Centre-Periphery-Difference in Low-Level Vision And Its Interactions with Top-Down and Sensorimotor Processes

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ABSTRACT

There is a profound difference in low-level vision between the retinal centre and the periphery (cpd). That contrast sensitivity declines from centre to the periphery is well established in humans. However, recently TMS on FEF was found to remotely affect visual cortex such that the cpd was reduced. No direct connections between FEF and occipital visual areas are known, but connections between FEF, the pulvinar and the occipital visual areas exist. I examined the cpd pattern in contrast sensitivity after real lesions in FEF and pulvinar areas by estimating visual thresholds. The results showed that real lesions of FEF do not have the same effect as TMS and are consistent with TMS causing subthreshold activation mimicking covert visuospatial attention. The cpd pattern in contrast sensitivity was different between FEF and pulvinar patients. Differences were prominent for foveal processing, while peripheral processing revealed parallel deficits, although these did not reach significance. In the second part of this work I focused on manual visuo-motor processes that have been found to differ between centrally and peripherally presented subliminal primes. For the periphery, when invisible primes are compatible with targets in their motor associations, RT's to targets speed up. However, for foveal primes, priming costs (negative compatibility effects (NCE)) can occur with compatible primes and targets. I examined the impact of perceptual sensitivity decline for the absence of NCE in the periphery by equating primes' strength via contrast threshold measurements. The results showed that perceptual equation does not equate priming effects. The critical factor, to trigger visuo-motor processes in periphery was found to be the prolonged time of the mask-target interval (SOA). This indicates that the functionally distinct retinal areas can both trigger visuo-motor processes, which are independent from visibility equation.

To my Family

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF FIGURES IN APPENDIX

LIST OF TABLES IN APPENDIX

LIST OF ABBRIVIATIONS

Bi	Bilateral
BOLD	Blood-oxygen-level-dependent
cpd	Center-Periphery Difference
cpdp	Center-Periphery Difference in Visuo-motor Priming
FEF	Frontal Eye Fields
FEF TMS	TMS over FEF
F	Fovea
fMRI	Functional Magnetic Resonance Imaging Technique
DTI	Diffusion Tensor Imaging
L	Left Periphery
MEG	Magnetoencephalography
M	Arithmetic Mean
mL	Middle Left
mR	Middle Right
NCE	Negative Compatibility Effects
P	Periphery Left & Right Combined
PCE	Positive Compatibility Effects
PET	Positron Emission Tomography
P/F	Ratio Periphery Combined/Fovea
pR	Posterior Right
SEM	Standard Mean Error
R	Right Periphery
TMS	Transcranial Magnetic Stimulation
VEP	Visual Evoked Potentials

CHAPTER 1

SCIENTIFIC BACKGROUND

1.1 Summary and Rationale

1.1.1 Summary of Chapter 1

The introduction begins with a brief overview of the rationale motivating this thesis, and then provides an overview of the main background topics needed to underpin the experimental chapters. The visual processing system, theories and models of top-down control and visuospatial attention are described, followed by a detailed description of brain areas involved. Chapters 2-5 of the thesis focus on the FEF and the pulvinar, and these are introduced in detail here. Following this, some relevant methodological issues are introduced between patient and TMS studies. The second part of the introduction focuses on centre-periphery difference in sensorimotor priming (cpdp), providing the essential background to Chapters 6 and 7.

1.1.2 Summary of Experimental Chapters

The experimental work presented here investigates how the decrease in perceptual sensitivity which is shown with increasing retinotopic eccentricity in humans links with top-down control of visuospatial processes and what its impact is on visuo-motor control processes. In the first part of the thesis the impact of top-down control of covert visuospatial attention on cpd in vision is examined. In the second part the impact of cpd in vision on automatic control mechanisms in sensorimotor processes is of interest. Previously it has been reported that transcranial magnetic stimulation (TMS) of the FEF modulates the retinal perceptual sensitivity drop from foveal to peripheral regions. Chapters 2-5 focus on two brain areas, the frontal eye fields (FEF) and the pulvinar, and assess the impact of damage to these areas on the centre-periphery differences in contrast sensitivity. Chapter 2 validates the experimental paradigm chosen to test centre-periphery difference in perceptual sensitivity to contrast (cpd). Chapter 3 shows that the cpd in contrast perception after real chronic right FEF lesions was not equivalent to the cpd pattern reported after transient right FEF TMS but mirrors oculomotor findings in FEF patients in previous studies. Chapter 4 investigates patients with pulvinar lesions as this thalamic nucleus is a hub for cortico-cortical connections and it is

known to be retinotopically organised in monkeys and involved in visuospatial processing and control in humans and therefore it is considered likely to pass the FEF signals which modulate visual processing in the occipital cortex. The results indicate involvement of the pulvinar in visuospatial processing, which might act as an amplifier of visuospatial signals from FEF. The data supports previously found fixation changes with pulvinar damage, however no clear contralesional effects for periphery were found in the second group analysis. Finally, Chapter 5 examines the proposal that FEF TMS changes cpd in contrast sensitivity due to top-down control of attentional shifts. The data suggest that both brain areas are specifically involved in visuospatial top-down attention, with possibly complementary mechanisms in fovea but parallel in periphery. Chapters 6-7 examine a previously reported asymmetry between fovea and periphery in visuo-motor (sensorimotor) priming effects and whether equating for the perceptual sensitivity drop could account for the lack of motor inhibition with peripheral primes. Chapter 6 shows that perceptual sensitivity loss alone cannot account for the lack of motor inhibitory processes in periphery and that attentional manipulation does not have any impact on that. Experiments in Chapter 7 suggest that the "time window" for eliciting motor inhibition processes in the periphery differs from that for foveal stimuli. This suggests dissociation between the perceptual strength and sensorimotor strength of a stimulus and indicates that the separation between visual and motor processing can be fused into a module or concept of visuo-motor representation, which is partially independent and equally accessible from fovea and periphery when certain sensorimotor criteria are met.

1.1.3 Rationale

The first part of the thesis is motivated by previous findings in humans that non-invasive transcranial magnetic stimulation (TMS) of the Frontal Eye Fields (FEF) directly modulates visual processing in occipital brain areas and increases peripheral contrast sensitivity relatively to that of the fovea (Ruff et al., 2006). Such modulation appears to be in line with psychophysical and behavioural studies in humans which have shown that processing of visual information can be enhanced by covertly directed attention to a location in the visual field (Posner et al., 1980; Hawkins et al., 1990; Muller and Humphreys, 1991; Handy at al., 1996; Carassco et al., 2000; Humphreys et al., 2004). However, there is more than one way in which TMS may have influenced the FEF, and therefore, converging evidence is provided in

this work by examination of cpd in contrast processing after lesions of FEF in brain injured patients.

Secondly, the FEF TMS results are surprising because no long-range connections between FEF and the occipital areas are known. However, a grey matter nucleus of the subcortical thalamus, the pulvinar, is well known to facilitate cortico-cortical processing having strong connections to both the FEF in the frontal lobe and visual areas in the occipital lobe. Both, the FEF in humans (Hagler and Sereno et al., 2006; Saygin and Sereno, 2008, Kastner et al., 2007) and the pulvinar in monkeys (Shipp, 2003) have been found to be retinotopically organised and both are known to be involved in visuospatial attention. This implies their involvement in visual functions and suggests likely functional links to cpd in vision. Therefore pulvinar patients are tested here in the same tasks as patients with FEF lesions. Thirdly, to investigate if the top-down visuospatial attention is the neural mechanism underlying the FEF TMS effect on cpd in vision, patients with FEF and pulvinar lesions were tested in top-down and bottom-up controlled visuospatial attention.

The second part of the thesis is concerned with previously reported cpd in sensorimotor processes found using manual motor responses following subliminally (below a conscious visibility threshold) presented visual stimuli or primes. Either facilitation or inhibition can be evoked (DeJong et al., 1990; 1995), and this was found to differ when initiated by primes in the center or in the periphery (Schlaghecken and Eimer, 1999). The main hypothesis for this difference is the cpd in visual sensitivity (Lingnau and Vorberg, 2005), and that hypothesis is tested here.

Figure 1 illustrates a framework for the topics to be studied in this thesis. It is proposed that visuo-motor systems have evolved for different kinds of behavior as relatively independent functional modules (Goodale, 1996; Milner and Goodale, 2006). However, in humans, visuo-motor processes need to be processed in flexible circuits. Thus, control circuits developed, to meet the demands of complex human-environment interactions (Goodale and Milner, 1992; Goodale 1993; Goodale and Humphrey, 1998; Goodale, 2001; Goodale et al., 2004; Goodale et al., 2005; Goodale, 2008; Sumner et al., 2008). Control is achieved in a variety of ways, including top-down processes of attention, but also automatic and unconscious mechanisms such as saliency maps, which provide a basis for stimulus-driven attentional and oculomotor shifts, and subliminal inhibition, as studied with sensorimotor priming. These topics will be introduced in the sections below. The perceptual sensitivity drop in the retina is well

established and precisely measured in humans. The psychophysical methods to measure cpd are one of the most reliable, accurate and objective among non-invasive methods in human experimental neuroscience. Therefore same measurement methods are applied to investigate both the cpd in patients with FEF and pulvinar lesions and sensorimotor processes in healthy participants.

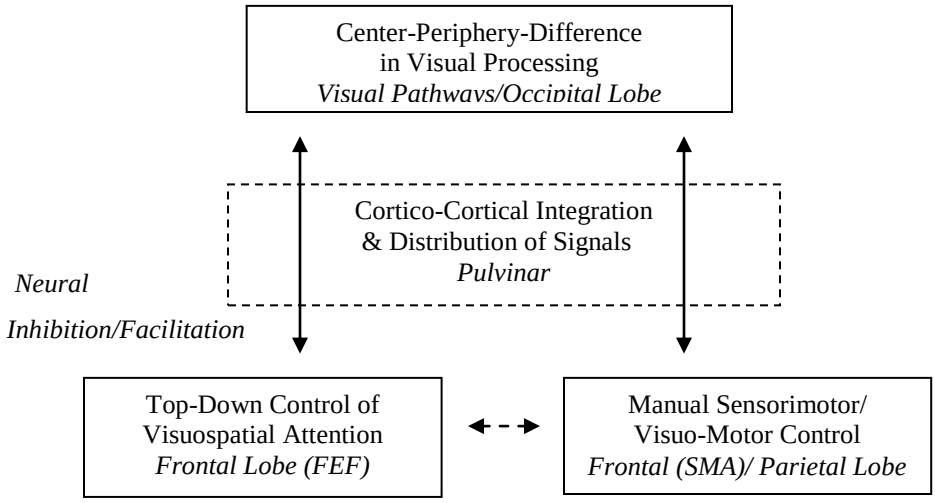


Figure.1. Illustration of the relationships to be studied in this thesis. Separate but interconnected visuo-motor circuits (cognitive top-down and automatic sensorimotor systems) which influence and are influenced by the fundamental differences in visual processing between center and periphery. SMA: Supplementary Motor Area.

1.4 Vision from Bottom-up Perspective

1.4.1 Two Cortical Visual Systems

Our perceptual experience and behavior seems unified in time and space. However, a wealth of research indicates that neural processing of visual input does not happen cohesively. Visual input can be processed independently and in parallel as early as its entrance through the retina of the eye. The first evidence for separated pathways of visual processing emerged with observations of brain injured patients at the beginning of the 20th century and converged to establish models of visual processing (Ungerleider and Mishkin, 1989; Milner and Goodale, 1992, 2006, 2008) which influenced the understanding of brain processes profoundly. In the following decades, supportive evidence has been gathered for two main

concepts which dominate the view at present: functional specialization and anatomical segregation of brain processing,

1.4.1.2 Dorsal and Ventral Pathway

In 1969 Schneider postulated an anatomical separation in visual coding of the location of a stimulus and the identification of a stimulus. This distinction between object identification and spatial localization, i.e. between the what pathway and the where pathway of visual input, has been adapted by later models of visual processing. The model of visual processing by Ungerleider and Mishkin, 1982 postulates, that the visual input as arriving in the striate cortex can be divided into two major streams: the ventral stream projecting up to the inferotemporal cortex and the dorsal stream projecting to the posterior parietal cortex (Fig.2). This model was based on studies in monkeys (Milner et al., 1977). In humans, the emphasis shifted from 'what and where' to 'what and how'; in other words, vision for perception and vision for action (Milner andoodale, 1992). This model will be discussed in more detail in later sections.

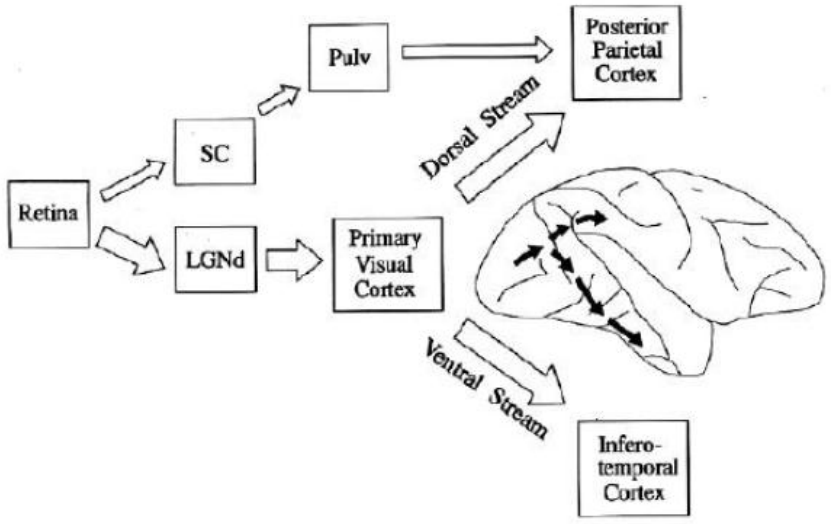


Figure 2. The major routes of visual input into the dorsal and ventral streams in the monkey brain. The diagram of the macaque brain on the right of the figure shows the approximate routes of the cortico-cortical projections from the primary visual cortex to the posterior parietal and the inferotemporal cortex, respectively. LGNd: laterale geniculate nucleus, pars dorsalis; Pulv: pulvinar; SC: superior colliculus. (Ungerleider and Mishkin (1982)). As the visual input enters the retina it can be passed via superior colliculus and via lateral geniculate nucleus (LGN). The SC projects on to the pulvinar which then projects to the parietal cortex. The LGN projects to the primary visual cortex which then can project to the posterior parietal cortex (dorsal stream) and to the infero-temporal cortex (ventral stream).

1.4.1.3 Functional Organization

The modular organization of the visual system in functionally separate areas is a fundamental principle established in monkey since the 1970's (Zeki, 1973, 1976; 1978; Wiesel and Hubel, 1974). Later it was shown that the human visual cortex in the occipital lobe has also a modular organization, i.e. the visual cortex is divided anatomically into several different functional areas (or functional modules), which specialize in processing different features of visual input (colour, motion, contrast, orientation) (Zeki et al., 1991) (Fig.3).

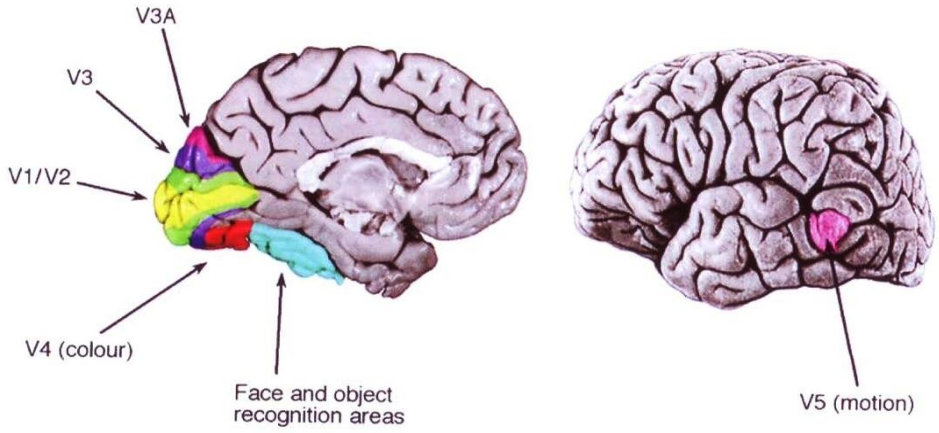


Figure 3. Medial (a) and lateral (b) view on human brain showing modular and functional organization in human visual cortex (occipital lobe). Functionally different areas are indicated by different colours. (Vision of the Brain, Zeki, 1999).

1.4.1.4 Hierarchical Organization

Hierarchical processing from simple visual features (contrast or orientation) to more complex visual percepts (motion, faces) has been revealed as another important principle in visual processing and it also defines the functional specialization of the visual areas (Fig.4). The V1 striate area of the occipital lobe has been found to process simple visual features such as orientation, colour and contrast (Wiesel and Hubel, 1974; Zeki, 1978, 1983, 1993). Area V2, which is a part of the extrastriate cortex, receives input from V1. The other visual areas include areas V3 and V3A, known for processing dynamic form (Hubel and Wiesel, 1965); Area V4, the colour processing area (Zeki, 1978); and Area V5, located in the middle

temporal sulcus, also referred to as MT, is involved in processing information about motion (Allman et al., 1973).

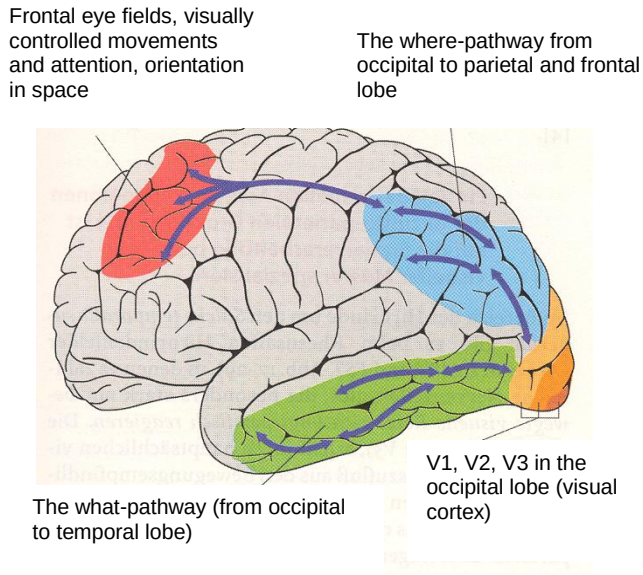


Figure 4. Visual processing in the human brain. Visual Pathways (Birbaumer N., Schmidt R. (1997) modified), areas in red: frontal areas involved in visuospatial and visual memory processing, blue: parietal areas and higher order visual areas, dark yellow: V2, orange: V1.

The functional specialization of visual areas in the occipital lobe has been continuously extended into areas like V6, V8, KO (kineto-occipital) and LO (lateral occipital) (Zeki et al., 2003). Further, areas in the frontal lobe, such as the Frontal Eye Fields (FEF) were identified which were linked with visual, visuospatial attention and oculomotor processes. The FEF have been suggested to be linked to the dorsal pathway of visual processing.

1.4.1. Centre-Periphery Difference in Visual Processing

Spatial Organization of Visual Input

The functional specialization of the two pathways for visual processing constitutes a fundamental entity of the visual system and starts immediately at the beginning of the visual processing in the retina. After the emergence of the two-pathway model by Ungerleider and

Mishkin in 1982 the division in two pathways has been found to begin at the very retinal level with two main cytological subdivisions of the retinal ganglion cells, which terminate different layers of the lateral geniculate nucleus (LGN) (Hubel and Livingstone, 1988). As a first approximation, most cells in the foveal area have been found to terminate in the parvocellular layers, and these go on to form the key innervations to the ventral stream. Cells from the periphery of the retina mainly terminate in the magnocellular layers in LGN, and produce the major input to the dorsal stream. In sum both ganglion cells, and receptor types and their respective numbers, all differ substantially between the fovea and the periphery of the retina. Accordingly, the organization of visual areas and the amount of neurons dedicated to different kinds of processing of visual input differ substantially for fovea and the periphery. This has fundamental implications on how stimuli displayed in the fovea or in the periphery are processed and responded to.

Retinotopic Organization of Visual Input

Numerous studies suggest that the most coherent image information within the visual system is its spatial organization in the form of visual field maps. "Without this element any realistic chance of reconstructing the original visual image would be lost" (Wandell et al., 2007). In monkeys and in humans, the neurons in lower visual areas (e.g., V1 through V5) were shown to be organized in the form of retinotopic maps (Sereno et al., 1995). Neurons in those areas form a 2D representation of the visual image displayed on the retina in such a way that neighboring regions in the visual cortex correspondingly represented neighboring regions in the retina. Thus, the regions of visual cortex, despite their functional specialization, preserve the visual field map so that the spatial relations of the visual inputs on the retina do not change during visual processing.

Cortical Magnification of Visual Input

However, it has been found that the passing of spatial organization can be nonetheless distorted in visual areas in many ways. Most importantly, there are profound differences between the cortical spaces that retinotopically map fovea and peripheral parts of the visual field (Wiesel and Hubel, 1974; VanEssen et al., 1984). As Fig.5 illustrates, it has been shown, both in monkeys and in post-mortem studies in humans, that the visual system allocates proportionally more grey matter to the fovea than to the periphery (Oesterberg, 1935; Curcio et al., 1989, 1989).

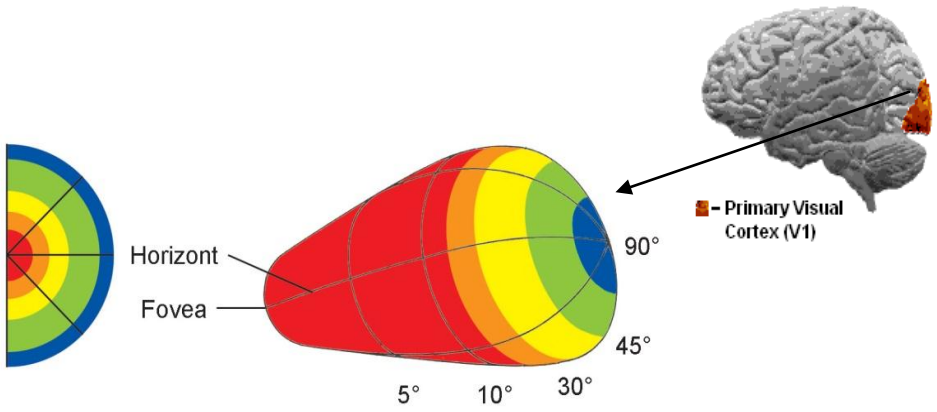


Figure 5. Illustration of Cortical Magnification of Central vs. Peripheral Parts of the Retina in V1 Cortex. (a) visual hemifield (half of retinal image) (b) space in the primary visual cortex dedicated to foveal and peripheral processing (c) lateral view of human brain with visual cortex in the occipital lobe. Eccentricity is shown in visual angle in degrees from 0 (fovea) to 90 degree visual field (periphery) labeled in colours from red to blue (adapted from the website of Prof. Gegenfuhrter Laboratory, Goetingen, Germany).

The "cortical magnification" was quantified in the monkey showing a linear decrease with retinal eccentricity. Retinal cells close to the fovea were found to project to 2-3 times more cortical space in V1 than a retinal cell from a peripheral locus (Talbot and Marshall, 1941; Daniel and Whitterige, 1961). Added to the fact that there are many more cells per unit area in the fovea than periphery to start with, such a difference has a profound effect on how the visual input is processed in the fovea in comparison to the periphery. For example, in both primates and in humans, visual sensitivity has been shown to drop with increasing eccentricity – from the very centre of the retina (fovea) to the retinal periphery (De Valois and Jacobs, 1968; Merigan, 1989). This has been shown in numerous psychophysical studies investigating contrast perception in humans (Robson and Graham 1981; Rovamo 1978; Rovamo and Virsu, 1979; Snowden and Hess 1990; Thibos et al., 1996; Rijsdijk et al., 1980, Cambell, 1980; Lie et al., 1980, Sereno et al., 1995).

