tool to improve the outcome of exposure therapy. Mental Illness 2: e6.

de Jong MC, van Engeland H, Kemner C (2008) The attentional effect of gaze shifts is influenced by emotion and spatial frequency, but not in autism. Journal of the American Academy of Child & Adolescent Psychiatry 47: 443-454.

II.2 Refereed abstracts

de Jong MC, van Steensel MJ, Hendriks RJM, Raemaekers MAHL, Leijten FSS, Ramsey NF, van Ee R (2010) Occipital reflections of perceptual decisions revealed by subdural electrode recordings in human. Society for Neuroscience, San Diego, USA.

de Jong MC, Knapen THJ, van Ee R (2010) Perceptual memory influences perception of a changing and a stable visual environment in opposite ways. Forum of European NeuroScience, Amsterdam, The Netherlands.

Stijl R, Petridou N, de Jong MC, van Ee R (2010) Investigating perceptual selection in ambiguous visual stimulation using high temporal resolution 7 Tesla fMRI. Forum of European NeuroScience, Amsterdam, The Netherlands.

de Jong MC, Kourtzi Z, van Ee R (2010) Perceptual memory increases amplitude of neural response in sensory brain regions. Vision Sciences Society, Naples, Florida, USA.

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Appendix III

Curriculum vitae

Maartje Cathelijne de Jong was born in Eindhoven, The Netherlands, on April 17th 1981.

She enrolled in the Bachelor's program in Biology at Utrecht University, The Netherlands, and took additional courses in Physics, Mathematics and Psychology. In her first year she was selected for the Excellent Track for outstanding students. She wrote her thesis at the Bioinformatics department and graduated in 2005. During this time she also worked as a mathematics coach for high school students and as a dancer.

Maartje was admitted to Utrecht University's prestigious Master's program in Cognitive Neuroscience. As part of this program she worked with Prof. Dr. Chantal Kemner, University Medical Centre Utrecht, to investigate abnormalities of visual processing in autism spectrum disorders. This work was granted the Talma-Eijkman award for outstanding undergraduate research work. As an intern she worked with Prof. Dr. Raymond van Ee, Helmholtz Institute, Utrecht University, investigating the perception of ambiguous images using neuro-imaging techniques. In the group of Prof. Dr. Victor Lamme, University of Amsterdam, she wrote her Master's thesis on subliminal visual priming. She received her Master's degree with honors ('cum laude', GPA= 4.0) in 2007.

Maartje returned to the Helmholtz Institute as a PhD-student and investigated neural mechanisms underlying temporal modulation of visual perception in the group of Prof. Dr. Raymond van Ee and the group of Prof. Dr. Frans Verstraten. She used a variety of techniques, including scalp and intracranial electro-encephalography, functional magnetic resonance imaging and psychophysics, as described in this thesis. As part of her PhD-research she collaborated with national and international colleagues. In support of her international travels she received awards from the Vision Sciences Society (VSS), the Forum of European NeuroScience (FENS) and the Dutch Society for Biophysics and Biomedical Technology (VvBBMT). In 2010 she won the 'Dance Your PhD'-contest in the category Biology (Science Magazine, Am. Ass. for the Advancement of Science). At Utrecht University she participated in the graduate school of Helmholtz Institute (Natural Sciences) and was a member of the PhD-council of the Science faculty and an editor of the Helmholtz Herald (letter of the Helmholtz Institute).

From 2012 until present Maartje works as a postdoctoral researcher in the group of Prof. Dr. Chris Dijkerman, department Experimental Psychology, Utrecht University. Her current research topic is visuo-tactile integration in near-body space.

Appendix IV

Nawoord (in Dutch)

Ik heb met veel plezier aan dit proefschrift gewerkt. Graag wil ik iedereen bedanken die aan dit proefschrift en aan dit plezier heeft bijgedragen.

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Casper Erkelens wil ik bedanken voor zijn betrokkenheid en goede adviezen. Ik vind het een genoegen om met Casper te discussiëren. Het maakt niet uit welk wetenschappelijk onderwerp wordt aangesneden, hij weet altijd iets te zeggen waar je wat aan hebt.

Toen de vakgroep Fysica van de Mens werd opgeheven heeft Frans Verstraten mij in zijn groep bij Psychologische Functieleer opgenomen. Ik wil Frans bedanken voor zijn inzet, de fijne en open samenwerking en de impuls die hij gegeven heeft aan de projecten in dit proefschrift.

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I would like to thank Zoe Kourtzi for inviting me to Birmingham and showing me how a research project can grow with creative thinking and a perfectly organized lab. It has been a privilege and a pleasure to work with her.

Chantal Kemner wil ik bedanken voor de wijze waarop zij mij heeft laten kennis maken met het werk als wetenschapper. Ze heeft mij geleerd om vertrouwen te hebben in de gekozen onderzoeksopzet. Sinds onze eerste ontmoeting, jaren geleden, zijn onze wegen zich blijven kruisen en ik hoop dat ze dat blijven doen.

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Ralph Hendriks wil ik bedanken voor zijn trouwe inzet en zijn vriendschap.

Ook wil ik al mijn collega’s en voormalig collega’s van de vakgroep Fysica van de Mens en de vakgroep Psychologische Functieleer bedanken voor hun collegialiteit en de vele leuke momenten, gesprekken en uitstapjes. Ik heb ik de loop der jaren met verschillende collega’s een kamer gedeeld, op conferenties en op de Uithof, en ik heb het altijd erg gezellig gehad. Tobias Borra is het langst mijn kamergenoot geweest. Ik wil hem bedanken voor de vele keren dat ik met (en om) hem gelachen heb. Chris Dijkerman wil ik graag bedanken voor de mooie nieuwe projecten die we hebben opgezet en voor zijn belangstelling in mijn persoonlijke omstandigheden.

Vanwege mijn persoonlijke situatie heeft de afronding van dit proefschrift een tijd moeten wachten. Ik ben blij en gelukkig dat ik tegen alle medische verwachtingen in lopend en wel mijn proefschrift kan verdedigen. Graag wil ik iedereen bedanken die mij een hart onder de riem heeft gestoken en heeft geholpen toen ik ziek was. In het bijzonder wil ik mijn echtgenoot, dochtertje, ouders, broer en schoonfamilie bedanken. Ik heb jullie nog nooit zo nodig gehad en jullie waren er voor me.