1.4.1 Contrast Perception

1.4.1.1 Processing of Visual Contrast

The visual system is able to compute contrasts between different colours and their hue, between luminance's of an image and can discern different objects of different texture (Zeki, 1973). Contrast has been defined as a low-level visual feature and it is known to be processed mainly in the primary visual cortex (V1) and is believed to be computed through feed-forward, feed-back and horizontal connections (Wiesel and Hubel, 1966). Without the property of the visual cortex to measure and compute visual contrasts no meaningful image would be visible to the eye.

1.4.1.2 Measurement of Contrast Sensitivity

Contrast sensitivity measures the ability of the visual system to discern between luminance of different levels in an image. Often contrast is defined as the difference between the highest luminance level (white) and the lowest luminance level (black). Contrast is calculated as a difference in luminance levels relative to mean luminance (Michelson, 1927) and can be estimated via visibility thresholds in visual detection or orientation discrimination tasks (Sharpe and Tolhurst et al., 1973; Robson and Graham, 1981; Cambel and Robson, 1968; Virsu and Rovamo, 1979).

1.4.1.3 Centre-Periphery Difference in Contrast Sensitivity can be modulated

The findings of Virsu and Rovamo, 1979 and many other studies in the late 1970s and 1980s found robust centre-periphery differences in visual perception and in contrast processing. However, more recently Ruff et al. (2006) showed in their study that visual processing of contrast in the periphery can be modulated remotely by Transcranial Magnetic Stimulation (TMS) over the Frontal Eye Fields (FEF). Ruff and colleagues (2006) reported improved contrast sensitivity in the periphery relative to the fovea. As a result, there was a relative equalization of cpd in contrast perception. This behavioural effect was consistent with an increase in the blood oxygen level dependent signal (BOLD response) for early visual cortex (V1-V4) in its peripheral parts (Ruff et al., 2006). The authors proposed that the causal effects of TMS on BOLD in visual brain areas and their behavioural manifestation in contrast

perception could reflect top-down control mechanisms in the form of covert visuospatial attention. These results, and the related hypothesis, formed the inspiration for the first part of this thesis (Chapters 2-5), and Ruff et al.s' study will be explained in more detail in Chapters 2 and 3. First, the background needed is provided in sections below, including introductions to the concepts of top-down processes and attention, the FEF and other essential brain areas, and methodology of TMS.

1.5 TOP-DOWN PROCESSES

Early brain imaging studies have shown that "perception arises through an interaction between sensory [visual] input and prior knowledge" (Frith and Dolan, 1997) and **"**attentional guidance represents prior knowledge on visual input" (Driver and Frackowiak 2001). Anticipation and expectancy of a visual feature or of its spatial position in the visual field have been reported to lead to faster and more accurate detection of visual targets (Posner, 1980, Posner et al., 1980a,b, 1982). Fig.6a. also demonstrates this and the dilemma to understand the stage at which top-down processes control the visual input towards meaningful visual precepts.

The early view on visual perception is based on early cognitive models and theories of visual processing in the brain, which assume that visual perception can be controlled in two ways via a) bottom up visual input and via b) top-down higher cognitive processes such as anticipation, expectation and knowledge of a visual image to emerge. Bottom-up driven visual input has been outlined in previous paragraphs (Ungerleider and Mishkin, 1982), while the top-down processes originally were believed to influence vision in the late stages of visual processing. However several studies (including Ruff et al., 2006) now suggest that top-down processes can influence vision at stages as early as contrast processing in V1-V4.

The definition of top-down processes is an umbrella term for a variety of higher cognitive functions. Intention, memory, prior experience or knowledge and attention have been suggested to play an important role in top-down anticipatory control and have been linked with conscious voluntary commands which selectively direct perception of and action to relevant aspects of the environment (Norman and Shallice, 1986; Milner, 2004).

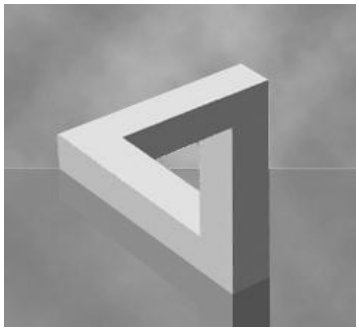
a)  b) 

Figure 6. Examples for top-down and attentional influence in visual processing. Higher order cognitive processes such as prior knowledge and expectation (or anticipation) can guide attention and eye movements towards the relevant aspect of the image. (a) Dalmatiner in landscape; the figure of the dog emerges only if the observer expects a dog, without the modulation of expectation (via verbal instruction or a cue) the picture remains a homogenous abstract pattern. (b) Ambivalent triangle or impossible figure: overt attention and eye movements to the right lower or left upper corner of the triangle changes the perspective of the figure in 3-D space (vertical or horizontal) (Zimbardo and Gerrig, 1997).

1.5.1 Attention

1.5.1.1 What is Attention?

Three fundamental aspects of attention have been proposed: selection, awareness and control (Baddley and Weisskrantz, 1993). All theories and models are based on these concepts (Lavie and Tsal, 1994; Driver, 2001; Chuan and Wolfe 2001; Ruff et al., 2006). Attention is also often understood in the form of neural processing capacity, which can be controlled via top-down voluntary conscious mechanisms. However attention can also be engaged subconsciously and involuntarily, as explained further below.

1.5.1.2 Forms of Attentional Selection

The selective nature of attention is based on the idea that there is a limited capacity of processing resources in the brain (Broadbent, 1957; Desimone and Duncan, 1995). The bottleneck or filter model of attention is the earliest one (Broadbent, 1957) and it is based on this assumption. Although selective allocation of attention is one of the key mechanisms in

top-down control of visual processing there are ongoing debates on how these processes are integrated.

One form of attentional selection is voluntary, which usually is defined as a top-down or endogenous process. Endogenous control of attention is for instance a result of external or internal instruction on a conscious perceptual level (Hophinger et al., 2000). The other form of attentional selection has been suggested to be of automatic origins and is often referred to as exogenous, bottom-up or stimulus-driven attention, or 'attentional capture'. In exogenous selection, attention is "caught" automatically from the periphery without conscious interference (Chastian and Cheal, 2001). Posner (1980) stressed that attention is a selective process, having a limited capacity, and that it is related to both reactive/ reflexive (stimulus-driven) and voluntary (top-down directed) processes, and it is associated with both inhibitory and facilitating effects.

1.5.1.3 How does Selective Attention in Vision work?

Attention seems a flexible cortical mechanism, which can act, independently from retinal sensitivity loss in the form of a supermodal control mechanism (Goodale and Milner, 2010a,b). Attention seems to enhance both foveal and peripheral processing. With attention less contrast seems necessary to attain the same response level in visual cortex, in the periphery and in the fovea (Kastner et al., 1999; Avidan et al., 2002, Hopfinger et al., 2000, Brefczynski and DeYoe, 1999; Tootell et al., 1998; Carrasco et al., 2001, 2006).

Kundsen, 2007 developed a model, which incorporates top-down processes into functions involved in selective attention. Although Kundsen speaks generally about a model of attention, it also applies to visuospatial attention. The model illustrates top-down sensitivity control in the form of higher cognitive processes, which regulate signal intensity in the information channels that compete for access to working memory (Egeth and Yantis, 1997).

Top-down signals from working memory, decision making processes, competitive selection mechanisms and bottom-up saliency filters control visual sensitivity and regulate the location in the visual field to which attentional resources can be directed.

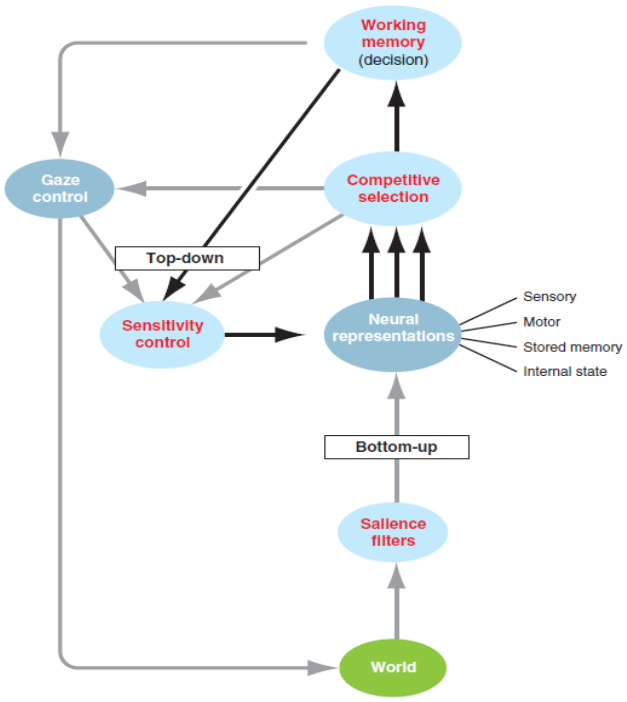


Figure 7. Model of functional components in visuospatial attention. Voluntary attention involves working memory, top-down sensitivity control, and competitive selection operating as a recurrent loop (dark arrows). In red are highlighted the processes that contribute to attention. Note that neural representations can exist in the form of sensory, motor, internal state and stored memory inputs. Neural representation in the form of visuo-motor links will play an important role in understanding sensorimotor processes in the second part of this work (Kundsen, 2007).

Importantly, Kundsen suggests a close interplay between top-down signals and the bottom-up saliency of infrequent stimuli and stimuli of instinctive and learned biological relevance (Koch and Ullman, 1985) which automatically evoke strong neural responses and which compete in the selective process (Itti and Koch, 2001). In fact it is known that stimulus-driven attention can override any top-down action programs in working memory (Miller and D'Esposito, 2005). Accordingly, the function of selective visual attention has been proposed to rely on perceptual salience (physical strength + perceptual strength) of a stimulus and its behavioural salience (behavioural relevance) within the goals of behaviour in progress (Desimone and Duncan, 1995).

1.5.1.4 The "Spotlight" Theories of Visuospatial Attention

William James (1890) described attention as having a focus, a margin and a fringe, which inspired David LaBerge (1983) to use the term "spotlight" when referring to attention. The focus of the spotlight has been proposed to be surrounded by fringe of attention which extracts information at low-resolution, which has its cut-off at a specific area called margin (Fig.7). Information inside the spotlight is thought to be processed quicker and with greater efficiency than information outside the spotlight (Luck et al., 1997). Thus, a detailed analysis of a whole visual scene requires a mechanism for selecting and shifting the focus of attention from one relevant location to another. However, what moves the spotlight to align with behavioural goals remains unresolved to date.

In the same tradition stands the zoom lens model (Eriksen and James, 1983). It proposes that any change in size of the attentional focus can be described by a trade-off between size of focus and the efficiency of processing. This model is based on limited processing resources (Broadbent, 1957; Desimone and Duncan, 1995) and assumes that the larger the visual area in focus of attention the slower processing will be of that region. Although it has been suggested that the focus of attention can subtend a minimum of 1 degree of visual angle (Eriksen and Hoffman, 1973), its maximum extent is unknown to date and certainly will be subjected to situational and individual variances.

Psychophysical studies have shown that an attentional gradient across the visual field exists based on the distance from the locus of a cue (Shulman et al., 1985; Downing and Pinker, 1985). Response latency to luminance-onset targets have been shown to increase monotonically with increasing target distance from the cued visual field location as tested in both endogenous and exogenous attentional manipulations (Shulman et al., 1985; Downing and Pinker, 1985; Handy at al., 1996, 2005).

1.5.1.5 Overt Attention versus Covert Attention

In 1980 Posner established that "attention can be allocated covertly, without eye movements". The increase of attentional focus and visual processing through the retinal fovea is usually referred to as overt attention and is interconnected and confounded with eye movements and ocular fixation. On the contrary, covert attention is considered to be

employed to monitor the environment without direct gaze and to prioritize the processing of some locations of the visual scene at the expense of others (Desimone and Duncan, 1995). Thus, peripheral visual processing can be covertly enhanced although the retinal fovea (highest point of visual acuity) has not been shifted towards it.

Thus the "spotlight" has been linked with increased perceptual sensitivity to the area of attention in the visual field (Treisman and Glade, 1980; Brefczynski and DeYoe, 1999). Fig.7 illustrates the spotlight metaphor and how this could overlap with cpd in perceptual sensitivity. Wherever the attentional focus is shifted, there is a relative enhancement of acuity and sensitivity In other words, processing becomes more fovea-like, and the fringe and margin of the attentional spotlight seems to match peripheral blurred vision. Until Posner (1980) established that attention could be shifted without eye movements, the two concepts of attention and perceptual sensitivity were not well distinguished. "Although there are a number of empirical approaches to the study of detection, most have not clearly separated between attentional factors and sensory factors and are thus incapable of providing an analysis of the relationship between the two".

Figure 8. Spotlight model of visual attention. The attentional spotlight and visual sensitivity is highest centrally and horizontally at null of y-axis as the picture indicates. The spotlight is of highest sensitivity in the centre usually where the fovea focuses on (retinal center), the blurry part of the attentional spot is the fringe, and it collides spatially with peripheral decrease of perceptual sensitivity when attention remains on the retinal center.

The ability to shift attention across visual space covertly can be understood as a cortical mechanism, which enhances neural processing directly in the cortex, and should be distinguished from the somewhat rigid bottom-up processing after the highest processing lens

(fovea) has been shifted towards a visual stimulus, which has been originally displayed in the periphery. This proposal seems to be supported by studies in monkeys and in humans, which reported activity in visual cortex when attention was covertly directed to a corresponding part of the visual field, even in the absence of visual stimulation (Hopfinger et al., 2000; Moore and Armstrong, 2003; Kastner et al., 1999, 2000, 2004; Kastner and Pinsk, 2004).

However, even though attention can be shifted covertly, eye movements and attention are thought to be strongly related. In monkey, Rizzolatti et al., 1987 have shown that action (oculomotor shifts) and attention are not necessarily different control mechanisms. Low current microstimulation in monkeys increased sensitivity to locations corresponding to the stimulated movement fields of FEF without evoking eye movements. This has been interpreted as the correlate of covert attention (Cavanaugh et al., 2006; Mueller and Rabbitt, 1989; Ekstrom et al., 2008). Investigations of attentional, eye movements and manual responses interactions to visual peripheral targets in humans strongly suggest that there is a supramodal representation of attentional space for all visuomotor functions (Hodgson et al., 1999).

1.5.2 Neuroanatomy of Top-Down Processes

Early studies in monkeys suggest that prefrontal cortex (PFC) could be a source of top-down signals necessary for maintaining sensory representations in the absence of bottom-up sensory input (Fuster et al., 1985; Luck et al., 1997). In humans, the first break through for evidence of brain areas involved in top-down control of visual processing emerged from early brain imaging studies. Frontal brain areas were shown to be activated for visual input (meaningless abstract pattern) when contrasted with visual recognition (a perceptual meaning was brought into the picture) (Ramachandran, 1994; Fink et al., 1996; Dolan et al., 1997). Depending on the visual feature attended (not only the locus in visual field), activation increased in specialized visual brain areas (Corbetta and Shulman, 1998; Corbetta et al., 1998, 2000). Friston et al., 1997 elucidated one of the types of top-down mechanisms in a brain imaging study showing that a set of areas was more active when attention was compared with passive viewing. Activation in that study included right prefrontal cortex, premotor cortex – and within it the frontal eye fields (FEF). Also several subcortical areas, among them the thalamus have been activated. Additionally, brain areas involved in selective attention have been found to be active even before the target has been achieved or presented

(Driver and Frith, 2000) while their sensory activity has been confirmed to be modulated by attention, memory and the intention to act (Egeth and Yantis, 1997). More studies followed which confirmed that anticipatory visuospatial attention involves stimulus-independent changes in BOLD signals from frontal, parietal, and visual cortical regions (Corbetta and Shulman, 1998; Freedmann et al., 2003; Bestmann et al., 2007; Berman and Colby, 2009).

1.5.2.1. The "Source" and the "Site" of Top-down influence

While the site of top-down modulation of vision is envisaged to be within the visual cortex, it has been long proposed that a priming, cueing or top-down signal arrives from some other brain regions ("source") (Zeki et al., 1991). Classically, brain areas known to be involved in top-down processes such as working memory, monitoring, execution and planning have been localized in the prefrontal cortex (PFC) (Fig.9). The PFC is highly interconnected with all sensory, neo-cortical and motor systems and with a wide range of subcortical structures and has been divided into three subparts: anterior, dorsolateral and ventrolateral as illustrated in Figure 9.

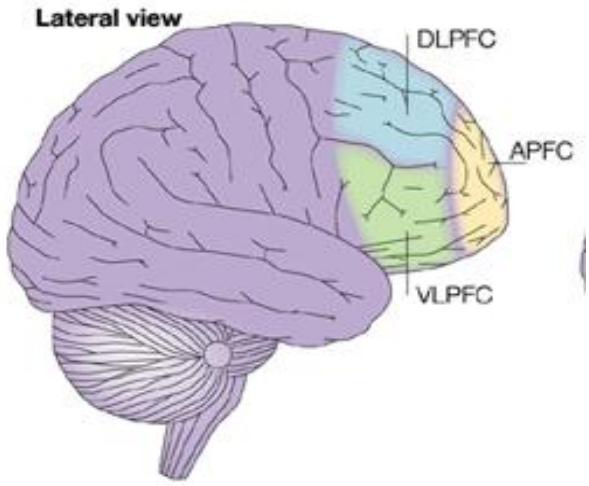


Figure 9. Illustration of human brain with its frontal cortex functional divisions in lateral view. The prefrontal cortex (PFC) can be divided into anterior (APFC, Brodmann area (BA) 10), dorsolateral (DLPFC, BA 46 and 9), ventrolateral (VLPFC, BA 44, 45 and 47) and medial (MPFC, BA 25 and 32) regions. BAs 11, 12 and 14 are commonly referred to as orbitofrontal cortex. (Adapted from Simons and Spiers, 2003, Nature Neuroscience).

These parts of the PFC are believed to be specific control instances monitoring and updating of task rules for all sensory and motor processes including attentional and occulomotor processes (Walker et al., 1998; Hodgson et al., 2007). Deactivation of the whole PFC has been reported to attenuate the activity of extrastriate neurons (beyond area V1) to a behaviourally relevant cue (Chafee and Goldman-Rakic, 2000), indicating involvement of PFC (or its sub-regions) in selective attention and in working memory.

During attention PFC enhanced the activity of brain neocortex and subcortical areas such as the pulvinar, superior colliculus and the occipital areas. Lesions to the PFC in humans and in monkeys confirm this role (Miller and Cohen, 2001) and PFC lesions have been reported not to show deficits in sensory discrimination or direct motor performance (Duncan et al., 1996). The Dorsolateral Prefrontal Cortex (DLPFC) has been especially focussed upon. Human brain areas which belong to the DLPFC are the cytoarchitectally distinctive areas BA 9, BA 46 (Brodman, 1909) (Fig.9). The DLPFC has been found to have wide back-projections on many brain areas and to influence their processes in a top-down manner via higher cognitive functions (Fuster, 1985). In brain imaging studies the DLPFC has been linked with working memory and attention in many visuospatial tasks (Smith et al., 1996).

More recently, however, the search for the neural basis of top-down control has broadened. Other brain areas in the frontal lobe such as the Frontal Eye Fields (FEF) or subcortical areas such as the pulvinar have been found to be potential sources of top-down control in visual processing and are the key areas investigated here.

1.5.2.2 A Model of Brain Areas involved in Top-Down Sensitivity Control

Kundsen, 2007, proposes a network of brain areas involved in executive control and attention as Fig. 10 illustrates. At the top of the hierarchy of neural processing Kundsen proposes prefrontal brain areas such as FEF and DLPFC. At the lower level Kundsen suggests the parietal cortex, in particular the lateral intraparietal area (LIP) which contains saliency maps and which is connected with FEF and other sensory areas. At the next lower level the model emphasizes a subcortical area – the superior colliculus (SC) which mediates automatic responses which influence attention.

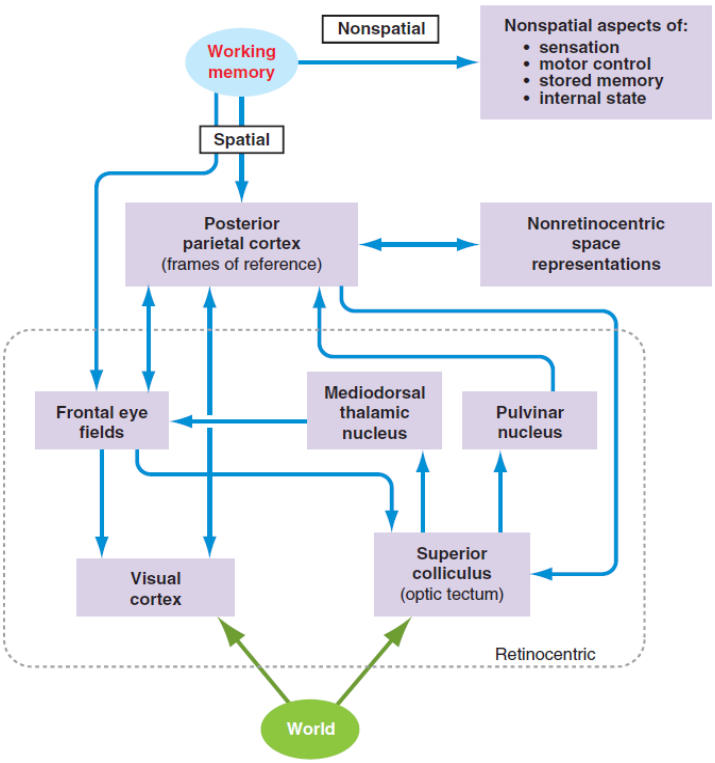


Figure 10. Model for top-down sensitivity control (Kundesen, 2007)**.** Blue arrows: Bias signal that regulate neural responsiveness. Green arrows: bottom-up information filtered for salience in the superior colliculus and in visual cortical areas. Top-down can bias signals from working memory which modulates the representations of nonspatial aspects of information. Top-down bias signals from working memory which also modulates the representation of information on the basis of object location, and which are transmitted to the posterior parietal cortex (PPC). There they are represented in various reference frames. Retinocentric biased signals are transmitted from working memory also to the FEF. Bottom-up signals arevcombined with top-down bias signals in all listed brain structures.

Neural processes such as lateral inhibition, which mediate the process of competitive selection through contrast enhancement, are proposed in accordance with earlier literature (Posner, 1980). Kundsen differentiated between brain areas involved in spatial (retinotopic) and nonspatial processes and suggests that parietal areas are not retinotopically represented. However the contrary has been found just recently (Sereno et al., 2008). In the model the FEF has been suggested to interact directly with the posterior parietal lobe, lower visual areas in the occipital lobe and the superior colliculus – which in turn interact with the pulvinar (Logothetis et al., 2010; Berman and Wurtz, 2008, 2010, 2011).

However, functional and anatomical links between the pulvinar and the FEF or the pulvinar and the occipital areas is missing in this model entirely. This illustrates a gap in the understanding of how these areas interact exactly in the human brain during such processes. Although white-matter connections between the FEF and the pulvinar were found previously, and the pulvinar does show connections to the occipital areas in monkeys (Shipp et al., 2003) and in humans (Leh et al., 2007) no direct white-matter connections between the FEF and the occipital areas have been found (Felleman and Van Essen, 1991).

1.6 THE FRONTAL EYE FIELDS (FEF)

One of the key focuses of this thesis is the role of the FEF in modulating low-level visual processing. Ruff et al., 2006 suggested that from the FEF "..pathways exist for top-down modulation of visual cortex, and stimulation of these pathways can produce attention-like behavioral effects" (Bressler et al., 2008). Subsequent studies have shown direct links between top-down modulation, visual attention and FEF using brain imaging and theoretical causality models (Sylvester et al., 2007; Bressler et al., 2008). Today, this brain area is considered as a multifunctional visual area which has been found to be involved in functions for guiding and enhancing visual perception such as oculomotor and attentional processes.

1.6.1 Localization and Connectivity

The FEF area was first determined in primates, when neural populations in the lateral frontal cortex were found to be active during oculomotor shifts. Connections with parietal and temporal brain areas and with the motion processing complex (MT+) were reported. However, no direct connections between FEF and visual areas in the occipital lobe are known to date (Shall et al, 1995; VanEssen et al., 2005) (Fig.11). The precentral sulcus (PrCeS) has been proposed to be the human homologue of the FEF (Paus, 1996). The relatively small region has been localized fronto-laterally at the junction of the superior frontal sulcus and precentral sulcus (BA8, BA 9) (Paus, 1996). The human FEF was found to be spatiotopically organized (Sereno et al., 1995; 2005) and white matter connections between FEF and other cortical and subcortical areas such as the pulvinar have been reported in humans recently (Leh et al., 2007).

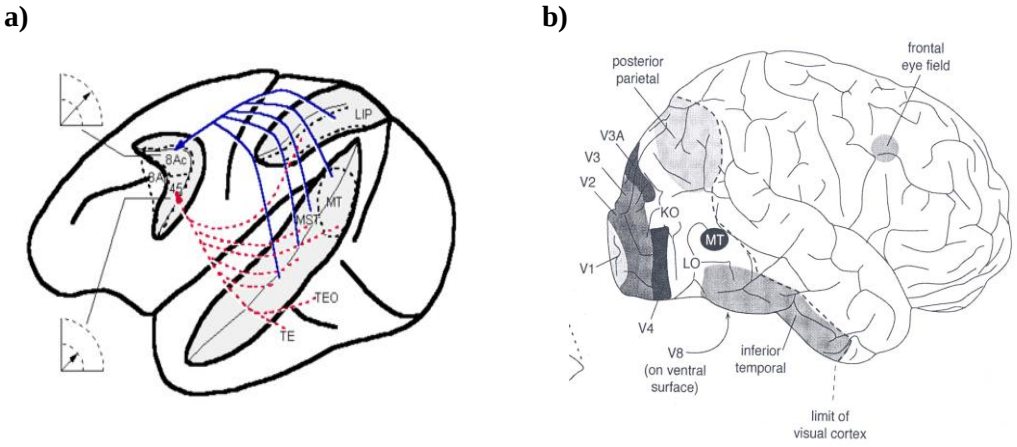


Figure 11. FEF position and connectivity in (a) monkey (b) humans; (note that the human and monkey brain images are mirrored here– the occipital lobes in both are to the inner side of the figure) (a) FEF position and connectivity in monkey; areas involved in low-level visual processing are placed remotely from FEF, but the temporal (TE and TEO) and parietal areas (LIP: Lateral Inferior Parietal) are connected with FEF, while no FEF connections to occipital areas were found, with the exception of MT and MST areas (involved in motion processing) (Van Essen, 2005). (b) Areas V1-V5, KO: kinetic occipital, LO: lateral occipital, MT: Middle temporal motion processing area are all areas involved in low-level visual processing and are placed remotely from FEF, which is localized fronto-laterally in humans. (Ramachandran VS., Vilayanur S. (2002). Encyclopedia of the Human Brain, Vol.4).

1.6.2 Functions

The FEF in monkeys was reported to contain properties for visual and motor processing and to be involved in the transformation of visual processing to saccade motor commands. The FEF were found to contain maps of visual space in which the amplitude and direction of saccades were organized in retinotopic coordinates (Goldberg and Bruce, 1990). More recent microstimulation studies have shown subpopulations of neurons, which seem to be specifically related to stimulus relevance, even without impending saccades and to be engaged in visuospatial processing indicating an attentional role of the FEF (Schall, 1995, Schall et al., 2007; Thompson et al., 1997; Moore and Fallah, 2001; Thompson and Bichot, 2005; Thompson et al., 2005). Similarly, transcranial magnetic stimulation (TMS) studies in humans (Schall et al., 2001; Ruff et al., 2006; Taylor et al., 2007) suggest that this originally believed oculomotor area is also involved in spatial attention processing and provides a basis for enhanced perceptual processing.

1.6.2.1 Eye Movements versus Attentional Shifts

In 1950, Penfield and Rasmussen found that stimulation of FEF did not produce visual precepts or phosphates but evoked saccades. However, later studies found more subtle perceptual effects. Schall et al., 1995 found that FEF neurons could specify a location in space without specifying stimulus attributes or a particular visual stimulus. Other studies reported a change of luminance discrimination performance during FEF stimulation (Moore and Fallah, 2001, 2004; Moore and Amstrong, 2003a,b; Moore et al., 2003). A brain imaging study of Corbetta and Shulman (1998) seems to support the view that there is no decoupling of attention and eye movements (Fig. 12). The same fronto-parietal network including the FEF has been activated during both functions. However, it has been proposed that anatomical integration between attention and eye movements could hold only for voluntary visual shifts of attention and eye movements (Corbetta, 1998; Corbetta et al., 1998; Corbetta et al., 2000; Shulman et al., 2010); i.e. accordingly with top-down functions of selective spatial attention. On the other hand, it was speculated that this could be generalized for reflexive visual orienting and stimulus driven attention.

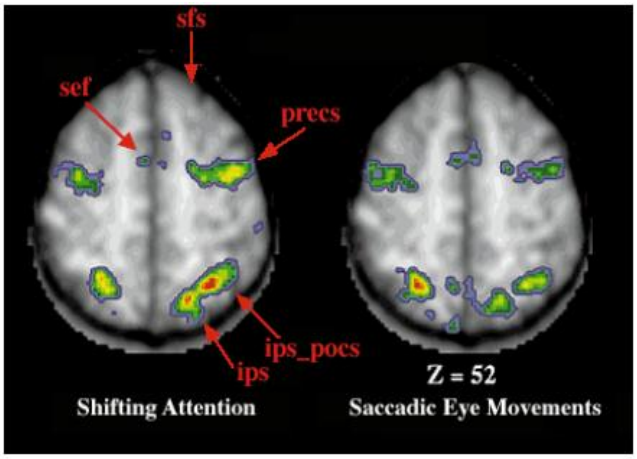


Figure 12. Common neurophysiological basis for shifting attention and eye movements to peripheral targets as shown in a fMRI study (Corbetta and Shulman, 1998). FEF is activated in both as indicated by precentral sulcus activation (precs). During attentional shifts parietal activation in the right hemisphere is dominant in the intra-parietal sulcus (ips) and in the postcentral sculcus (ips_pocs).

FEF activation was obtained in the same study of Corbetta and Shulman, 1998 when attentional shifts were performed to the periphery and contrasted with central detection. Also

a series of other brain imaging studies found activation of FEF when attention was directed covertly to peripheral stimuli (Nobre et al., 1997; Vandenberghe et al., 1997). This indicates that the FEF is indeed engaged in covert attentional shifts in humans during top-down control.

1.6.2.2 Top-down Signals

Most evidence from involvement of FEF in the distribution of top-down signals in different sensory modalities has been gathered by single recording studies in monkeys (Reynolds at al., 2000; Moore et al., 2003; Thompson and Bichot, 2005; Thompson et al., 2005; Awh et al., 2006). In humans, Corbetta et al., 2000 reported that FEF maintained the most sustained level of activation during a 7-sec delay, when subjects maintained attention at the peripheral cued location. Also a prestimulus top-down signal during expectation of a stimulus to a certain location was found to activate a distributed fronto-parietal network of areas including the FEF (Kastner and Ungerleider, 2000). Importantly, only in the FEF (and parietal area), BOLD was found to be modulated by the direction of attention (Corbetta et al., 2000), which suggests that these areas control the endogenous (top-down) allocation and maintenance of visuospatial attention. Based on these findings Corbetta and colleagues proposed a model of a regulatory system for visuospatial attention describing its neural circuits in which the FEF plays a crucial role (Fig.13).

The model integrates two largely dissociated neural networks mediating top–down and bottom–up control of visuospatial processing. Importantly it suggests that the right FEF plays the key role in both types of attentional control (Fig.14). This also indicates that top-down and bottom-up attentional processes are difficult to distinguish or only partly disintegrate within the right FEF. The right FEF might be a crucial neural hub for any visuospatial processing and therefore accessible by top-down and bottom-up guided visuospatial attention.

While Corbetta et al., 2000 suggest that FEF and parietal areas contribute together to visuospatial attention circuits in the brain; other studies provided evidence that FEF and parietal areas can process distinct aspects of attentional control. For instance, it has recently been argued that frontal areas (in particular, FEF and LPFC) may be more involved in top-down or endogenous aspects of visual attention, whereas parietal areas may be involved in more bottom-up or exogenous aspects.

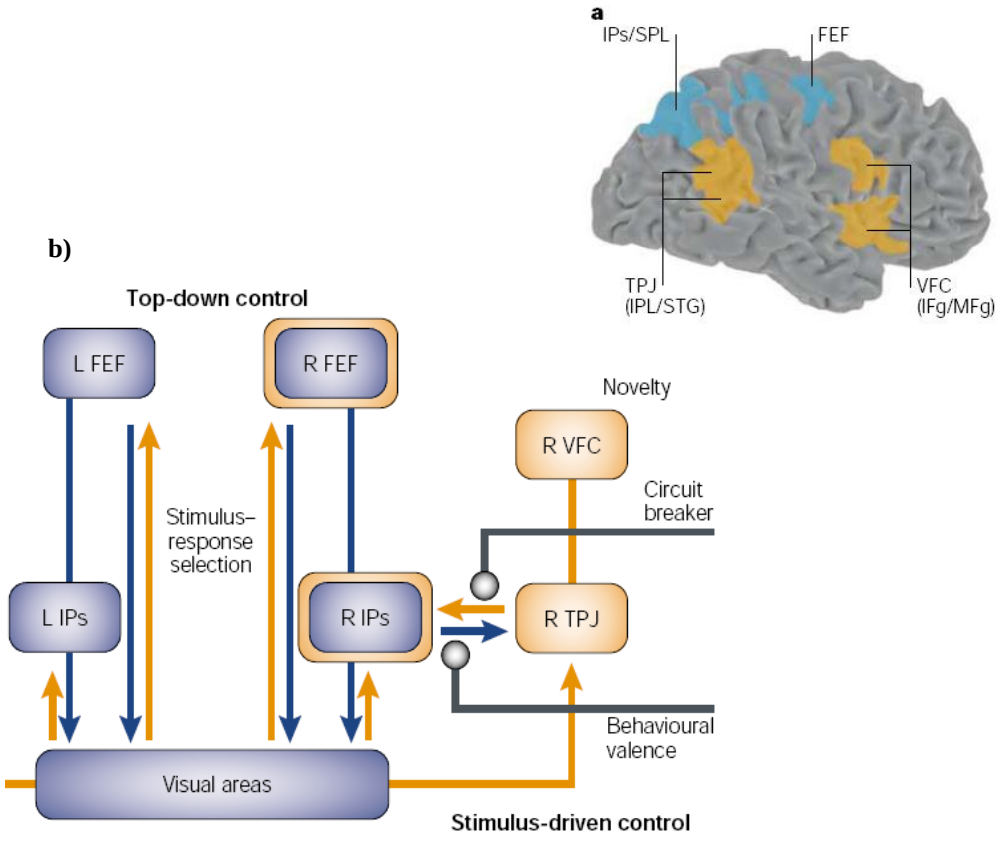


Figure 13. FEF involvement in top-down and stimulus-driven attention within the neuroantomical model of attentional control (Corbetta et al., 2000). The model is based on research results from patient studies and fMRI studies. **a)** Areas in blue indicate the dorsal frontoparietal network (FEF, IPs/SPL, interparietal sulcus/superior parietal lobule). The areas in orange indicate the stimulus driven ventral frontoparietal network. TPJ, temporoparietal junction (IPL/STG, inferior parietal lobule/superior temporal gyrus): VFC, ventral frontal cortex (IFg/MFg, inferior frontal gyrus/middle frontal gyrus). The areas damaged in neglect (right) better match the ventral network. **b)** Anatomical model of top-down control. The IPs-FEF network is involved in top-down control of visual processing (blue arrows). The TPJ-VFC network is involved in stimulus driven control (orange arrows). The IPs and FEF are also modulated by stimus-driven control. Connections between the TPJ and IPs interrupt ongoing top-down control when unattended stimuli are detected. The VFC might be involved in novelty detection. L: left; R: right.

In monkeys, it was found that FEF neurons registered top-down shifts of attention with a shorter latency than the parietal cortex (Buschman and Miller, 2007) while, automatic shifts of attention to a salient stimulus showed the opposite latencies. Human TMS-fMRI studies (Ruff et al., 2006; 2008; 2009) seem to support that the frontal and parietal cortex may exert qualitatively different influences on visual cortex. Accordingly, the direction of flow of information has been postulated to be reversed for top-down in these areas.

1.6.2.3 Is Right FEF special?

The classical understanding of visuospatial attention and attentional orienting came from clinical work in neglect and extinction patients after right parietal lesions (Heilman et al., 1983). Accordingly, spatial selective attention is widely considered to be right hemisphere dominant. However, in healthy subjects early fMRI studies have reported bilateral BOLD responses in dorsal frontoparietal regions during anticipatory shifts of attention to a location (Kastner et al., 1999; Corbetta et al., 2000; Hopfinger et al., 2000). Right-lateralized activity has mainly been reported in ventral frontoparietal regions for shifts of attention to an unattended target stimulus (Arrington et al., 2000; Corbetta et al., 2000). Accordingly, Corbetta et al., 2000 reported that stimulus-driven shifts of spatial attention and target detection showed asymmetries with a preference towards right hemispheric specialization, which differs from the rather bilateral network of top-down control of selective attention. Thus, top-down control of selective attention seemed to involve a less lateralized network of brain areas than stimulus-driven attention. However, bilateral BOLD responses have ben found to increase with the target's increased unpredictability, indicating engagement by stimulus-driven orienting (Hahn et al., 2006).

Ruff et al., 2006 claimed that TMS over the right FEF mimicked top-down control on visuospatial attention and later Ruff et al., 2009 found for both frontal and parietal stimulation clear differences between effects of right- versus left-hemisphere TMS on activity in the visual cortex. Frontal TMS over either hemisphere elicited similar BOLD decreases for central visual field representations in V1-V4, but only right frontal TMS led to BOLD increases for peripheral field representations in these regions. Thus, the right FEF seems to play a very specific role in peripheral enhancement of visual processing indicating its engagement in covert shifts of attention.

1.6.2.4 Insights from Real FEF Lesions

Previous sections described FEF functions through microstimulation and recording studies in monkeys and in behavioural, stimulation and brain imaging studies in humans. Studies of lesions in a brain area of interest also provide a good source of evidence for FEF functions. Both, lesion analysis of FEF in monkeys and in humans reported attentional and oculomotor deficits (Posner et al., 1984; Pierrot-Deseilligny et al., 1993; De Renzi, 1982). However, in

monkeys surgical ablations of the FEF had little effect on oculomotor behavior when the other hemisphere is preserved.

In humans, a range of saccade, antisaccade and cueing tasks with variations in fixation offsets has been applied to investigate the immediate and the long-lasting effects of FEF lesions. Pierrot-Deseilligny et al., 1993, 1995 found that FEF disengages fixation, and triggers intentional saccades to visible targets and to remembered target locations, or to the location where that target will reappear. The following functions were further reported as impaired: eye movement control, triggering saccades, control of smooth pursuit, and intentional visual exploration (intentional saccades). However, the oculomotor impairments were often transitory and patients recovered fast while chronic functional impairments after FEF lesions were more difficult to trace and required sensitive and accurate measurement methods.

Acute Impairments after FEF Lesions

Acute frontal lesions in humans (probably including FEF) resulted in an ipsilateral eye deviation, which lasted no more than a few hours or days (Tijssen, 1991; Tijssen et al., 1994). During this time, contralateral eye movements (saccades, smooth pursuit, visual orientation reflex (VOR)) were reported to be present but being performed with difficulty. Further, acute lesions of FEF in humans influenced saccade triggering by increasing contralesional saccade latency for left and right FEF (Rivaud et al., 1994; Gaymard et al., 1995, 1998, 1999; Milea et al., 2002). This was the case for the overlap task during which the fixation point is still displayed when the lateral target appears.

Chronic Impairments after FEF Lesions

All saccades (intentional and reflexive) were reported to be hypometric to the contralateral side of the lesion in chronic FEF patients. Machado and Rafal (2004a,b,c) found that some patients showed errors in the form of reflexive glances towards contralesional targets and the presence of a fixation point inhibited the initiation of ipsilesionally directed saccades. Rafal (2006) concluded that FEF lesions result in disinhibition of reflexive saccades towards the contralesional field and an impairment of reflexive saccades towards the ipsilesional field. Also patients with chronic unilateral FEF lesions showed a reduced effect of a fixation point on saccade latency to contralesional targets; and strategic modulation of this effect was

compromised for saccades to ipsilesional targets (Rafal et al., 2002). In an anti-saccade paradigm Machado and Rafal (2004c) found that a fixation point inhibited the initiation of contralesionally directed saccades less than those directed ipsilesionally, thus the inhibition effect of a fixation point was deficient for the contralesional side in FEF patients. Saccade preparation in response to a cue (top-down or reflexive) did not reduce the inhibitory effect of a fixation point on initializing anti-saccades to either of the hemifields.

Top-down and stimulus-driven modulation on spatial orientation has been tested in patients with chronic FEF lesions mainly in oculomotor behaviour. Saccadic initiation deficits were reported in FEF patients to the contralateral hemifield for goal-directed orienting while benefits with reflexively summoned saccades were found to the ipsilesional hemifield (Henik et al., 1994). However, as investigated via reaction times (RT's) and saccadic latencies no effects with covert attention to targets placed in further periphery were reported (Henik et al., 1994). However, in those studies attentional effects were tested in conjunction with oculomotor behaviour measuring RT's or saccadic latencies but not perceptual thresholds of visual targets appearing in the periphery. Thus overall, voluntary control of fixation and saccades has been found to be compromised in FEF patients, but the perceptual, attentional and oculomotor impacts have not been entirely disentangled.

1.7 THE PULVINAR

1.7.1 Localization

The pulvinar is a grey matter nucleus belonging to the thalamic nuclei complex which is placed subcortically and therefore is well positioned to regulate cortico-cortical transmission as a hub (Fig.14a/b). The pulvinar is placed just above the LGN but it is perhaps up to 5 times bigger than the LGN. It shows fine grain structure and none of magno and parvocellular layers as the LGN does. In humans, the pulvinar has been found to consist of a large mass of nuclei forming the most caudal portion of the thalamus (the dorsal thalamus), overhanging the geniculate bodies and the dorsolateral surface of the midbrain (Fig.14a/b). The pulvianr itself is a complex structure found to be divided in at least four subareas. In humans it has

been subdivided into medial, lateral, inferior, and anterior nuclei which have also been divided in terms of their functions.

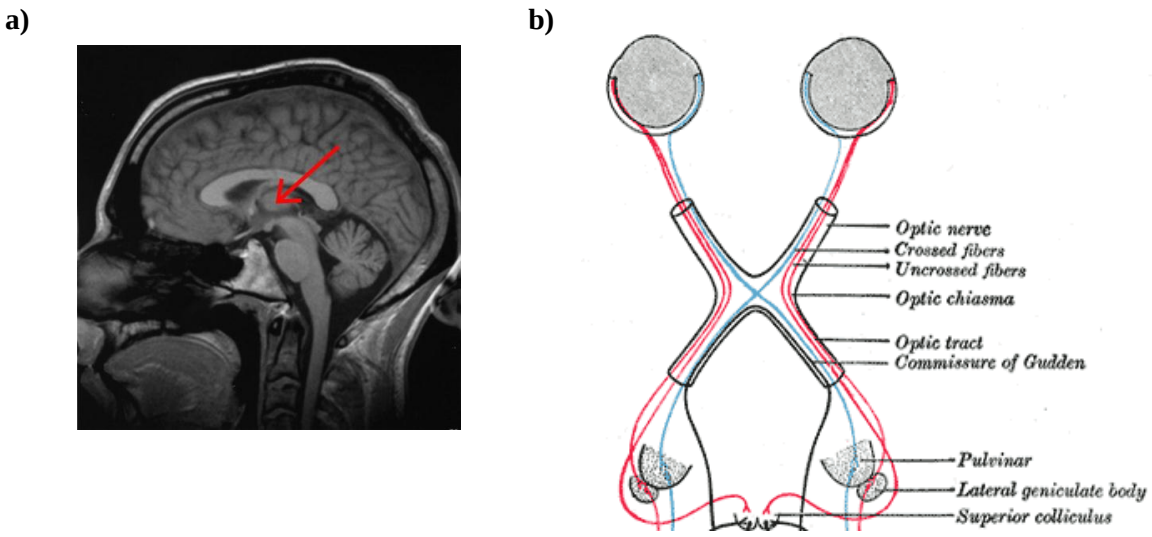


Figure 14. Pulvinar's central position (a) Midsagittal view of the human thalamus where pulvinar is placed **(b)** Optic chiasma and nerves with location of pulvinar nucleus. The pulvinar nuclei are part of the subcortical structure called thalamus and lie posterior, medial and dorsal to the laterale geniculate nucleus, and cover the underlying superior colliculus (SC). They form a big and diffuse mass around the axonal tract that arises from SC, the brachium of the SC.

1.7.2 Subdivisions and Connectivity

The very first anatomical studies of the pulvinar have been conducted in the macaque monkey of which the pulvinar has been divided on the basis of cytoarchitectonic criteria into four parts: the lateral, medial, inferior, and oral pulvinar nuclei. The lateral and inferior nuclei have been found to be retinotopically organized (Bender, 1981a,b, 1982). Also anatomical studies in mammals revealed that the pulvinar receives inputs from subdivisions of visual cortex and back projects to these (Chalupa et al., 1972; Romanski et al., 1997; Casanova et al., 2001; Guillery and Sherman, 2002a/b; Sherman and Guillery, 2002; Shipp et al., 1998; Shipp, 2001, 2003, 2004; Sherman, 2005; Kaas and Lyon, 2007) via long-range interneurons, while visuo-somatomotor connections via the pulvinar have been suggested a long time ago (Shipp et al., 1995; Shipp and Zeki, 1998).

Recent anatomical studies in monkeys indicate that the pulvinar anatomy reflects the topography of the cortices and is subdivided according to its connections, dividing the pulvinar into several distinct maps (Shipp et al., 2003). Each pulvinar subdivision has been found to have a distinctive pattern of reciprocal projections with multiple cortical areas. For the inferior and lateral pulvinar restricted anatomical connections have been found, in contrast to the wider connections of the medial pulvinar (Weller et al., 2002). Additionally, the pulvinar has been found to be connected with many non-visual areas (Chalupa et al., 1972; Romanski et al., 1997; Casanova et al., 2001; Guillery and Sherman, 2002a/b; Shipp, 2003, 2004).

Similarly, the human pulvinar has been found to be interconnected with various subcortical structures and with a wide range of brain regions involved in visual and attentional processing such as V1, V2, visual inferotemporal areas (area 20), posterior parietal association areas (area 7), frontal eye fields (FEF) and prefrontal brain areas (Leh et al., 2007). In accordance with suggested connectivity-based anatomy in monkey pulvinar (Shipp, 2003), damage to different parts of the human pulvinar has been found to produce deficits similar to the areas to which they are connected (Ward et al., 2002; Ward and Arend, 2007).

1.7.3 Functions

Non-human studies have provided convincing evidence for major contributions of the pulvinar to visual processing, spatial visual attention, and oculomotor behavior (Petersen and Robinson, 1986; Robinson et al., 1990; 1992, 1993, Shipp, 2004; Grieve et al., 2000).

1.7.3.1 Visual Processing

Pulvinar neurons in monkeys have been found to respond selectively to a number of visual stimulus features, including colour, orientation, or motion (Petersen and Robinson, 1985). Anatomical tracer and electrophysiological animal studies on cortico-pulvinar circuits suggest an important role in visual spatial attention, visual integration (Shipp, 2004) and higher-order visual processing (Villeneuve, 2005). There is growing evidence supporting the view that inferior and lateral pulvinar nuclei are retinotopically organized in monkeys (Stepniewska and Kaas, 1997; Adams et al., 2000; Lyon and Kaas, 2007). Accordingly, the inferior and lateral nuclei have been found to be involved in visual salience processing (Robinson and

Peterson, 1992; Grieve et al., 2000). Further divisions have been reported in the inferior pulvinar in squirrel monkeys, macaque monkeys, and in marmosets (Stepniewska et al., 2000). Studies have shown divisions in the inferior pulvinar to be separated functionally into subsets creating subcortical components of the dorsal stream (Ungerleider and Mishkin, 1982) and subsets which were more devoted to the ventral stream processing (Adams et al., 2000; Gutierrez et al., 2000; Kaas and Lyon, 2007; Saalmann and Kastner, 2009).

1.7.3.2 Oculomotor Functions

Some pulvinar cells were found to show enhanced responses to visual stimuli which are targets of eye movements and when the eyes are moved towards or away from the stimulus (Wurtz et al., 1980; Wurtz and Albano, 1980). This kind of response pattern is called eye-movement dependent but spatially non-selective and is associated with "the role of signalling changes in state when stimuli take on relevance as targets for particular movements" (Robinson and Petersen, 1992). Other pulvinar cells were found to respond following the eye movements, and about 30% of cells were seen with eye movements in total darkness (Robinson et al., 1986; Petersen and Robinson, 1987; Robinson et al., 1990, Robinson et al., 1993). It was proposed that this might be interpreted as the cells are "signalling the act of shifting the image of an object to the fovea or the beginning of a new visual scene" (Robinson and Petersen, 1992).

1.7.3.3 Visuospatial Attention

The enhancement of response of the pulvinar cells to a stimulus has been seen shortly before saccadic eye movements towards a visual target or during attention to a peripheral stimulus (covert attention) (Petersen et al., 1987). Furthermore, most cells in the pulvinar were found to be responsive to a wide range of stimulus movement during periods of fixation and also during total darkness. However, when the eye movement was made, those cells did not respond during exploration of the stimulus to which the receptive field was shifted. It has been suggested, that the pulvinar cells' properties enable suppression and therefore increase salience of visual signals. Davidson and Bender, 1991 have shown that at certain eye positions visual excitability of cells are blocked while allowing for higher excitability to stimuli in the surrounding visual field. These pulvinar cells have been proposed to be activated by a non-visual input, an extraretinal signal (coming from the superior colliculus

(Benevento and Fallon, 1975) that were assumed to prevent these pulvinar cells from responding to visual input during eye movements.

1.7.3.4 Top-Down versus Bottom-up Attentional Control

It has been shown that the visual characteristics of the pulvinar cells might depend more on the input from the striate cortex. More recently, Wilke et al., 2011 found that monkeys with pulvinar damage were severely disrupted in their visually guided behaviour contralaterally in functions such as spontaneous visual exploration and saccades into the ipsilesional field, which had abnormally short latencies and tended to overshoot their mark.

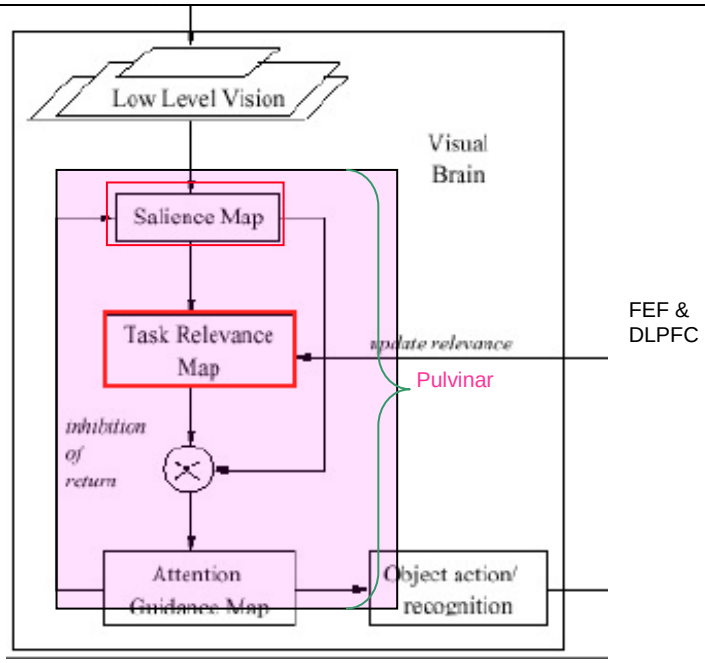


Figure 15. A modified model of interacting saliency and top-down control on visuospatial processing (Iitti et al., 1998). The pink square encompasses saliency and task relevance maps which converge in the pulvinar in the form of attentional guidance maps. Top-down signals creating task relevance maps are assumed to originate from DLPFC and FEF, while saliency maps are assumed to be created from signals in the visual cortex.

Based on these findings the role of the pulvinar in visual attention has been suggested in the form of "saliency map" formed from top-down and bottom-up processes (Koch and Ullman, 1985; Iitti and Koch, 2000, 2001; Iitti et al., 2000) (Fig.15), which determine the location and

spatial scale for the next attentional shift, followed by activation of parietal and inferotemporal areas, in dorsal and ventral streams respectively. The pulvinar has been found to be anatomically separated for dorsal and ventral visual processing paths (Kaas et al., 2007) and it has been suggested that the ventral pulvinar would mediate involuntary attentional shifts only while the dorsal mediates voluntary attentional shifts (Van Essen, 2005).

1.7.3.5 Evidence from Patients with Pulvinar Damage and Neuroimaging Data

Functions

Data from patients with subcortical lesions suggest pulvinar involvement in attentional orientation to visual stimuli (Danziger et al., 2001; Ward et al., 2002; Ward and Arend, 2007; Arend et al., 2008), in visual attention processing like attentional engagement (Rafal and Posner, 1987), visual filtering (Danziger et al., 2001; LaBerge and Buchsbaum, 1990; Snow et al., 2009), feature binding (Ward et al., 2002) and the analysis of target surround (Michael and Desmedt, 2004). Patient data also suggest that the pulvinar might be contralaterally organized, as contralesional deficits were reported in visual and attentional processing (Rafal and Posner, 1987; Snow et al., 2009; Arend et al., 2008) and more recently this has been supported by neuroimaging studies (Cotton and Smith, 2007; Smith et al., 2009; Kastner et al., 2004). Further lines of evidence indicate that the pulvinar is part of a distributed network subserving visuospatial attention (Desimone et al., 1990; Kastner and Ungerleider, 2000). Second, patients with lesions in the pulvinar exhibit visuospatial hemineglect, impairment in directing attention to the contralateral hemifield (Karnath et al., 2002; Rafal and Posner, 1987). The lesion sites of neglect patients have been located in the dorsomedial pulvinar (Kastner, 2004).

Functional Subdivisions

Studies in patients with pulvinar lesions reported functional dissociations between anterior and posterior areas of the pulvinar (Arend and Ward, 2008). The medial and posterior maps were suggested to be involved in both the temporal and the spatial aspects of perceptual tasks. Lesions of the anterior parts of the pulvinar in humans have revealed spatial deficits only (Rafal and Posner, 1987; Arend et al., 2008; Snow et al., 2009). The anterior maps were suggested to be connected to visual areas, and to be organized spatially and retinotopically.

The anterior parts of the human pulvinar therefore seem to correspond functionally to the inferior and lateral pulvinar in monkeys while the posterior parts seem to show features of the medial and posterior medial parts of the monkey pulvinar (Fig.16). However, the correspondence of the functional areas has not been fully confirmed yet.

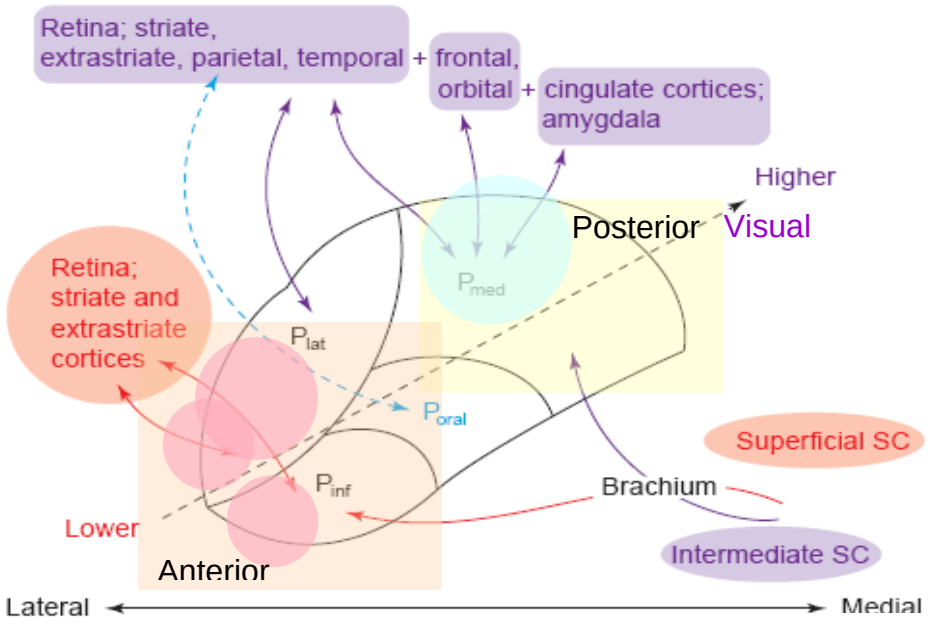


Figure 16. A modified schema of divisions and connections in monkey pulvinar (Grieve et al., 2000). Pink circles: retinotopic maps found in monkey's lateral and inferior pulvinar. Blue circle: visuospatial maps found in medial pulvinar (Pmed) in monkey. The light pink square and the yellow square are superimposed on the schema of monkey pulvinar and indicate human pulvinar divisions of similar functions.

Conclusion about Pulvinar Functions

In sum, due to its central position the pulvinar has been suggested to facilitate cortico-cortical communication in the form of a sensory gating system, providing a nexus where activity of one area can modulate activity of another one (Arend et al. 2008; Guillery and Sherman, 2002; Sherman and Guillery, 2002; Shipp, 2003, 2004). It is believed to mediate and/or drive the integration of visual information flexibly and reciprocally (Logothetis et al., 2010;

Berman and Wurtz, 2008, 2010, 2011). But currently, the data about the pulvinar in monkeys is very rich compared with the knowledge of functions and divisions of the pulvinar in humans.

1.8 METHODOLOGICAL ISSUES CONCERNING TMS AND PATIENT STUDIES.

1.8.1 Human Lesion Studies

This thesis will investigate patients with brain damage as a convergent technique to TMS for providing insights on the roles of FEF and pulvinar for cpd in low-level visual processing. A brief introduction to the relative merits and problems with each technique is given below.

1.8.1.1 Why are Real Lesion Studies in Humans still relevant today?

Patient studies have played a critical role in understanding the neural mechanisms regulating human behavior. Before the onset of non-invasive and in-vivo brain imaging methods the only way to access functions in the human brain was through examination of patients with brain injuries, combined with postmortem studies of their brain tissue (Harlow, 1848; Wernicke, 1874; Broca, 1861; Scoville and Milner, 1957; Sperry et al., 1961; Zeki et al., 1993).

Today, there is still a high demand for precise assessment and prediction of functions in patients after brain damage. The numbers of brain-injured patients is high due to demographic (stroke, dementia) and technical (accidents) developments. Lesion–function or lesion-behavior mapping studies can help in both directions (a) making predictions for patients with acute and chronic lesions after brain injuries and (b) to infer from their functional impairments about localization of functions and neural networks. The critical impact of patient studies can be seen in many established theories of brain processing such as the two-visual-pathways model (Ungerleider and Mishkin, 1982) (and its redefinition into what and how pathways model by Milner and Goodale, 1992, which will be explained in later paragraphs).

1.8.1.2 Disadvantages of Brain Lesion Studies in Humans

Nonetheless, patient studies are vulnerable to misinterpretation and require precise methods and statistical validation for reliable brain-function mapping. For instance, there is a considerable amount of flexibility and plasticity in the brain, so that different areas can change their functions in response to damage in another area. It is also known that many brain functions are carried out in a distributed manner, with large portions of the brain working together rather than each region having a fixed function (Corbetta et al., 2000). Furthermore, focal lesions in the human brain are rare. Extensive and multifocal lesions are the case after stroke or accidents at present. It is then difficult to localize the necessary node for functional impairments shown by patients. Further, it is often difficult to know whether impairment is due to grey matter lesions, or damage to white matter tracts passing through the damaged area. In addition, it is crucial to make the distinction between chronic and acute lesions, as there is considerable plasticity and reorganization in the brain, which can change the functional impairments over time – usually, but not always to a better behavioral/ functional outcome.

1.8.1.3 Novel Approaches to Lesion Studies in Humans

Recently, techniques of lesion analysis have become statistically more accurate and are improving constantly (Rorden et al., 2000, 2007, 2009; Rorden and Karnath, 2004). There are techniques to group all patients with the same functional impairment and analyze their lesion overlaps (Kartesz et al., 1979). Another novel approach provides comparison with a control group of healthy people or of other brain-damaged people (Roden and Brett, 2000; Price and Friston, 2002; Bates et al., 2003; Mort et al., 2003). Such statistical methods are promising but require a high number of patients and therefore their application is out of scope of the work presented here. Instead, with the very few patients available the most sensitive and precise method, a psychophysical thresholds measurement, has been successfully applied to capture otherwise elusive functional impairments.

1.8.2 Transcranial Magnetic Stimulation (TMS)

Another approach to test brain functions non-invasively and with relative precision in humans is the so-called “virtual lesion” method of transcranial magnetic stimulation (TMS).

1.8.2.1 What is Transcranial Magnetic Stimulation?

Transcranial magnetic stimulation (TMS) is a non-invasive brain mapping method applied in humans to investigate brain functions in vivo through induction of weak electric currents induced by rapidly changing magnetic fields from a coil placed above the scalp region of interest (Barker, 1991). The TMS stimulation is believed to modulate the neural activity transiently in superficial brain tissue and to reveal the necessity of that brain region for a particular behaviour or cognitive function, suggesting a causal link between them. Therefore, TMS can be understood to test causal links between behavior and the site of activation/stimulation. However, the neurophysiological effects of TMS are not fully understood yet, which leads to difficulties in interpreting TMS results (Pascual-Leone et al., 1999a/b; Walsh and Conwey, 2000; Sack and Linden, 2003).

1.8.2.2 Limitations of TMS

The TMS method deals with several theoretical and methodological issues, which makes the causal interference not less ambiguous from real lesions in patients. Recently, the traditional approach to TMS as "virtual lesion" has been updated (Silvanto and Muggleton, 2007, 2008a,b) and now it is believed that TMS can modulate behaviour in a more subtle and complex way than just simply disrupting it. If TMS stimulation causes signal suppression/ disruption i.e. so-called "virtual lesion" or if TMS stimulation is a facilitator of neural processes as 'subthreshold activation" (Harris et al., 2008) depends on several factors which are described below.

1.8.2.3 "Subthreshold Activation" or "Virtual Lesion"?

Technical Constrains

TMS can be administrated as a single (single-pulse TMS) or as a train of rhythmic pulses at a specified frequency (repetitive TMS (rTMS)). rTMS has been reported to produce effects that last longer than the period of stimulation. Depending on the intensity of stimulation, coil orientation and frequency of stimulation, rTMS can increase or decrease the excitability of corticocortical pathways. Low frequency rTMS was found to produce a transient reduction in

cortical excitability and to produce no substantial effect on cortical inhibition (Fitzgerald et al., 2006). High frequency rTMS above 5Hz was reported to lead to a reduction in cortical inhibition (Fitzgerald et al., 2006). Furthermore, the pattern of facilitation vs. inhibition has been reported to depend on stimulation intensity (Moliadze et al., 2003). Strong stimuli above 50% of maximal stimulator output could also lead to an early suppression of activity during the first 100-200 ms, followed by stronger facilitation.

The Time Point of Stimulation and the Initial Activation State of Neuronal Population

The behavioural effects of TMS have been suggested to depend on the initial activation state of the stimulated brain region and on the time point of TMS application during particular perceptual or cognitive task. While behavioural facilitation was found when single-pulse TMS was applied shortly before the onset of a task (Grosbras and Paus; 2002, 2003), the "virtual lesion" effect was found when TMS was applied during the perceptual and cognitive processes (Fernandez et al., 2002; O'Shea et al., 2004; Cowey, 2005; Muggleton et al., 2010). This has been explained as follows: when TMS is applied before the onset of a process it is suggested that all activity in differently tuned neural populations is at a baseline and so there is no difference in the activation states between them. Thus, the increase in cortical excitability would lead to a heightened sensitivity to subsequent sensory stimulation.

On the other hand, when TMS is applied during perceptual or cognitive processes it is believed that an activity imbalance already exists; certain neural populations being activated while others are inactive or even being inhibited. There are indications from studies that TMS might activate the less active (or inhibited) neurons when applied during a perceptual process (Silvanto et al., 2007) resulting in activation of neurons that are not involved in the currently ongoing cognitive or perceptual process (preferential facilitation) (Hotson et al., 1994). This would reduce the signal-to-noise ratio and consequently produce behavioural interference or disruption of the process.

Alternatively, it could be argued that TMS inhibits the activated neurons. However, it was shown that in most neurons TMS induces an initial short period of excitation, which is very likely to cover the duration of a brief perceptual process. It has been found that visual stimuli can be detected within 500ms after presentation (Amano et al., 2006). Thus, TMS has been more often referred to in terms of facilitation than inhibition (Kammer et al., 2005a,b) and

has been found to be followed by a longer lasting (up to a few seconds) period of suppression (Moliadze et al., 2003; Aydin-Abidin et al., 2006). Additionally, inhibition cannot explain a facilitation effect prior to onset of a stimulus (Silvanto and Muggleton, 2007).

On the other hand, the noise increase approach mentioned above has not been supported by a study (Harris et al., 2008), which compared the effects on detection thresholds of Gabor patches after noise induction into the image (image noise) (added noise paradigm, Pelli and Farell, 1999) or noise induction with the TMS stimulation (phosphenes induction) on occipital regions. Both procedures were found to increase perceptual thresholds for orientation discrimination (impair the perceptual process). TMS interacted in a multiplicative manner with the image noise induction and was interpreted not to occur independently, resulting in interruption of the neural process as shown by loss of signal strength. Thus, TMS was found not to add noise but to interrupt the neural process. In the study reporting such results the TMS pulse was applied on each trial after the presentation of the stimulus.

Conclusions

In summary, the initially promoted concept of TMS as a tool for inducing reversible "virtual lesions" seems to be out of date while more complex patterns of TMS effects have been shown to depend on several factors. Therefore, it is useful to validate the TMS method with real lesions in patients, which is the approach taken with in the experiments described in chapters 2-5.

1.9 SENSORIMOTOR PROCESSES

1.9.1 Introduction

The second part of the thesis is concerned with centre-periphery difference in sensorimotor processes. It investigates the proposal that "vision did not begin as a system for perceiving the world, but as a system for the distal control of movement" (Goodale, 1983).

1.9.1.1 What are Sensorimotor Processes?

Sensorimotor processes are understood as "pertaining to, or having both sensory and motor functions or refer to motor activity caused by sensory stimuli" (http://www.definitions). The term sensory refers here to visual processing and sensorimotor processes are synonymous to visuo-motor processes.

1.9.1.2 Role of Vision in Motor Processing

Goodale, 1988 and later Sparks and May, 1990 proposed that the modularity and functional specialization of the visual system in the brain, which has initially been described from the point of visual input i.e. from the view of "vision-for-perception", should be based on output requirements in the form of motor responses to visual objects – that is: "vision-for-action". In particular that view has been accepted for automatic saccadic eye movements (Sparks and May, 1990), but this idea goes beyond oculomotor functions. Accordingly, in a recent review Goodale, 2008 stated that in the 1970's and 1980's vision was identified with visual perception only – and its direct role in the control of movement was essentially ignored". Today the broader perspective is that "the functional organization of the visual system ("like the rest of the brain") has been shaped by its functional role for control of movement" (Goodale, 2008) seems more justified.

1.9.1.3 The "vision-for-action" Model

In the "vision-for-action" model of visual processing the ventral stream (Ungerleider and Mishkin, 1982) remained as the "what" pathway for object perception. However, the dorsal pathway has been redefined by Goodale and Milner in 1992, from the "where" pathway to the "how" pathway i.e. how to act (or react) to an object. Interestingly, although this model is mainly based on monkey studies (Goodale and Milner, 1992), the first indications for functional separation of the visual streams for object recognition versus motor response to objects emerged from patient studies. Damage to the temporal cortex has been found to result in visual agnosia (Goodale et al., 1993) the inability to consciously recognize or name the object. Damage to the parietal cortex (belongs to the dorsal stream) has been reported to result in apraxia, inability to know the function or how to use an object. More recently, however it is assumed that both systems are often simultaneously and in parallel activated

providing visual experience during skilled actions (Goodale and Milner, 1992) and studies indicate that there is reasonable crosstalk between both pathways (Wolfensteller et al., 2004).

1.9.1.4 Visual Consciousness in Visuo-Motor Processing

Conscious Visual Processing Route

The visual system has traditionally been divided into the conscious and subconscious pathways of processing. Data from patient studies suggest that the two cortical pathways for vision (ventral and dorsal) might differ in respect to access to consciousness. Information in the dorsal system (especially signals originating in the retinal periphery) can be processed without reaching consciousness while perceptual operations performed via the ventral system (especially originating in fovea) result in awareness. Goodale and Milner, 1992 suggested that for conscious visual experience the ventral system is necessary to be activated and claimed that processing of subliminal stimuli (stimuli presented below threshold of conscious perception) is evoked through partial or diffused activation of neural assemblies in the ventral system or activity in the dorsal stream.

Conscious Visuo-Motor Processing Route

Traditional models of visuo-motor interactions suggested that visual perception and motor response are discrete stages, activated successively (Sanders et al., 1980). More recent models assume a continuous flow of information from sensory to motor systems, thus making it possible that a motor response is conducted before perceptual analysis is finished, and therefore not necessarily requiring full conscious visual analysis (Coles et al. 1985; Schmid et al., 2007). Studies in monkeys suggest that the visual system mediating conscious visual experience developed much later than the system which controls visuo-motor actions (Goodale, 1993), and therefore it does not need to be a precondition for visuo-motor processing. Also patient data suggest that visuo-motor performance and visuo-motor associations can be build up without conscious visuo-motor processing or conscious procedural memory.

Subconscious Visuo-Motor Control Mechanisms

In addition to conscious cortical motor control systems, Goodale, 2008 proposed that "representational systems have emerged...[ ].. from which internal models of the external world can be constructed". Such representations can exist for visuo-motor associations and can be manipulated via a number of control mechanisms in the conscious and subconscious level. One such cortical control mechanism is automatic motor inhibition (DeJong et al., 1990).

1.9.1.5 Visuo-Motor Links as revealed by Subliminal Visual Primes

Neumann (1993) suggested that subliminal motor response activation can indicate the existence of direct perceptuo-motor links, which allow the perceptual system to affect the motor system without conscious experience of that process. Accordingly, it has been shown that stimuli presented near or below the threshold of conscious awareness (subliminal stimuli) can trigger activation of motor responses and are referred to as subliminal primes (Neumann et al., 1993; Neuman and Klotz, 1994; Dehaene et al., 1998; Klotz and Neumann, 1999; Klotz and Wolf, 1995).

What are Subliminal Primes?

Subliminal primes are stimuli and cues (visual or auditory) below a threshold of conscious perception, which are associated with a certain behavioral outcome or motor response, which they can trigger.

Masked Prime Paradigm

The common method to obtain an invisible or visually subliminal prime is the "masked prime paradigm". A briefly presented prime stimulus (prime) is immediately followed by another visual stimulus (mask) before the target follows. This method renders the first stimulus invisible to the observer, thus below the threshold of conscious visual perception (Daheane et al., 1999, Neumann and Klotz, 1994).

Priming Effects

Subconscious primes can reveal performance benefits in the form of faster reaction times (RT's) and lower error rates (ER's) when the associated responses in the prime and in the target are identical or compatible. This pattern of benefits to compatible prime and target are usually referred to as a "*Positive Compatibility Effect*" (PCE). When the prime is associated with a contrary response than the target stimulus, e.g. prime and target were incompatible, performance costs in the form of slower RT's and higher ER's have been observed. This pattern of compatibility effects described is usually reported at short mask-target stimulus onset asynchrony, SOA, (0-100ms) when presented foveally (Schlaghecken et al., 1998).

Negative Compatibility Effects

A reversed pattern of priming effects has been observed more recently when delaying the time point of target display i.e. at longer mask-target stimulus onset asynchrony (SOA) (Eimer and Schlaghecken et al., 1998; Eimer, 1990). For SOA of around 150 ms the priming effect reverses polarity, producing a negative compatibility effect (NCE) for compatible prime-target associations when presented in the fovea. Fig.17a/b/c illustrates the paradigms tested in previous studies on NCE and Fig. 18 demonstrates PCE at short SOA's and NCE at long SOA's.

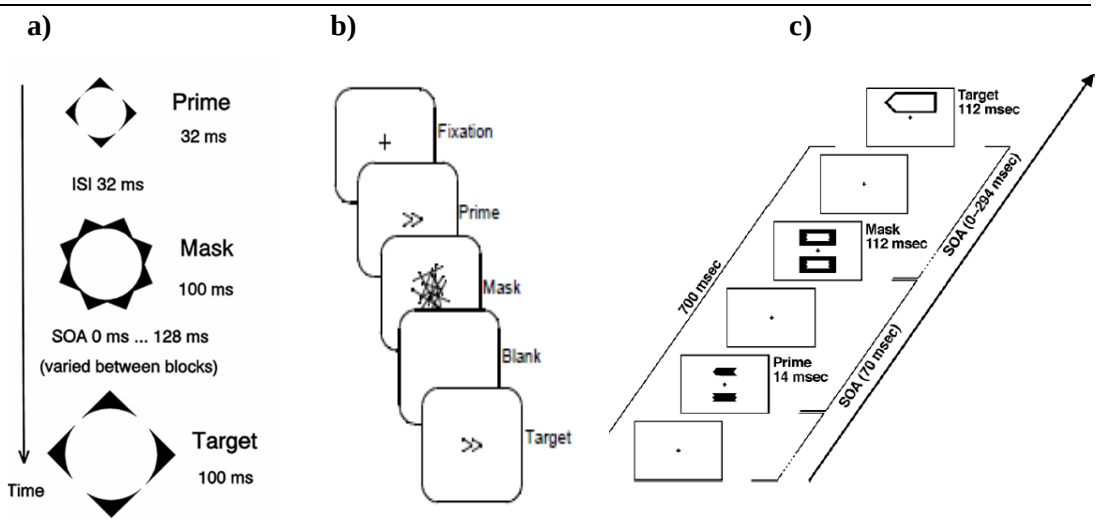


Figure 17a/b/c. Masked priming paradigms showing stimuli and timing parameter used to test NCE. a) Schlaghecken and Eimer, 1998; b) Sumner et al., 2008; c) Lingnau and Vorberg, 2005.

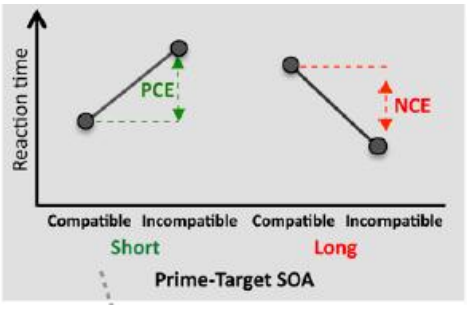


Figure 18. The reversal of priming effects as shown with long or short prime-target SOA's for compatible prime-target and incompatible prime-target trials (modified from Boy et al., 2008). Positive Compatibility Effects (PCE) indicated in green. Negative Compatibility Effects (NCE) indicated in red.

Negative Compability Effects indicate Inhibitory Motor Control Mechanism

While the PCE has been explained by subliminal sensorimotor facilitation i.e. motor activation triggered by primes, the NCE has been explained by motor inhibition in the form of active suppression of primes' firstly triggered activation. This results in faster response on incompatible trials as compared to compatible trials (the NCE). The activation of the alternative response is simply allowed as a longer SOA allows for neural processes for activation and inhibition of the irrelevant prime to take place. Thus, the pattern of activation followed by inhibition suggests an automatic, self-generated inhibitory motor control process involved in sensorimotor processes (De Jong et al., 1990, 1995; Eimer, 1994, 1995).

Localization of the Motor Processes indicated by Negative Compatibility Effects

NCE was tracked down in a distinctive form of lateralized readiness potential (LRP) in the motor cortex in humans by Eimer and Schlaghecken (1998, 1999, 2003) (Fig.19). Sumner et al., 2008 found that a patient with a focal lesion in the supplementary motor area (SMA) did not show NCE as tested at fixation. Therefore, it is very likely that the SMA is highly involved in programming and control of visuo-motor links and perhaps in the generation of inhibitory motor control (Fig.20).

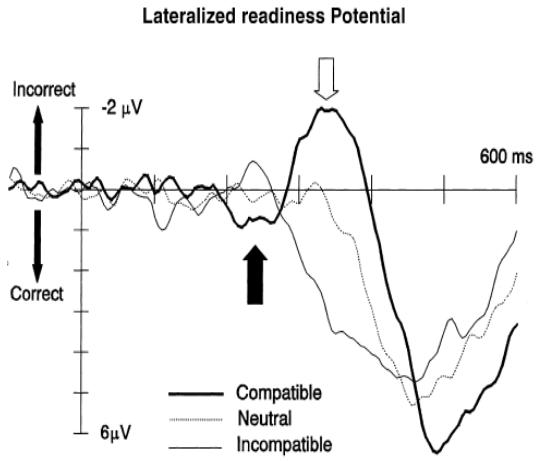


Figure 19. Lateralized readiness potentials measured in an experiment (Eimer and Schlaghecken, 1998). LRP waveforms obtained in compatible, neutral, and incompatible trials in the time interval between prime onset and 600ms after prime onset. Downward going (positive) deflections indicate activation of the incorrect response. The black arrow indicates the time interval where the initial response activation was observed; the white arrow indicates the subsequent reversal of this effect.

Two further studies have also implicated the SMA: Boy et al., 2010a found that the BOLD signal in SMA was modulated during the masked prime paradigm, while Boy et al., 2010b found that the NCE correlated across individuals with the concentration of GABA in the SMA, as measured by magnetic resonance spectroscopy.

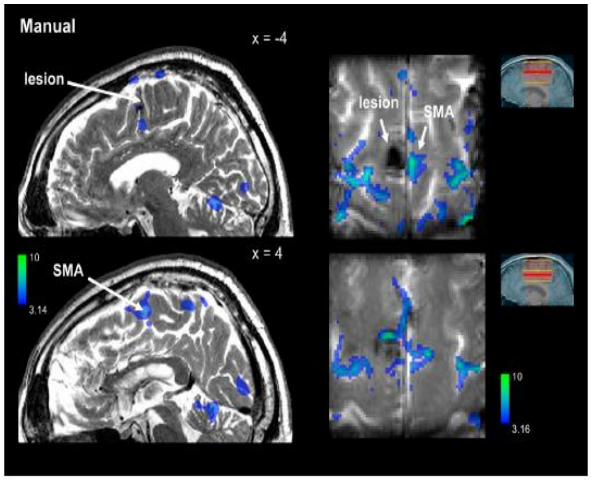


Figure 20. Functional Localization of the Lesion in the pre-SMA in a patient who did not show NCE (Brain imaging data from Sumner et al., 2008).

1.9.1.6 Centre-periphery Difference in Sensorimotor Processing

Sensorimotor Processing in Fovea and Periphery

The functional separation of streams in perception and action has been proposed to start at the very early level of visual processing starting with the retina. The fovea is known to process detailed visual input facilitating conscious inspection and perception, while the same visual stimuli presented peripherally can easily evoke saccades and attentional shifts to facilitate further foveal processing. However, visual processing in the periphery requires stronger visual stimuli to be recognized or to evoke active motor responses such as adequate manual action towards an object (Schlaghecken and Eimer, 2000, 2006). Consequently, links between perception and motor action might differ for fovea and periphery fundamentally. Accordingly, qualitative functional division for peripheral versus foveal processing of visuo-motor associations has been proposed as mentioned earlier (Ungerleider and Mishkin, 1982; Goodale and Milner, 1992).

NCE shows Centre-Periphery Difference

NCEs at fixation have been replicated in many studies (Eimer, 2000, 2001, 2002, Vorberg, 2000; Klapp and Hinkley, 2002; Klapp, 2005).

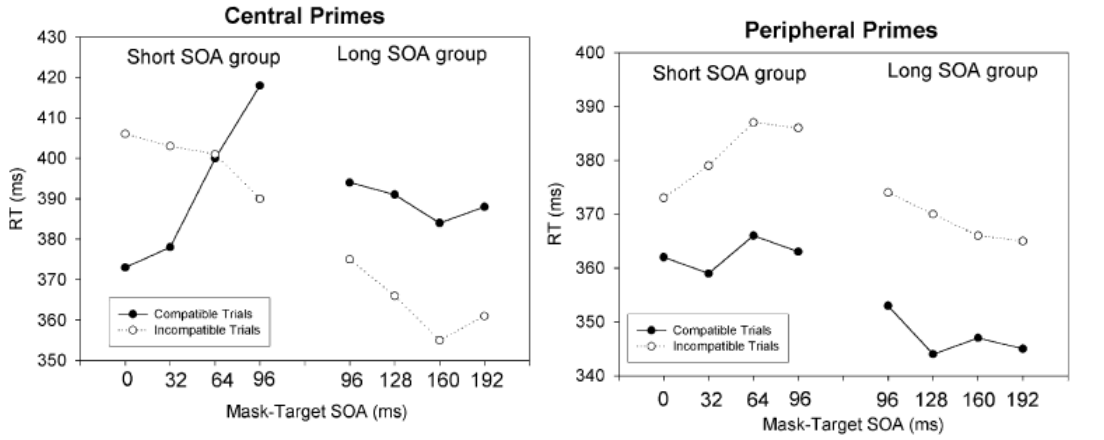


Figure 21. Mean reaction times (RTs) observed in compatible and incompatible trials for different mask- target SOAs. Left panel: Results obtained for central masked primes. Right panel: Results obtained for peripheral masked primes. (Data from Schlagecken and Eimer (2000), Exp.1).

However, when the same primes were presented to the near periphery (peripheral primes) at 2.8 ° above or below fixation – initially no NCE's were reported (Schlaghecken and Eimer, 1997; 2000; 2003) for any type of response, including manual, saccadic eye movements or vocal responses (Eimer and Schlaghecken, 2001) (Fig.21). With masked primes at increasing retinal eccentricity, the NCE gradually turned into a PCE. This effect has been called the "*centre-periphery asymmetry*" referred to as "centre-periphery difference in priming" (cpdp) (Schlaghecken and Eimer, 2000) (Fig.21). Electrophysiological recordings in motor cortex revealed distinctive modulation of LRP waveforms for periphery and fovea. With longer SOA's the activation-inhibition pattern occurred with foveal primes but only activation with peripheral primes (Eimer and Schlaghecken, 2003).

Retinal Sensitivity Threshold Account for Sensorimotor Centre-Periphery Difference

Schlaghecken and Eimer (2000) observed that when foveal primes were reduced in their perceptual strength by random dot noise, no NCE's occurred (Fig.22).

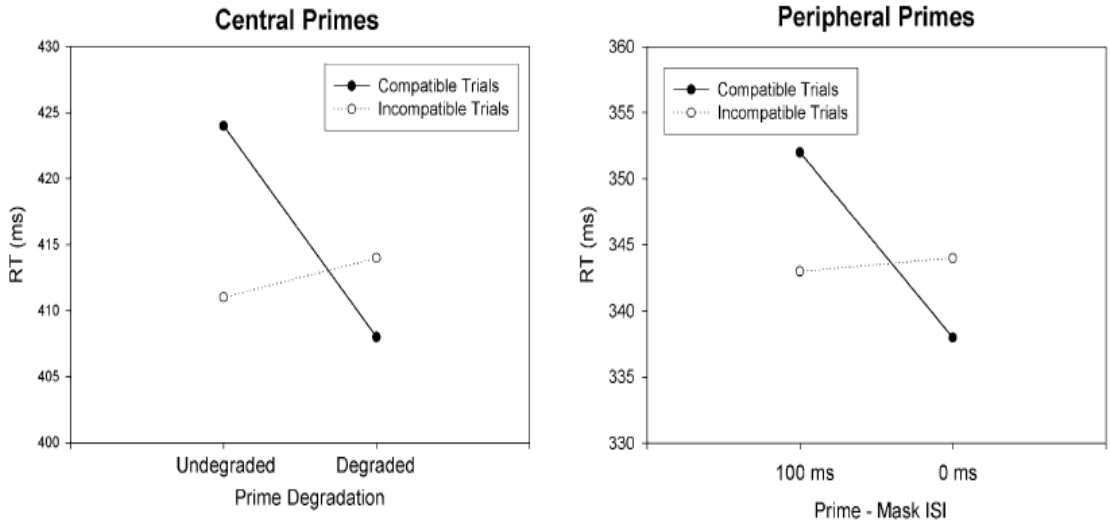


Figure 22. Mean reaction times (RT's) observed in compatible and incompatible trials. Right panel: Results obtained for peripheral masked primes when prime-mask interval was either 100 or 0ms. Note that the shorter interval produces weaker primes. Left panel: Results obtained for undegraded and degraded central masked primes. Data from Schlaghecken and Eimer (2000).

For peripheral retinal locations when perceptual strength of primes was increased by extending the interval between prime and mask, the NCE became evident. This has been interpreted as cpdp being closely linked to the retinal sensitivity decrease with retinal eccentricity and Schlaghecken and Eimer (2000) proposed that NCE occurrence depends on the strength of sensory traces elicited by masked primes.

A second experimental support came from the study of Lingnau and Vorberg (2005) in which they adjusted stimulus size in an attempt to compensate for the cortical magnification factor in visual areas (DeValois and DeValois, 1988; Serano et al., 1995). With larger peripheral stimuli, NCEs were detected (Lingnau and Vorberg, 2005). The paradigm used by Lingnau and Vorberg (2005) has been shown in Fig.17c (see paragraphs above).

Thus, it became accepted that no fundamental cpdp remains when cortical magnification (or perceptual sensitivity) is controlled for (Lingnau and Vorberg, 2005). However, none of these studies provided evidence for NCE at extended retinal eccentricities. More importantly, it has not been tested whether the central and peripheral stimuli were objectively equated in perceptual salience.

Subconscious Visuo-Motor Representations Proposal

Having a subconsciously accessible "module" for visuo-motor association in the form of a neural representation should not require distinctive visuo-motor pathways for fovea and periphery but on the contrary should allow flexible motor responses on an automatic level at any retinal eccentricity. However, the requirement to access a neural representation for a certain visuo-motor link might still differ for fovea and periphery – in the form of sensorimotor strength of the stimulus.

What is Sensorimotor Strength of a Prime?

Sensorimotor strength of a visual stimulus can be defined as its probability to trigger a visuo-motor association and therefore its probability to access visuo-motor representations. Sensorimotor strength can depend on the automatic and unconscious processing power of a visual stimulus. The sensorimotor processing power needs to be high enough to account for visual and motor activation thresholds. Sensorimotor strength is not necessarily the same as

'perceptual strength', as measured by perceptual discrimination or detection tasks, and this distinction will become important when the results to the second part of the thesis are discussed.

"Sensorimotor Time Window" Approach

Adjusted size of primes and increased interstimulus interval (ISI) between prime and mask were important factors for NCE in the periphery (Schlagheacken and Eimer, 2000; Lingnau and Vorberg, 2005). Simultaneously, the time interval between the mask and the target (SOA) has been prolonged which resulted in NCE in para-foveal retinal loci up to 4.4 visual angles. The prime-mask interval was suggested by Lingnau and Vorberg (2005) to present the amount of motor activation until the mask arrives whereas the mask-target SOA would determine the time available for motor inhibition process to develop. However, these two conditions have not been separated in the studies cited above. NCE with prolonged SOA in the periphery suggests that there is a certain "time window" for triggering inhibitory processes, which could differ for periphery and fovea.

Model of Early Motor Control to Explain Sensorimotor Centre-Periphery Difference

Schlaghecken and Eimer (2000, 2002, 2006), Schlaghecken et al., 2003, 2004, 2006, 2007 developed a functional model of early motor control, which is based on two thresholds, which when reached by sensory stimuli should allow the triggering of automatic motor inhibition. Weaker activations from perceptually weak primes remain below hypothetical inhibition threshold. Only a strong sensory trace can result in increased activation that crosses the inhibition threshold (Fig.23). This model explains why NCE do not occur in the periphery. Motor tendencies triggered by foveal primes are stronger than motor tendencies elicited by peripheral primes (Eimer and Schlaghecken, 2000).

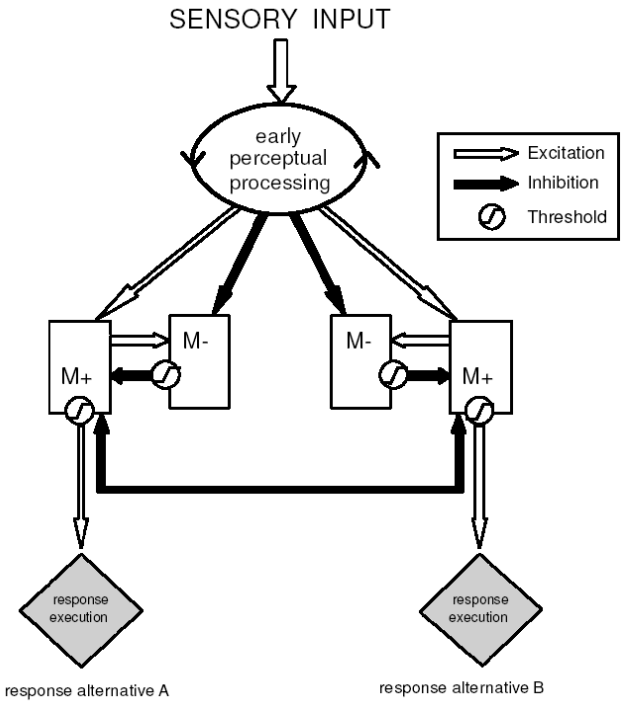


Figure 23 demonstrates the model, which consists of an early sensory processing subsystem, a motor control subsystem and a response execution stage. In the motor control system activation (M+) and inhibition (M-) modules are assumed to receive a common input specific for their acting direction (- or +) from the early perceptual processing stage. The modules are interconnected in an asymmetric activation/inhibition loop; i.e. M+ is assumed to activate M- continuously, while M- was proposed to inhibit M+ only if the activation level (from M+) exceeded a criterion value (the inhibition threshold). Execution of an overt motor response would be initiated only if M+ activation exceeded a motor output threshold. An above-threshold activation of M- should be possible only if a strong perceptual input is subsequently masked.

1.9.1.6 Alternative Explanations and Factors for NCE and Cpd in NCE

Shared Visual Features in Prime and Mask

Numerous studies have found that when the mask and prime are sharing the same visual features the priming effects occur more easily (Lleras and Enns, 2004; Verleger et al., 2004; Jaskowski and Przekoracka-Krawczyk, 2005; Jaskowski et al., 2007, 2008; Sumner

et al., 2007). Therfore, perceptual theories have been proposed which might also explain the NCE (Fig. 24).

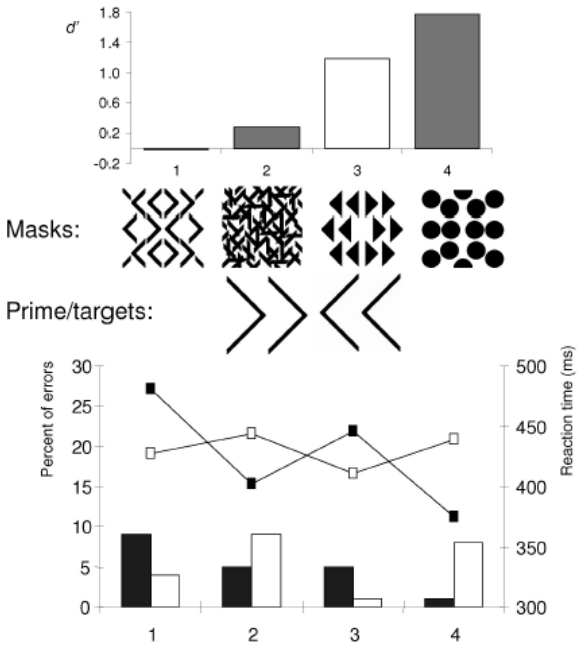


Figure 24 Shared feature hypothesis as tested by Jaskowski and Przekoracka-Krwaczyk (2005), Experiment 1. Upper plot: Stimuli and results: d' for the masks showed. Lower plot: reaction times (lines), and percentages of incorrect responses (bars) for congruent (filled symbols/bars) and incongruent (open symbols/bars) trials for all masks used The masks which did contained recognizable features of the prime did produce NCE (mask 1 and 3) while the masks with no features (mask 4) or less recognizable prime features (mask 2) showed no NCE.

Object Updating Theory

The "object updating" or "mask-induced priming" theory holds that a mask could prime the contrary response to one of the masked stimulus, in particular when there are shared features in the mask and masked stimulus (Verleger and Jaskowski, 2004; Klapp, 2005; Lleras and Enns, 2004, 2006). It is believed that novelty or feature differences are exagerated by the visual system, the features in the mask that are also in the prime may be relatively reduced in salience. Such imbalance in mask feature saliance could trigger response priming in the opposite direction from that expected from the prime, and hence

create NCE. Accordingly, it has been shown that when masks did not share perceptual features of the primes and targets the NCE's disappeared (Lleras and Enns, 2004; Verleger et al., 2004; Jaskowski and Przekoracka-Krawczyk, 2005; Sumner et al., 2007). Thus, the althernative model to inhibition hypothesis has been proposed based on "active mask" which account for NCE's, to which Sumner (2007) refers to as mask-induced priming.

Sumner (2008) investigated the "mask-induced priming" hypothesis by using masks composed of random lines, which were arranged in certain orientations, and primes composed of two lines of certain orientation. It was found that whether the masks included features (orientation) of the primes and targets or not, similar NCE effects were produced. Furthermore, when the masks obtained features (orientation) of one target but not the other, representing the extreme possible case for mask-induced priming, the priming effect produced was small and insufficient to account for the prime-related NCE. Thus mask-induced priming is not an adequate explanation for the NCE, at least for the stimuli employed in that study.

Stimulus-triggered Inhibition Hypothesis

Stimulus-triggered inhibition hypothesis suggests that the inhibition of the prime is triggered by the sudden onset of the mask. In such a case an unconscious "whoops response" occurs to inhibit the present motor activation which does not seem relevant anymore (Jaskowski, 2007; Jaskowski et al., 2008). Thus the role of the mask is not to cause priming, but to trigger the inhibition of previously caused priming. However, the role of stimulus similarity between prime and mask then remains an open question. It has been suggested that inhibition is triggered in particular when the mask contains features that are task relevant.

Boy et al., 2008, had provided evidence for the importance of mask onset recently. A mask is applied, which appears before prime presentation and moved towards the location of the prime to eventually mask it. In this way, no new stimulus appears after the prime and only PCE were found, whereas when the mask was not displayed before prime presentation NCE were found. However, it is important to mention that while mask onset plays a critical role eliciting the NCE (Boy et al., 2008) the direction of motor priming causing the NCE does come from the prime, not the mask.

For the purposes of investigating the cpd in priming, it is not important whether inhibition is triggered by the mask stimulus, or is self-triggered as in the original theory by Eimer and Schaghecken, 1998.

Neural Habituation Model

Note that it is important to distinguish these mask-induced priming theories from theories which suggest purely perceptual or attentional accounts for NCE i.e. perceptual processing of targets might be delayed when they share features with the primes (Bavelier et al., 2000; Huber, 2008; Sohrabi and West, 2009). Huber et al, 2001, 2002; Huber, 2008 suggested a "neural habituation model", which postulates processes similar to adaptation and habituation ("repetition blindness" (Johnston et al. 2002)), whereby the visual system becomes less sensitive to features it just processed which serves the purpose of resolving source confusion (Huber, 2008). Sohrabi and West (2008) proposed in their model that NCE emerges due to an attentional refractory period, which would act to slow the perceptual processing of the target in compatible trials. Repetition blindness has been ruled out by early studies of Schlaghecken and Eimer (2000), but the more sophisticated habituation and source confusion model of Huber deserves attention.

Mask Onset Account

Boy et al., 2008, had provided evidence for the importance of mask onset recently. A mask has been applied, which appeared before prime presentation and moved towards the location of the prime to eventually mask it. In that way, no new stimulus appeared after the prime and here PCE only were found, whereas when the mask was not displayed before prime presentation NCE was found. However, it is important to mention that while mask onset plays a critical role eliciting the NCE (Boy et al., 2008) the direction of motor priming causing the NCE does come from the prime, not the mask.

Training Effects

Previous studies indicated that practice is necessary to obtain robust positive and negative priming effects (Klapp and Hinkley, 2002; Schlaghecken et al., 2007; Sumner, 2008), which implies that it is not a purely sensory phenomenon, but rather one that relies on building sensorimotor associations. However, training effects in priming were not

mentioned in studies in which well established stimulus-response associations such as right-pointing arrows for right button response etc. were applied (Jaskowski and Slosarek, 2007). The development of NCE over the time course of training in subliminal reaction task was described in detail by Boy et al., 2008. Positive priming has been found to be influenced by training when new and arbitrary links between stimulus and responses are learned (Boy and Sumner, 2009). Mirroring the training effect of PCE and NCE has been found to increase over the time course of training (Boy and Sumner, 2009). Most importantly, a switch in the stimulus-response mapping switched the PCE and NCE around, until the new mapping was learnt. This is strong evidence that the effect is sensorimotor, not due to perceptual or attentional habituation. This has not been tested for peripheral primes which might require longer training times with novel S-R associations.

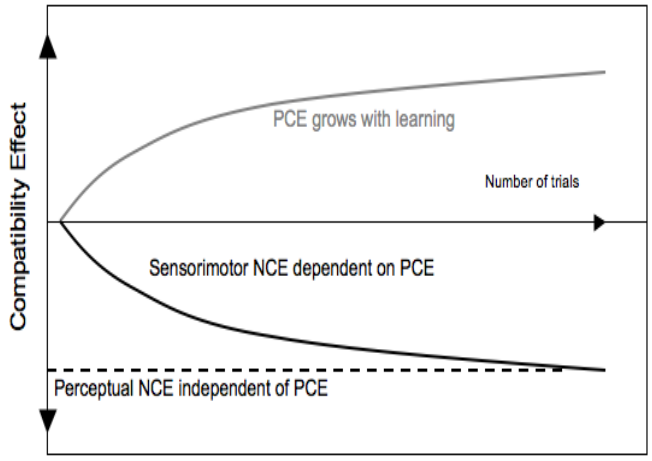


Figure 25 demonstrates the development of PCE and NCE over time with practice. The higher number of trials the higher both priming effects, which in their size mirror each other exactly (Boy and Sumner, 2009).

Attentional Processing

Studies on masked priming showed that focusing attention in time or space can modulate the effectiveness of invisible stimuli (Schlaghecken and Eimer, 2000; Handy et al., 2003; Handy et al., 2005). Focused attention in fovea might facilitate faster and stronger visuo-motor processing, which reaches the activation-inhibition thresholds earlier, while in periphery covert visuospatial attention processing does not. However, Sumner et al., 2006

demonstrated that attention can directly enhance sensorimotor processes and this in a different manner to enhancing perceptual representation or visual salience of stimuli (perceptual strength). In their study, the attentional manipulation did not mimic physical stimulus enhancement. Attentional accounts for NCE were also considered in several other studies (Bavelier et al., 2000; Huber, 2008; Sohrabi and West, 2008). Sohrabi and West (2008) proposed in their model that NCE emerges due to an attentional refractory period, which would act to slow the perceptual processing of the target in compatible trials. However, there was no study, which tested the impact of attentional processing differences for cpdp between fovea and periphery directly. In fact, previous experiments on the cpdp have not always taken attentional effects into account, and these may have contributed to the differences measured. This methodological issue will be discussed in more detail in chapters 6 and 7 which are concerned with cpdp.

CHAPTER 2

EXPERIMENTS 1 and 2

COMPARISON OF PSYCHOMETRIC METHODS FOR CENTRE-PERIPHEY-DIFFERENCE in CONTRAST SENSITIVITY

1. INTRODUCTION

The first experiment introduced in this chapter is the validation experiment conducted to compare two psychophysical methods measuring centre-periphery difference for contrast perception. The second experiment examines the impact of target duration for cpd for contrast perception. The experiments are based on the behavioural study of Ruff et al., 2006, which found that FEF TMS changes the centre – periphery difference in low-level vision at the physiological and behavioural level. The study is described in detail below.

1.1 FEF TMS Study, Ruff et al., 2006 – Description

1.1.1 Methods

Ruff et al., 2006 combined fMRI and TMS of the FEF to test the causal influence of FEF upon remote retinotopic visual cortex as compared with TMS stimulation upon a control area (vertex[1]). Vertex sites are routinely used in the behavioral TMS literature as a control of non-specific, general effects of TMS application (Walsh and Convey, 2000; Walsh and Pascual-Leone, 2005). Frontal TMS was applied over the right posterior middle frontal gyrus, just ventral to the junction of superior frontal sulcus and ascending limb of precentral sulcus in each participant tested. This site has been shown by previous studies to correspond to human

[1] *the vertex site was selected to control for non-specific effects of TMS, such as the 'clicking' sound and tactile sensation associated with TMS application. Vertex was not expected to affect the visual cortex unless in a non-specific way*

FEF (Ro et al., 1999; Grosbras et al., 2002; Grosbras et al., 2003). Figure 26 shows both sites of TMS stimulation and the stimuli sequence applied.

In both fMRI studies (FEF and vertex), TMS was applied in short temporal "gaps" between the acquisition of subsequent MR image volumes. Five TMS pulses of 9 Hz in a repetitive manner (rTMS) were applied in a gap of stimulus presentation. In separate sessions, TMS was administrated to FEF or vertex at four different intensities. Participants viewed a blank display or were presented with stimuli with a coloured or black-and-white checker board pattern which changed their form and colour every 500 ms over the whole visual field. This stimulus was designed to activate many regions of the visual cortex in which the BOLD signal was measured, providing an index of neural population activity (Logothetis, 2002).

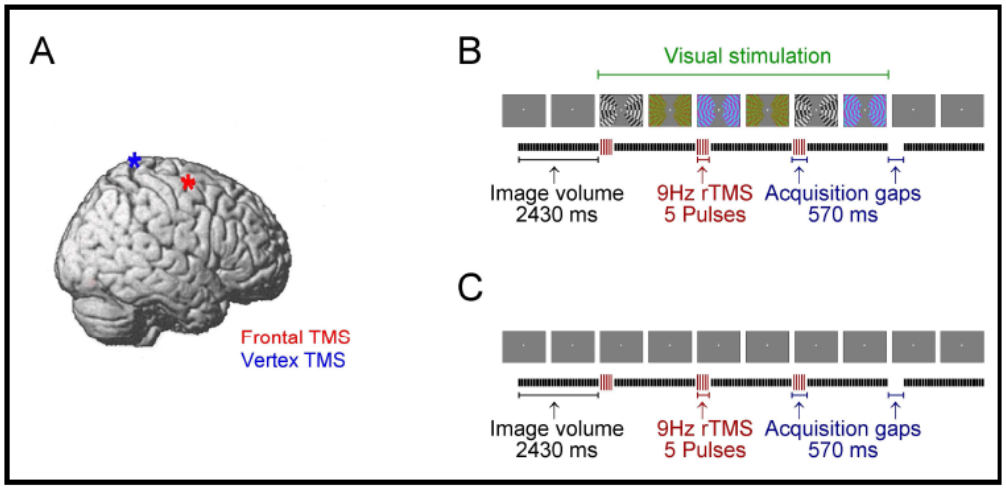


Figure 26. TMS stimulation sites and stimulus presentation sequence in study of Ruff et al., 2006 (modified). a) Red star: right human FEF, blue star: vertex control on a normalized brain template. b) and c) Schematic time course of TMS relative to MR volume acquisition during combined TMS-fMRI: b) Trials with visual stimuli on the screen during TMS. c) Trials without visual stimuli. For each trial, three TMS trains were delivered in the 570 ms gaps between acquisition of subsequent image volumes, and seven rest scans were included between successive trials. Visual stimuli (when present, as in b) remained visible during all three TMS trains and during the acquisition of the three image volumes following the TMS trains.

1.1.2 Results

Retinotopic Activation in Visual Brain Areas

Ruff et al., 2006 found that with increasing TMS intensity the activity change arose in occipital areas in a top-down manner regardless of visual input. TMS to vertex did not produce such increasing activity effects. Fig.27a/b/c/d shows activity maps for different eccentricities of visual areas as modulated by TMS.

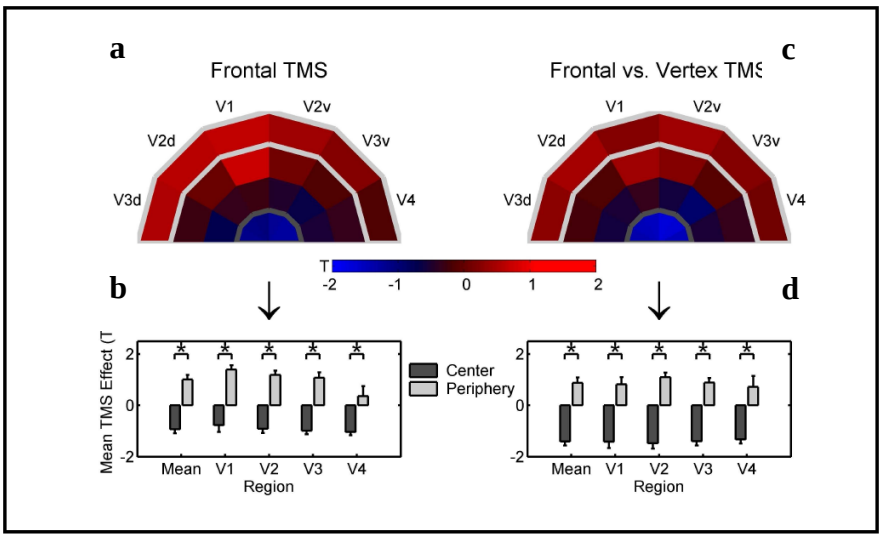


Figure 27a/b/c/d Mean effects of FEF-TMS intensity for different eccentricity sectors in the retinotopic visual areas. (a-d) The correlation of TMS-intensity with BOLD (quantified as T-value) was extracted from each individual retinotopic flatmap, separately for four different eccentricity sectors in each region. a) Shows the mean effect of frontal TMS-intensity for each area and eccentricity sector, averaged across flatmaps and voxels within each sector. The effects are colour-coded according to the scale below. c) indicates that increased intensity of frontal TMS produced activity increases for peripheral visual field representations in V1-V4, but activity decreases in the most central eccentricity sector. (b) and (d) plot the corresponding mean. TMS-induced effect with its standard error b) for frontal TMS; d) for frontal-minus-vertex difference for the most central and the most peripheral eccentricity sectors, when averaged across visual areas (leftmost two bars) or separately for area V1 through to V4 (pooling across dorsal and ventral subdivisions). In all these retinotopic visual areas, increased frontal TMS-intensity produced activity increases for the peripheral sector but activity decreases for the central sector (stars indicate $p < .05$ in paired t-tests).

Parallel with increasing intensity of FEF TMS, activity in the peripheral visual field representations for each retinotopic visual area bilaterally were found to increase, while in representations of the central visual field (around the foveal confluence) decreases in activity were found. Note that eye movement data was also analyzed and there were no differences

for eye position found with the increase of TMS intensity. Thus, the activity increase in peripheral areas could not have been due to eye movements. Additionally, no phosphenes were reported in participants, which are in line with findings that phosphenes occurred during TMS stimulation on occipital areas only (Walsh, 2005).

Contrast Sensitivity during FEF TMS

In a subsequent psychophysical study, Ruff et al., 2006 tested the behavioural relevance of the above described FEF TMS centre-periphery modulation of retinotopic activity in visual cortex. It was predicted that TMS to the right FEF would enhance peripheral vision relative to central, for both hemispheres. This was found to be the case: the perception of contrast appeared enhanced in both left and right periphery relative to fovea, consistent with previous studies reporting that BOLD increases in early visual areas were associated with increases of contrast perception (Ress and Heeger, 2003; Olman et al., 2003, 2004) (Fig.28a/b/c).

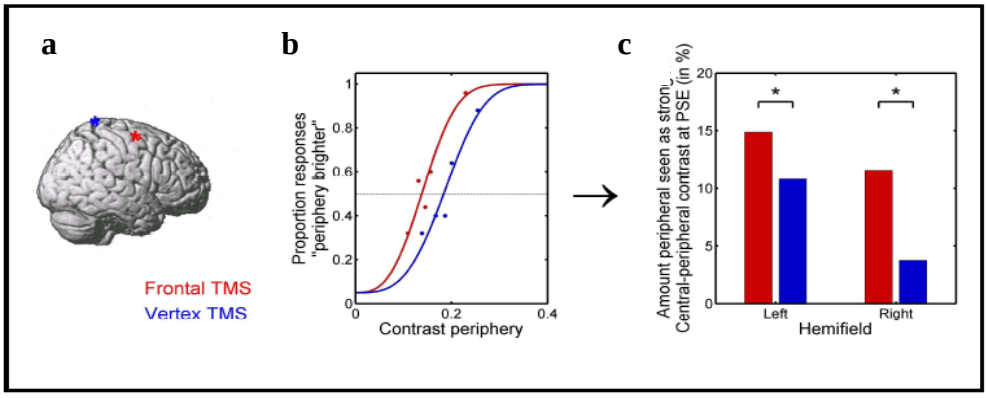


Figure 28a/b/c. Psychophysical results on cpd in contrast perception during FEF TMS. Frontal but not vertex TMS enhances perceived contrast for peripheral relative to central visual stimuli, for both hemifields. a) frontal (red star) and vertex-control (blue star) TMS sites, selected according to the same criteria as in the neuroimaging experiments. b) psychometric curves fitted to the psychophysical data of an illustrative participant for one hemifield, when judging which of two concurrent Gabor patches appeared higher in contrast. Separate psychometric functions were obtained with frontal TMS (red curve) or vertex TMS (blue curve) co-occurring with the visual displays. The intersection of the dashed horizontal line with either curve indicates the Point of Subjective Equality (PSE) value for the peripheral patch in the corresponding TMS condition. c) displays inter-participant mean contrast-value differences between central and peripheral stimuli at the derived PSE. For both TMS conditions and both hemifields. Due to the subtraction of contrast values at the PSE higher values represent more enhancement of peripheral relative to central perceived contrast.

1.2 Rationale for Experiments 1 and 2

Ruff et al., 2006 conducted a perceptual comparison task, estimating the point of subjective equality (PSE) in contrast perception between retinal centre and periphery of which results have been introduced in the paragraph above. Participants had to report which of two simultaneously appearing Gabor patches, one in the centre and one on the right or left in the periphery was of higher contrast (Fig.29).

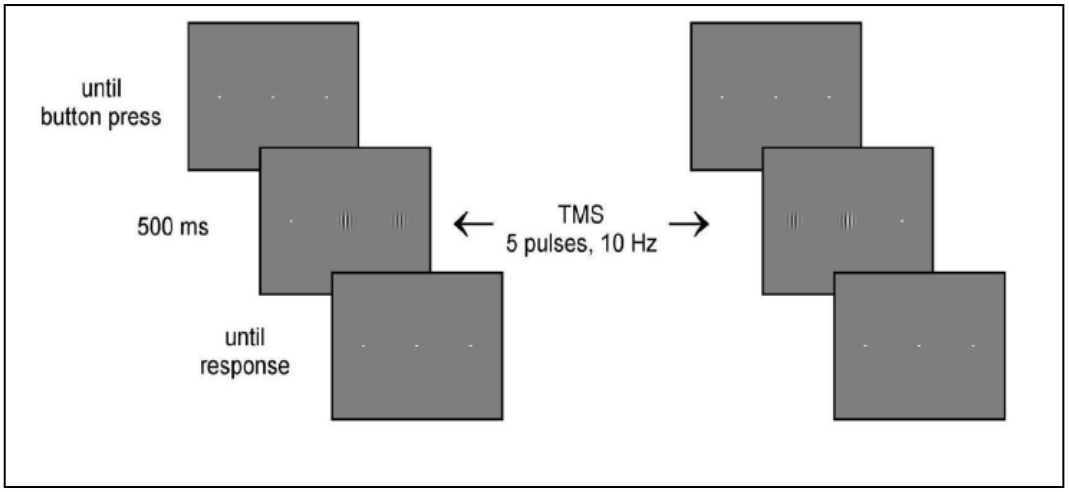


Figure 29. Stimulus Sequence applied in the psychophysical measurement of contrast perception during TMS (PSE method) according to original (Ruff et al., 2006, thesis). Two vertically oriented Gabor patches were displayed simultaneously centrally and peripherally left or right for 500ms, during the display TMS was applied. Participants maintained fixation and rated which of the displayed stimuli was of higher contrast. The contrast of the peripheral stimuli was adapted while the contrast of the central stimulus was at fixed value. The point of subjective equality has been estimated between the central and peripheral stimuli according to the response. In general, this is a highly subjective method, vulnerable to attentional momentum and capacity of the observer.

This PSE method is however well known for its subjectivity and decision biases and therefore cannot be considered to measure pure contrast sensitivity. Additionally, the PSE method requires a good ability to maintain concentration and dedication during the task. The total duration of the PSE experiments is relatively long and requires many repetitions which need to be averaged to ensure reliable results particularly in patients with brain injuries who are not trained on these kinds of tasks. For this reason, the PSE method was considered inadequate for brain injured patients, who are known for poor concentration abilities and their overall vulnerability to enduring cognitive tasks.

A further consideration is that Ruff et al., 2006 employed stimuli of a relatively long duration, which would be inadequate for FEF lesioned patients who tend to lose fixation. A longer display of a stimulus in the periphery would very possibly increase the probability of eye movements which would lead to misleading results. Eye movements would increase the detection and accurate identification of a target which would increase artificially peripheral sensitivity. The increase of sensitivity could not be led back to covert attention abilities in these patients but to their eye movements. This would create a serious confound in the study. Also, shortening stimulus duration in the PSE method would increase the difficulty of the task decreasing the reliability of the task or requiring longer training sessions. In addition, some of the FEF patients available for experiments showed more extensive lesions involving DLPFC, which has been found to affect functions such as decision making, attention and working memory. A task which is biased by judgment abilities and the attentional momentum of an observer may therefore prove incapable of testing visual sensitivity objectively in patients with frontal brain damage.

Therefore it was necessary to change the task from the one Ruff et al., 2006 employed, to an alternative task to measure cpd in contrast perception which could meet all the requirements to provide a reliable, valid and precise test of contrast sensitivity in brain injured patients. In this chapter I introduce an orientation discrimination (OD) task, in a format suitable for patients, and test whether its measure of cpd is correlated to the contrast judgement task used by Ruff et al., 2006.

The Orientation Discrimination Task

In the orientation discrimination task (OD) participants are asked to indicate the orientation of the stimulus (2 alternative choices), while contrast is systematically decreased until errors are made in a staircase procedure. Thresholds at certain performance level (here 79% accuracy) can be estimated for fovea and periphery individually and a ratio periphery divided by fovea (P/F) can be calculated. There are two potential advantages of the OD task: 1) it is an objective measurement of perceptual ability, rather than a subjective measurement of perceptual decision; 2) It may reveal greater cpd than the judgement task, and thus allow greater sensitivity to changes in cpd in patients. Two experiments were conducted in healthy participants (Ruff et al., 2006 also used a young healthy population), in order to validate and optimise the OD paradigm.

1. In the first experiment both methods were tested in a within-subject design. If the new contrast estimation task via orientation discrimination was equivalent to PSE a high correlation of the cpd ratios was expected.

2. In the second experiment the impact of target duration for cpd in the orientation discrimination paradigm was examined to optimise the cpd estimation for patients who might move their eyes to look at a stimulus if stimulus duration is too long (i.e. more than the typical saccade latency of around 200 ms).

2 EXPERIMENT 1

2.1 Methods

2.1.1 Orientation Discrimination Procedure

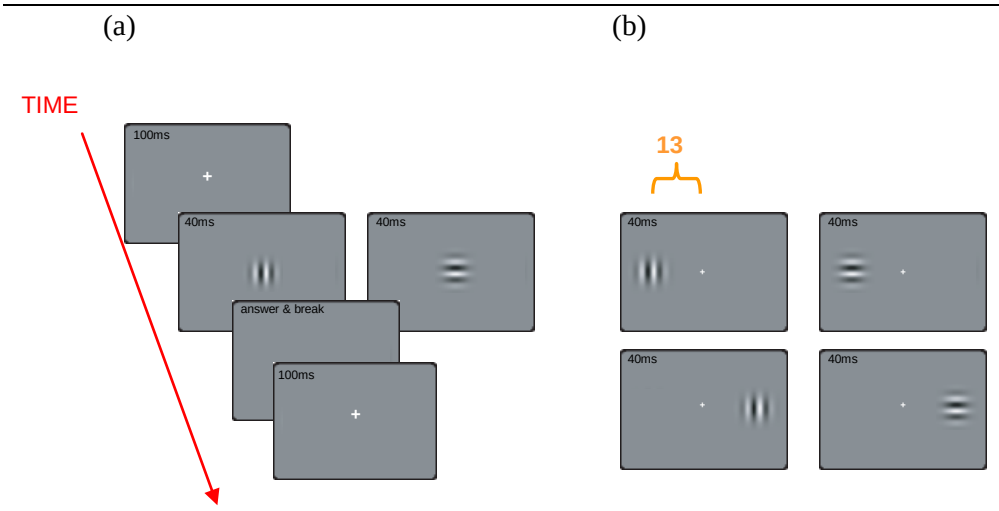


Figure 30. Orientation discrimination paradigm used for all experiments with patients described in chapter 3-5 (a modified version of this is applied to test visuo-motor processes in chapter 6-7). Trial sequence for (a) central and (b) peripheral retinal loci left and right at 13 visual degrees. The stimulus sequence started with a fixation point display for 100ms, followed by the display of the target – either a horizontally or vertically oriented Gabor patch of 40 ms duration. A blank screen appeared, and when the participant identified the orientation of the stimulus via a button-press, next trail sequence started with fixation point. The contrast of the Gabor patches was adapted to accuracy of the responses. Two correct answers were required to lower the next stimulus contrast, and with one failure the stimulus contrast was increased again (two-alternative forced-choice task (2AFC)).

In experiment 1 the PSE method used by Ruff et al., 2006 was replicated as far as possible, employing similar stimulus size and duration. This technique was compared to the orientation discrimination (OD) paradigm which was considered more appropriate for patients. Stimulus size and target duration was reduced to ensure precise retinotopic position of the stimulus. Equivalently to Ruff et al., 2006 spatial frequency was constant for foveal and peripheral presentation in both paradigms (Fig.30) and the stimuli were centred on the same retinal loci in both paradigms. Each of the peripheral loci was stimulated at 13 degrees from fixation horizontally. The paradigms were counterbalanced for each participant in the order ABBA or BAAB.

Stimuli

For the orientation discrimination paradigm Gabor patches, phase-randomized sinusoidal gratings were presented within a sinusoidal envelope with a SD of 0.5 visual angle and were of either vertical (90 degrees) or horizontal (180 degrees) orientation. All Gabor patches were of constant spatial frequency, 2 cycles per degree for all three retinal locations tested. Gabors were displayed with initial luminance amplitude (peak to trough) of 12.5 candelas per square meter (cd/m^2) in foveal and 20 cd/m^2 peripheral retinal positions. All stimuli had a mean luminance of 55 cd/m^2 and were displayed against a grey background of a luminance of 55 cd/m^2.

Estimation Procedure

In a two-alternative forced-choice task (2AFC) participants indicated the orientation (horizontal or vertical) of the displayed Gabor patches. Gabors were randomly displayed left, right or center after fixation offset. Each trial of a fixation – target sequence was self-initiated by a button-press, triggering a brief display of a fixation cross for 100 ms, followed by a brief Gabor patch display of 40 ms proceeded by an interval display until the button-press response. Participants pressed one of two keys with the index- and middle finger of their right hand to indicate the orientation of a displayed Gabor patch. Index finger (left key on the response box) was assigned to vertical orientation whereas the middle finger (right key on the response box) was assigned to indicate the horizontal

orientation, equivalently for all three retinal loci tested. Auditory feedback was provided after each response, indicating hits and errors.

A three-down, one-up staircase with a value adjustment step at 1.2 ratio of the Gabor's contrast was applied. 1 block of 90 trials in the center and 2 blocks each of 70 trials in the periphery were performed. 2 retests were performed for each participant (3 tests in total). With each retest the initial contrast of Gabors was adjusted according to the results from the previous test. In the adaptive staircase procedure, the decrease in threshold (Gabor contrast) required three sequential positive responses to the orientation displayed but only one negative response to increase. This adaptive procedure is known to reduce systematic biases (which occur with the method of limits and the method of adjustment), as well as increase measurement accuracy and efficiency as the number of target values and a range of values to test can be reduced fast. Reversals were counted and a mean of the last 5 reversals produced the threshold value.

2.1.2 Point of Subjective Equality Paradigm

The task was designed to be similar in all respects to the paradigm applied in the TMS study of Ruff et al. 2006. Gabor patches were displayed in pairs i.e. one constantly in fovea and one randomly alternated in the left or in the right peripheral visual field. In a two-alternative forced-choice task (2AFC) participants indicated which Gabor patch of the pair displayed was of higher contrast.

Stimuli

Gabor patches were presented within a sinusoidal envelope with a SD of 2 degrees and were of vertical (90 degrees) orientation only. All Gabor patches were of constant spatial frequency 2 cycles per degree for all three retinal locations tested. Gabors were displayed with mean luminance of 55 cd/m^2 and an initial luminance amplitude value of 12.5 cd/m^2 in both foveal and peripheral retinal positions. This created an initial Michelson contrast of 23%. However, the foveal stimuli remained constant whereas peripheral stimuli were adjusted depending on participants' response to the preceding trial. All stimuli were displayed against a grey background of a luminance of 55 cd/m^2.

Estimation Paradigm

At each trial, a fixation – two-targets sequence was self-initiated by a button-press, triggering a brief display of a fixation cross of 500 ms, followed by a simultaneous display of two Gabor patches (foveal and peripheral) for 500 ms proceeded by an interval display until the button-press response triggered the next trial. Participants pressed one of three keys with fingers of their right hand to indicate on which side the Gabor patch was of higher contrast.

As in the OD method auditory feedback was provided after each response, indicating only the errors when the wrong button was pressed. In such cases, the response was discharged and the stimulus was displayed again. One testing sequence was of 90 trials. This procedure was repeated twice.

Apparatus

Stimuli were displayed in a dark room, on a Sony Triniton 19 inch GDM-F400T9 monitor, driven by a Cambridge Research System (CRS) ViSaGe graphics board at 100 Hz, which was calibrated with a CRS ColorCal and associated software. Viewing distance was 72 cm. Manual responses were made using a CRS CB6 button box. The subject's head was stabilized by a chin rest and a head rest. Stimulus control was provided by Matlab.7.3. Eye tracking analysis was performed online. Trials on which saccades or blinks occurred e.g., where the eyes deviated outside a 1.5 degree window from fixation were discarded and the subsequent trial of the staircase was drawn randomly.

Participants

Seven paid naive volunteers, 3 female and 4 male with normal or corrected to normal vision were tested. All participants were right-handed and of academic background, aged between 20 and 26 years (mean: 23 years). None had a history of neurological or psychiatric disorders or any sign of colour blindness or visual field defects. All gave informed consent in accordance with the local ethics committee before the study.

Analysis

In the OD method visibility thresholds obtained from reversals of adaptive staircase procedures were calculated as centre-periphery ratio for each participant. In the PSE method ratios were obtained from direct performance of the participant – the ratio was calculated from the peripheral stimuli that were judged equally often to be of higher or lower contrast than the foveal stimulus. For both methods, a mean of the values for left and right was used. A Pearson's Correlation was estimated with ratios for OD and PSE using SPSS.16. Additionally, two-tailed, paired sample *t*-test in SPSS.16 was performed to test ratio differences obtained from OD vs. PSE.

Results

Fig.31a demonstrates a high positive correlation for ratios obtained with the OD and PSE method, r^2 = .80, *p* (two-tailed) < .01.The mean centre-periphery ratio for OD method was 1.7 (*SEM* = 0.15) while for PSE the mean centre-periphery ratio was 1.2 (*SEM* = 0.09). Importantly, centre-periphery ratios were significantly higher in the OD method than in the PSE method (*t* = -6.61, *df* = 6, *p* = .001). Fig.31b illustrates the correlation of the threshold values obtained with the OD and PSE method for each participant (for individual values see Table 1 in appendix).

a) Correlation of cpd with lesion size **b) Cpd measured with both methods**

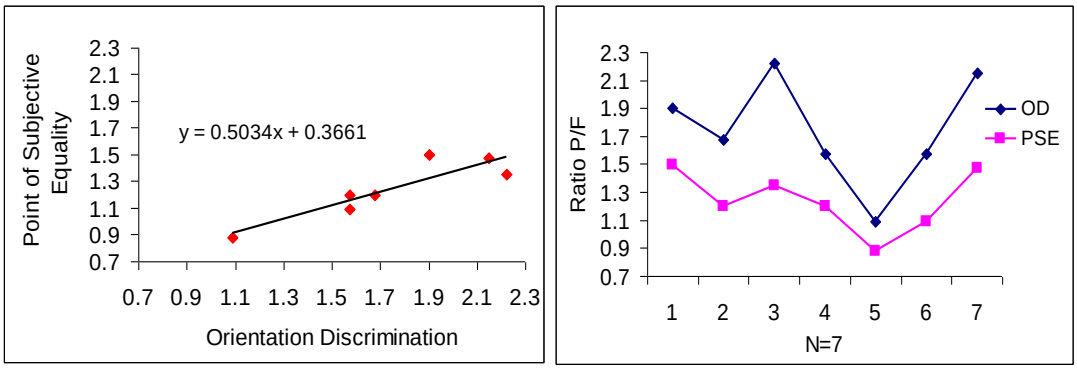


Figure 31a/b. Contrast perception ratios for center versus periphery obtained with OD and PSE. (a) Correlation between methods for each of the participants. (b) Individual participant's data for each of the paradigms applied.

Discussion

Results obtained in experiment 1 will be discussed below in the context of the second Experiment.

3 EXPERIMENT 2

3.1 Introduction

Having found that in young participants who have no problem complying with both tasks, the cpd measured by the OD method is highly correlated with the cpd assessed by the PSE method, and given that patients are more likely to be able to comply with, and provide stable results with, the OD method, I accepted the OD method as a suitable one for the patient studies in Chapters 3 and 4. It then remained to optimise the parameter of stimulus duration. In order to investigate the impact of visual stimulus duration for the cpd, participants were presented with short and long stimulus times in the fovea and in the periphery. As mentioned in the introduction above short stimuli were considered as more appropriate for FEF patients to prevent eye movements. Additionally, the cpd size might benefit from shorter stimulus displays, and a larger cpd would make it easier to detect any differences between patients and controls.

3.2 Experimental Procedure and Analysis

All methodological and analysis procedures were identical to the OD paradigm described above. Participants were presented with separate blocks of Gabor patches of 40 ms or 120 ms in ABBA or BAAB order and reported targets' orientation via button-presses.

Participants

Eight undergraduate psychology students (age range 21-31, mean: 24) were tested. None had reported neurological or visual impairments.

Results

As shown in Fig.32a/b and in Table 2 (appendix) for threshold values obtained in the fovea and the peripheral loci, with brief target presentation times (40 ms) centre-periphery ratios, (*M* = 2.1, *SEM* = 0.29) were significantly higher than with long presentation times (120 ms) (*M* = 1.3, *SEM* = 0.07) (two-paired t-test, (*t*=2.4, *df* = 9, *p* = .042)).

a) Cpd at two target durations **b) Visual thresholds at three retinal loci**

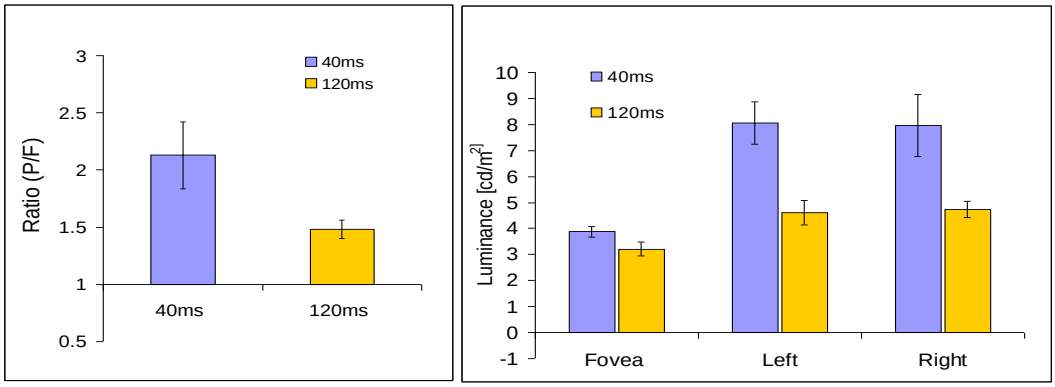


Figure 32a/b. Thresholds obtained at two different target durations (40ms and 120ms) for ten healthy young participants (N=10). (a) Centre-periphery ratio for fovea (blue) and periphery (left and right combined) (yellow) which was significant (two-paired t-test, (*t*=2.4, *df* = 9, *p* = .042)). (b) Thresholds obtained for fovea and periphery (left and right). Legend: blue: 40ms target duration, yellow: 120ms target duration).

4 DISCUSSION

Experiment 1 revealed that the cpd measures obtained with the two methods are strongly related. However, the OD method was found to measure significantly higher cpd, indicating that OD is a more sensitive method for detection of cpd for contrast perception than the PSE method.

In the OD method observers were asked to determine orientation of Gabors presented either in the center or periphery left or right, without employment of eye movements. Here the observers were not aware of the purpose of the task, while in PSE a) observers were asked to rate, which of the stimuli displayed were of higher contrast and b) judged the contrast directly but subjectively which exposed the performance on this task to observers'

preferences. Therefore, the OD method ought to be the more objective (judgment independent), in which also attentional effects were minimised.

In the OD method, the stimulus presentation was extremely brief, resembling flashed stimulus and the size of the stimuli was almost ¼ of those used in the original method. The small size of Gabor patches ensured that each stimulus activated only a limited set of early cortical neurons that filter orientation information and respond to small sectors of the visual field. Additionally, stimuli that are more compact in visual space (distributed over a small fraction of visual space) might reduce attentional and spatial uncertainty. In other words, with large stimuli, it is not clear whether the participants judge the center or the edge of the patch, which might give different results if contrast sensitivity varies over the extent of the stimulus.

In sum, the orientation discrimination paradigm seemed the most preferable to test cpd in patients and age matched controls. The advantage may come from all or any of the methodological differences stated above.

Experiment 2 indicates that increased ratios can be expected with shorter target presentation times. Thus, the target duration might be the critical parameter that leads to an advantage of OD over PSE method. However, it was out of the scope and main interest of this thesis to investigate if other differences between these two methods contribute to OD advantage. The crucial conclusion was that displaying targets of short duration of 40 ms in combination with the OD procedure is a robust and even more sensitive measurement tool for detection of cpd than the PSE method employed by Ruff et al., 2006.

5 CONCLUSIONS

Experiment 1 showed that the OD method measures cpd successfully and has close correspondence to the PSE measure. Additionally the OD measurement produces larger ratios than the PSE method, making it a potentially more sensitive measure for any differences in cpd between patients and controls. Thus, the OD method is the core estimation method applied for further experiments as described in Chapters 3-5.

CHAPTER 3

EXPERIMENT 3

CPD IN CONTRAST SENSITIVITY AFTER FEF LESIONS

1 Rationale

Ruff et al., 2006 proposed that the modulatory effects of TMS on cpd in visual processing could reflect top-down signals increasing processing sensitivity in a selective manner which result in a relative increase of visual processing and contrast sensitivity in visual periphery. The TMS stimulation was applied during the visual stimulation (100 ms after visual stimulus onset) which could both disrupt or activate perceptual processing. Thus it is not entirely certain if the TMS disrupted or enhanced the FEF effects on visual brain areas. To test if TMS acted as a "virtual lesion" or as "subthreshold activation" of FEF, cpd was tested in patients with real FEF lesions. Fig.33 illustrates the predictions which are described below.

2 Hypothesis

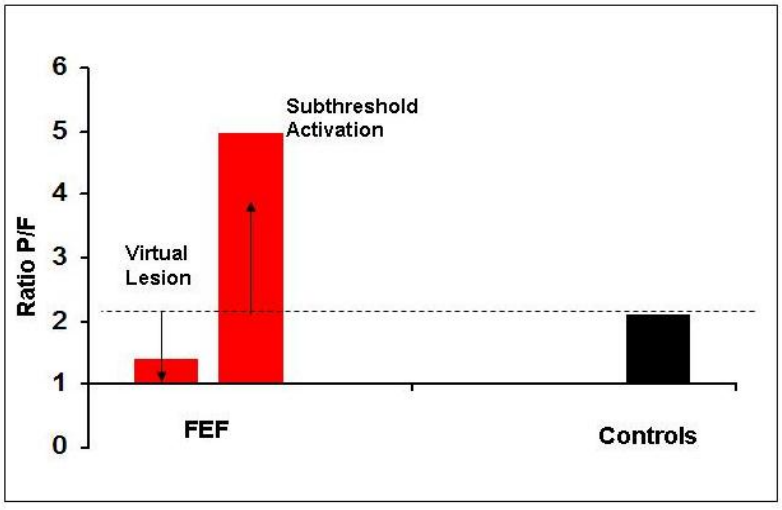


Figure 33. Predicted centre-periphery difference in FEF patients and healthy controls based on the FEF TMS results (Ruff. et al., 2006) calculated as ratio for visibility thresholds in periphery (left and right combined) divided by visibility thresholds in the fovea (P/F). Hypothesis A: Centre-periphery difference (Ratio P/F) decreases in patients if TMS acted as "virtual lesion". Hypothesis B: Centre-periphery difference (Ratio P/F) increases in patients if TMS acted as "subthreshold activation". Arrows and the red bars indicate Hypothesis A or Hypothesis B.

Two-rival predictions for the FEF TMS effect can be postulated when tested in patients with real lesions of FEF. TMS stimulation could act as a "virtual lesion" in FEF (Pascual-Leone et al., 1998a/b, Walsh and Pascual-Leone, 2005; Conwey, 2005; Silvanto and Muggleton, 2008). In that case, patients with FEF lesions would show similar effects to those produced by TMS – relatively enhanced peripheral contrast perception compared to fovea (or, in other words, reduced foveal contrast perception relative to periphery), resulting in a decrease of centre-periphery ratio in FEF patients (Fig.33).

However, if the TMS effect is due to remote effects on visual cortex resulting from non-specific sub-threshold activation of FEF (as suggested by Ruff et al., 2006) patients should show the opposite effect – relatively impaired peripheral contrast perception, resulting in increased centre-periphery ratios (Fig.33). The main idea would be that activation of FEF (naturally or using TMS) leads to a relative improvement of visual processing in the periphery (Grosbras and Paus, 2002, 2003). Patients with FEF lesions would not be able to achieve this improvement.

3 Methods

The orientation discrimination paradigm for estimation of contrast thresholds was described in chapter 2 in detail and therefore is not repeated here.

3.1 Sessions

Three right FEF lesioned patients and one bilateral FEF patient were tested. Three patients were tested in two sessions (T1, T2). Session T1 was an initial pre-testing stage. The testing sessions were conducted within a period of 4 months at the Wolfson Center for Cognitive Neuroscience, Bangor, UK.

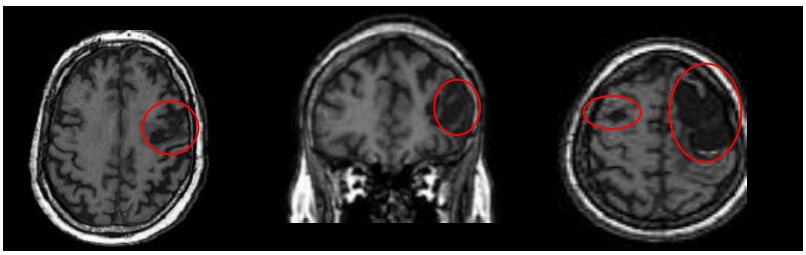
3.2 Participants

Multislice images are shown in figure 1a in the appendix (p. 204) for each of the patients tested. Three stroke patients, 1 male (M.J. (age: 75) and 2 female G.H. (age: 71), L.B. (age: 56)) with lesions including right FEF took part in the first two experiments (T1, T2). In patient L.B. the bilateral lesions were the result of haemorrage caused by sagittal sinus

thrombosis while the lesions of the three other patients were due to strokes. A full overview of the brain lesions are provided in the appendix figure 1a (p. 204). The scans demonstrated in Fig.34 show best the extent of cortical lesions including FEF. The scans are according to neuro-anatomical convention (left lesion is left and right is right). All patients were tested with normal or corrected to normal vision and all patients had motor impairments of their contralesional arm.

Eight healthy age matched controls (mean age: 66) were recruited from the Community Panel of the School of Psychology, Bangor University. Healthy participants aged over 70 were usually not motivated to participate in experiments and showed a high rate of drop-out. None of the participants in the healthy control group reported a history of neurological or psychiatric disorders or any sign of colour blindness or visual field defects. All participants (including patients) were right-handed and of varying professional background.

All participants – healthy elderly and patients gave informed consent in accordance with the local ethics committee before participating in the study. All participants were tested with the Hamilton-Veale Contrast Sensitivity Test based on the Pelli-Robson contrast sensitivity test (1988), and Acuity Test on a chart was performed prior to psychometric testing on a computer monitor. The testing served not only as a cross-validation of tests but also in the experimental setting it was a useful "ice breaker" between the experimenter and the particularly vulnerable participant group, the patients and elderly participants.



M.J **G.H** **L.B**

Figure 34. MR scans for three FEF patients. From right to left in axial view: M.J., C.W., G.H., L.B. All patients showed frontal right hemispherical lesion of different size, patient L.B. showed FEF lesions bilaterally, the more extensive in the RH.

Case Descriptions

Patient M.J

The 76-year-old (at the time of testing) male stroke patient M.J. showed on an MRI scan, lesions subcortically (basal ganglia) and in the lateral prefrontal cortex including the right FEF. Lesions were reported to be scattered including the right parietal lobe. The brain damage was reported to indicate an infarct. Time from infarct was 3 years at the time of testing. The following remaining impairments were reported: sensory loss in the left side of his face and slight astereoagnosis. M.J. was reported to be severely colour blind, which did not affect the discrimination performance of a black and white pattern.

Patient G.H

The 72-year-old (at the time of testing) female stroke patient G.H. showed on an MRI scan discrete right FEF damage, also affecting the motor cortex. Time from infarct was 4 years at the time of testing. Patient showed contralesional motor remaining impairments.

Patient L.B

The 56-year-old (at the time of testing) female patient L.B. showed on an MRI scan large, multi-loculated lesion in the right frontal lobe, with a surrounding area of gliosis extending into white matter and up to the ventricles. The chronic lesion has been reported in medical protocols (Bangor Clinical Center) to involve hand area of the motor cortex, the frontal eye fields, the pre-motor cortex and parts of Brodman's area 9, 10, 45 and 46. In the left hemisphere focal damage lateral to the frontal eye fields was reported. In 1998 L.B. was diagnosed with sagittal sinus thrombosis with bilateral superior frontal haemorrhage. Thus, the lesion developed nine years prior to testing. The patients' age was 47 at the time of the stroke. The remaining impairments were in the left arm, which was spastic and useless also at the time of testing. Examination five years after the acute phase reported that the extraocular movements were full in all directions and convergence was intact although L.B. was found to have some difficulty in executing anti-saccades and she was unable to wink. There were no visual fields cut or visual extinction found.

3.3 Set up and Testing Sequence

In T1 and T2 patients M.J, G.H and L.B were tested. In testing session T1 and T2, to obtain reliable results combined with as few lapses and biases due to attentional and tiredness effects, as well as for convenience of patients, all participants were presented with only one block of 90 trials in the center and two blocks of 70 trials in the left and right peripheral condition (140 trials in total for periphery). Such a procedure also allowed also for fast acquisition of threshold values. Reversal values obtained from those blocks served to estimate the mean threshold value for each peripheral location tested.

4 Analysis

All data analysis was performed in Matlab.7.3, Excel, WindowsXP 2006, SPSS 19. For testing sessions 1-2 mean luminance thresholds for Gabors' orientation discrimination were obtained from the last 30 values occurring in a staircase for each location tested. The centre-periphery ratios were calculated. For comparisons with Ruff et al., 2006 mean threshold values were transformed into Michelson's contrast in percent, calculated as mean luminance threshold value multiplied by backgrounds' mean luminance and converted into a percentage. For statistical comparison between few neurological patients and controls, non-parametric tests were used. Results for session T1 and T2 were averaged and are shown in Fig.35 below and in Table 3a (in appendix).

5 Results

5.1 Contrast Sensitivity

The mean perceptual thresholds for fovea in FEF patients and controls are shown in Fig.35 and Table 3a/b in appendix. The mean perceptual thresholds for fovea in FEF patients were 22.3% Michelsons Contrast (SEM=8.4) for periphery left 59.8% (SEM=23.3) and right 50.9 % (SEM=20.2) with combined left and right 55.5 % (SEM=21.4). Contrast sensitivity thresholds for individual patients and controls are shown in Table 3a/b in appendix. In controls, in fovea mean, perceptual thresholds for fovea were 7.9 % (SEM=1.1) for periphery, left 16.7 % (SEM=2.4) and right 17.1 % (SEM=3.2) while combined left and

right 16.9 % (SEM=2.7). Although contrast thresholds for all retinal loci tested seem to be elevated in the three tested FEF patients when compared with controls, the non-parametric Mann-Whitney U test revealed that this was not significant for fovea ($p > .05$) or periphery (left and right combined) ($p > .05$). However, this could have been due to a small number of FEF patients tested. This will be tested again in similar conditions in Chapter 5 with one more FEF patient who was available only later.

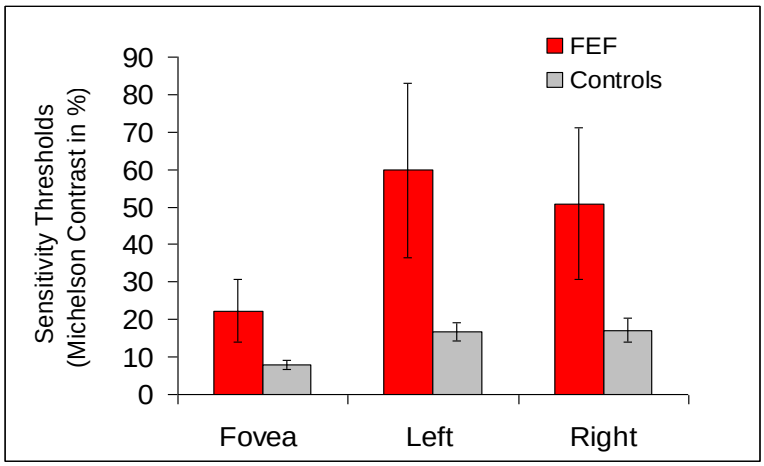


Figure 35. Perceptual sensitivity thresholds calculated as Michelson Contrast in % obtained for fovea and periphery left and right (13 degrees eccentricity) for 3 FEF patients and 8 healthy controls (p > .05) (Table 3a/b in appendix).

5.2 Centre-Periphery Difference and Lateralization Effects

Fig. 36a/b and Table 3a/b in appendix shows the cpd and lateralization effects obtained from this data set. Cpd in perceptual sensitivity was highly significant (t-test (two-tailed), t=5.451, df=7, p=.001) in the healthy participants group, while cpd was not significant in the FEF patient group tested (Wilcoxon Sign Test, p >.05). This will be reassessed with a higher number of FEF patients in an experiment with similar conditions described in chapter 5. Cpd when compared between FEF and healthy controls was not significant for the left visual field (FEF: M=2.6, SEM=0.3; Controls: M=2.1, SEM=0.2) or for the right visual field (FEF: M=2.2, SEM=0.1; Controls: M=2.1, SEM=0.1) or for periphery combined (FEF: M=2.4, SEM=0.2; Controls: M=2.1, SEM=0.1), (independent Mann-Whitney U test, p > .05).

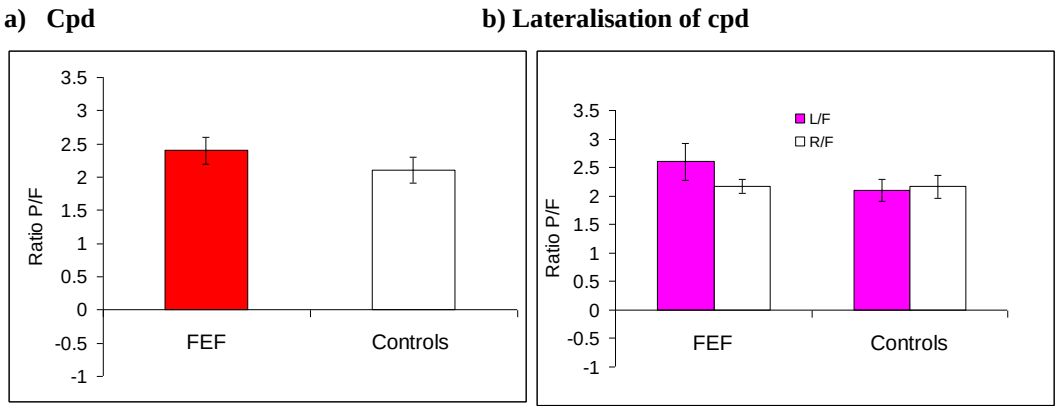


Figure 36a/b. Centre-periphery difference as calculated for contrast threshold in periphery divided by contrast threshold in fovea (Ratio P/F) and averaged for three FEF patients and eight healthy age matched controls. L/F: ratio left periphery/fovea; R/F: ratio right periphery/fovea (a) Cpd combined ($p > .05$). (b) Lateralization effects left visual field (L/F) (contralesionally for FEF patients) and right visual field (R/F) (ipsilesionally for FEF patients) ($p > .05$).

5.3 Correlations between Lesion Size and Performance in FEF Patients

Lesion volume has been ranked in all three patients after careful viewing of whole brain scans by an expert (Prof. Robert Rafal) and a novice (the author of this work) individually and a consensus was reached for the following ranking of lesions extents: L.B. > M.J. > G.H. The perceptual sensitivity impairments have been ranked for each patient resulting in a following rank: M.J. > G.H. > L.B.

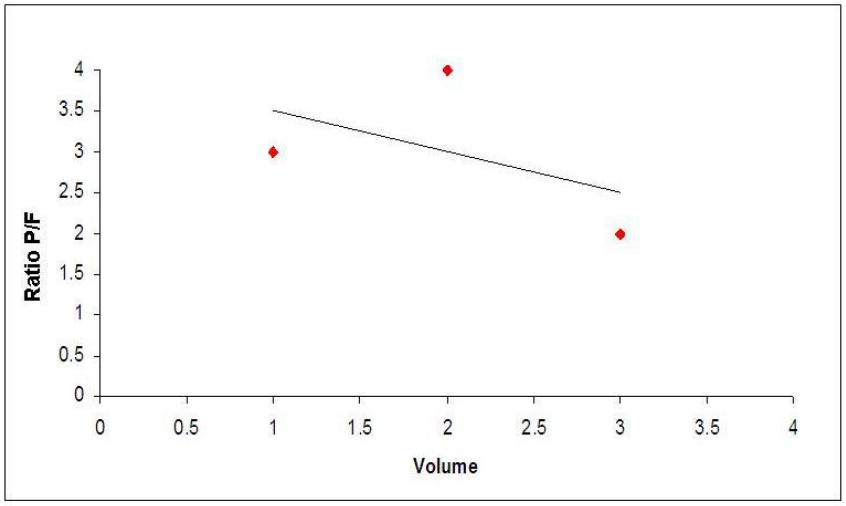


Figure 37 demonstrates small negative Spearman's correlation for cpd calculated as ratio for periphery divided by fovea (P/F)) and the extent of lesion rated by an expert and a novice in three FEF patients tested (*p* (two-tailed) > .05).

A nonparametric correlation test calculating Spearman's correlational coefficient for one-tailed test was performed. The results are shown in Fig.37. There was a negative correlation of perceptual sensitivity with the extent of lesion in FEF patients (r = -.80), which however was not significant (Spearman's correlation, *p* (two-tailed) > .05.). This shows that the impairment does not increase with more extensive lesion, on the contrary if anything, the trend is the other way round – the more focal the lesion, the greater the relative impairment of peripheral vision. This tendency could be interpreted as an indication of functional involvement of FEF in peripheral perceptual sensitivity; however this correlation was not significant with only three FEF patients.

6 Discussion

The experiments described above showed no differences in cpd in FEF patients when compared with healthy age matched controls and therefore did not show significant effects in either direction hypothesized. Therefore, at this stage no conclusions for TMS effects in Ruff et al. study can be made based on these results.

The results seem rather to suggest that FEF chronic lesions do not have the same effects as transient TMS FEF. This might be due to the chronic nature of lesions associated with brain plasticity and reorganization. Previous studies have shown that oculomotor impairments after FEF damage are reversible in patients after short periods of 2-3 days (Rivaud et al., 1994; Gaymard et al., 1998, 1999; Milea et al., 2002; Pierrot-Deseilligny et al., 2002). However, the tests have shown highly impaired contrast sensitivity in FEF patients at all locations tested which were retinotopy unspecific. Although this was not significant due to the low number of FEF patients, statistical comparisons are uncertain. Therefore, the tested FEF patients sample should be increased to reach clear conclusions. In chapter 5 results for cpd in contrast sensitivity from 4 FEF patients are described. Additionally, in healthy participants there was a clear cpd difference, perfectly in accordance with previous research in contrast perception in healthy populations.

Important to mention in this context is that previous studies of patients with chronic unilateral FEF lesions showed a reduced effect of a fixation point on saccade latency to contralesional targets; and strategic modulation of this effect was compromised for saccades to ipsilesional targets (Machado and Rafal, 2002). According to this the foveal

decrease in perceptual sensitivity could be associated with fixation neurons deficits in patients with chronic FEF lesions. Nonetheless, it is crucial to mention that influences of FEF on contrast sensitivity might be related to its contributions to covert visuospatial attention, which has been examined in a series of experiments described in chapter 5.

CHAPTER 4

EXPERIMENT 4

CPD IN CONTRAST PERCEPTION AFTER PULVINAR DAMAGE

1 Rationale

Experiments described in chapter 3 showed that chronic right FEF lesions result in lateralization effects in visuospatial processing. This result supports partly the FEF TMS study of Ruff et al., 2006, and might indicate that according to the lesion in FEF contralesional peripheral areas in the occipital lobe are less activated. However, nothing is known about direct white matter connections between the FEF and visual areas in the occipital lobe which could transmit visual signals. It is known that all sensory signals in the brain pass the thalamus. Within the thalamus there is a grey matter nucleus, called pulvinar which has been shown to be visuotopically organized in monkeys and to be involved in visuospatial processing in humans (Allman et al., 1972; Shipp et al., 2003, 2004; Kastner et al., 2004; Smith et al., 2007). Therefore, the human pulvinar is a likely candidate for computation and transmission of low-level visual signals between remote visual centres. Visuospatial impairments have been shown in patients with pulvinar damage (Rafal et al., 1987; Snow et al., 2009; Arend and Ward, 2008). Fig.38 shows a hypothetical model of pulvinar contribution to the networks of visual processing (Ungerleider and Mishkin, 1982). Occipital visual areas, the pulvinar and the FEF form an important functional network for visuospatial and low-level visual processing. The function of the pulvinar within this network shall be investigated here in patients with chronic pulvinar lesions. Firstly, the contribution of the pulvinar to centre-periphery differences in contrast perception will be examined and considered in relation to the cpd changes in patients with FEF lesions.

2 Hypothesis

The hypothesis that the pulvinar is involved in the FEF-occipital transmission of low-level visual input can be tested in patients with pulvinar damage. If the pulvinar nucleus is involved in visuospatial processing, specific impairments in cpd in contrast perception should be expected after its damage. In line with previous research, contralesional deficits in visual processing in the periphery can be hypothesized (Rafal et al., 1987; Arend et al., 2008; Snow et al., 2009). Some differences in foveal

sensitivity between pulvinar patients and healthy participants can be expected due to deficits in release of fixation neurons for saccades reported in pulvinar patients in earlier studies (Watson et al., 1979; Ogren et al., 1984; Rafal et al., 2004). Due to "sticky" fixation at the visual centre in pulvinar patients, longer fixation and therefore enhanced perceptual processing in fovea can be expected, simultaneously resulting in perceptual impairments in periphery.

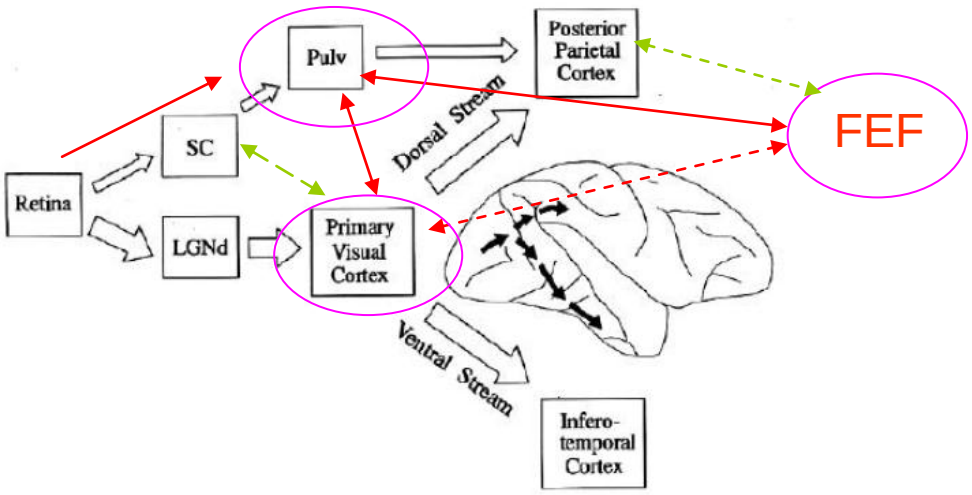


Figure 38. The occipital visual areas, the pulvinar and the FEF form an important functional network for visuospatial processing. This is a model of cortico-cortical projections for low-level visual and visuospatial processing including the pulvinar, which is superimposed on the two-pathways model of vision (Ungerleider and Mishkin, 1982). The FEF has not been previously included in the two-pathways model of vision by Ungerleider and Mishkin in 1982. Originally FEF was considered as an oculomotor and higher-order visual processing area, which does not contribute to low-level visual processing directly. However, novel study of Ruff et al., 2006 and Taylor et al., 2007 strongly suggest that FEF contributes to low-level visual and visuospatial processing. There are indications for retinotopic organization of FEF in humans similar to that in occipital visual areas (Sereno et al., 2005). The pulvinar was shown to be retinotopically organized in monkeys (Shipp et al., 2005). **Legend:** Pink circles: areas of interest in the work presented here, which compose the higher order neural network for processing and integration of visual signals. Green dashed arrows indicate connections known from previous research, not directly tested here. Solid red arrows indicate known connections of white matter between visual areas. The red dashed arrow indicates the influences between areas suggested by monkey and by TMS and brain imaging studies in humans for which no anatomical support in the form of white matter connections is known.

3 Methods

3.1 Set up and testing Sequence

All experimental set ups and paradigms were identical to those described in Chapters 2 and 3. One session for testing one participant was of 1.5 - 2 hours duration, as adjusted

for patients and elderly controls. The same session in young healthy participants was of 20 minutes duration.

3.2 Participants

The elderly control group was exactly the same as for the FEF patients tested. Eight healthy age matched controls (mean age: 66) were recruited from the Community Panel of the School of Psychology, Bangor University. One of the pulvinar patients (C.R) was aged 20 at the time of testing, therefore a much younger cohort of healthy controls (N=10, mean age 24) was recruited from the Community Panel of the School of Psychology, Cardiff University. Multi-slice images for pulvinar patients were not available for viewing; however multi-slice views do not add further information here as the lesions are very focal.

Patients Case Description

Lesion sites in the four pulvinar patients tested are illustrated in Fig.39. Three were elderly stroke patients, T.N., D.G., J.L. (60, 70, 65 – year-old). One patient was young and had a closed head injury (C.R., age 20). To compare results obtained from the young patient C.R., 10 young healthy undergraduate Cardiff University students (mean age: 24) were tested. Patient C.R. was tested with uncorrected vision, as he showed normal vision. All other patients and controls were tested with uncorrected vision

C.R

Damage History

C.R. is a 20-year-old man who suffered closed head injury in a fall, resulting in a focal haemorrhagic contusion and avulsion of the posterior pole of the pulvinar and no other contusions to the brain. The time of the brain injury was 3 years prior to testing. The chronic lesion is very focal in the posterior left pulvinar. No motoric impairments were diagnosed. No behavioural or cognitive impairments were revealed and also the visual field was intact. For about six months after the injury the patient had reported some difficulties with vision; e.g. difficulties seeing words on the right end of the page during reading, and it appeared to the patient that he would miss some words in sentences while reading because the sentences did not make sense and he had to reread it to understand. These visual symptoms had resolved some years before testing. A few

months after participation, patient C.R. entered university for engineering studies. However he dropped out during the first year, for reasons unknown to the experimenter.

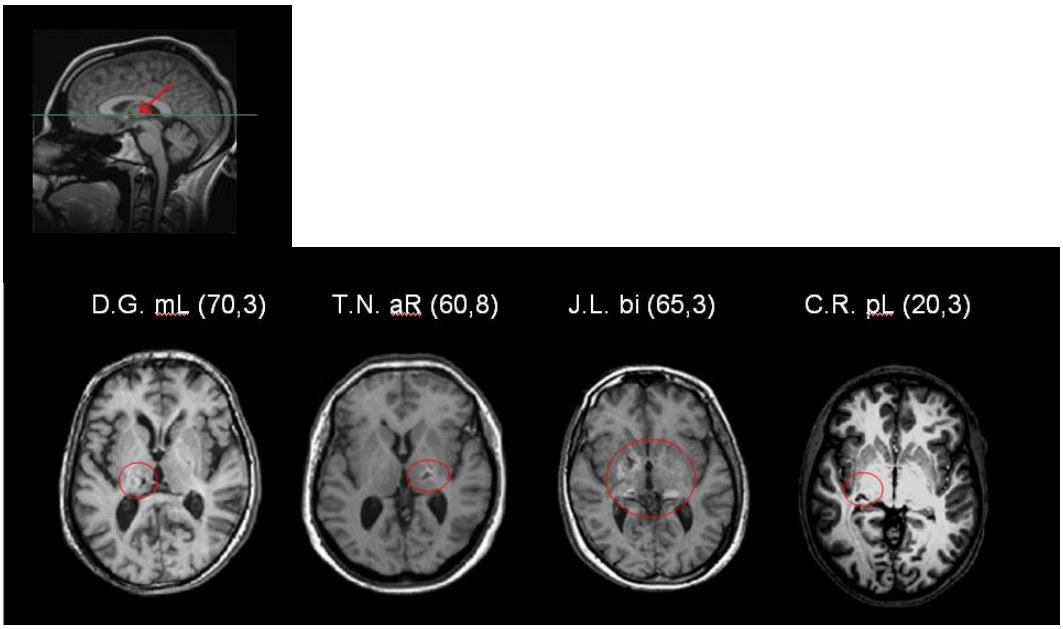


Figure 39. Axial view in neurological brain scans for each of the four pulvinar patients tested. The green line in the sagital view above patient scans indicates the scan level at which the pulvinar is located in the human brain. Red arrow indicates the approximate location of the pulvinar within the thalamus. In the axial views red circle indicate individual's lesion in pulvinar. Above: Initials, age and age of lesion when tested. Abbreviations: mL: middle left, aR: anterior right, bi: bilateral, pL: posterior lateral. Note the multi-slice views do not add further information here as the lesions are very focal.

Functional Deficits

In previous examinations, C.R. showed small deficits in selecting low-saliency targets at four visual angles in the periphery and higher deficits with vertical distracters (Snow et al., 2009). Other studies reported temporal attention deficits (Arend et al., 2008), spatial shifts costs for reallocating (slowing of attentional reallocation) into his impaired field (contralesionally) and increased dwell time (Arend et al., 2008) in a dwell task (Duncan, 1996). Thus, while clear temporal binding deficits were found, signs for potential spatial binding deficits in C.R. were shown with feature binding errors (feature not presented reported in target) more than illusory conjunction errors (feature belonging to distracter reported in target) defined as a function of search array location (Arend et al., 2008). In summary, after a discrete lesion in the left posterior pulvinar, C.R. showed mainly temporal perception impairments (Arend et al. 2008), no asymmetry with anti-saccades, but contralesional deficits with perceptual decisions.

T.N

Damage History

T.N. is a 60-year-old, right handed, hypertensive woman who suffered a 3cm intercerebral haematoma cantered in the right thalamus 8 years prior to testing. The lesion is focal, including the lateral thalamic nucleus and anterior-lateral pulvinar 2mm dorsal to the AC-PC line (anterior-posterior commissure). Impairments were found in the lower left visual fields. She has motoric impairments in the left arm and leg, but the patient is mobile with a cane.

Functional Deficits

T.N. showed lesions in anterior and lateral pulvinar and was found to have mostly spatial deficits (Warden et al. 2002). In the presence of nearby distracter features in her impaired quadrant, which is the lower left, stimuli were more likely to be misallocated and so more likely to be incorrectly bound to features at nearby locations. T.N. also showed a deficit in target localization in the contralesional field.

D.G

Damage History

D.G. is a 70-year old, right handed man who suffered a hypertensive haemorrhage in the left thalamus with a remaining lesion in the middle part of the pulvinar 3 years prior to testing. Slight motoric impairments (weakness) remain in the right arm and leg but the patient is mobile with a cane.

Functional Deficits

D.G. has left pulvinar lesion anterior (partly like T.N), which extends into posterior (combines the lesions of T.N. and C.R). Contralesional impairments were apparent in perceptual tasks (Arend et al., 2008).

J.L

Damage History

J.L. is a 65-year-old woman who suffered an intercerebral haemorrhage bilateral posterior thalamic bleed 3 years prior to testing. On the right side the haematoma was

small and limited to the pulvinar nucleus, while on the left the bleeding was slightly more extended.

Functional Deficits

This patient has not been tested in any other studies before.

4 Analysis

Data analysis was identical to procedures described in Chapters 2 and 3. The same elderly control group as for FEF patients were applied for statistical comparisons (Table 3b in appendix). The non-parametric Mann-Whitney U test has been preformed for statistical comparison of cpd and lateralization effects between the few pulvinar patients tested and eight healthy controls.

5 Results

5.1 Perceptual Sensitivity

Contrast sensitivity thresholds for individual patients and controls are shown in Table 4 in the appendix. The mean perceptual thresholds as calculated in Michelson contrast in % in pulvinar patients for fovea were 9.9 % (SEM=2.1) for periphery left 20.4 % (SEM=4.4) and right 34.4 % (SEM=4.1) while combined left and right was of 27.4 % (SEM=3.1). In controls mean perceptual thresholds for fovea were 7.9 % (SEM=1.1) for periphery left 16.7 % (SEM=2.4) and right 17.1 % (SEM=3.2) while combined left and right 16.9 % (SEM=2.7).

5.2 Lateralization Effects

The data described above indicate differences in perceptual sensitivity in left and in right visual fields in pulvinar patients. Cpd has been calculated for each of the peripheral loci separately. As Fig.40a/b illustrates in pulvinar patients cpd for left visual field (calculated as a ratio of perceptual thresholds in left visual field divided by perceptual thresholds in fovea) was M=2.1, SEM=0.2 while for right visual field it was of elevated ratio M=3.9, SEM=0.9 (Table 4 in appendix). Non-parametric independent Mann-Whitney U test revealed that the left visual field ratio (M=2.1, SEM=0.2) was not significantly higher than in healthy controls (M=2.1, SEM=0.2) ($p > .05$). However, the right visual field ratio (M=3.9, SEM=0.9) was significantly elevated in pulvinar patients when compared with healthy controls (M=2.1, SEM=0.1) (p=.017). Although

there is high variability of cpd for right visual field within the pulvinar patients group, there were no systematic perceptual sensitivity impairments, for example depending on the lesion side. For instance the right pulvinar damage did not always result in left visual field deficit, and left pulvinar damage did not always result in right visual field deficit. Therefore, results from all pulvinar patients have been averaged to see the general trend.

5.3 Centre-Periphery-Difference

Centre-periphery differences were combined for the left and right visual field for the pulvinar patients and using non-parametric independent Mann-Whitney U test revealed significantly elevated cpd in pulvinar patients (M=3.0, SEM=0.4) when compared with age-matched controls (M=2.1, SEM=0.1) (p=.016).

a) Lateralization of cpd **b) Cpd**

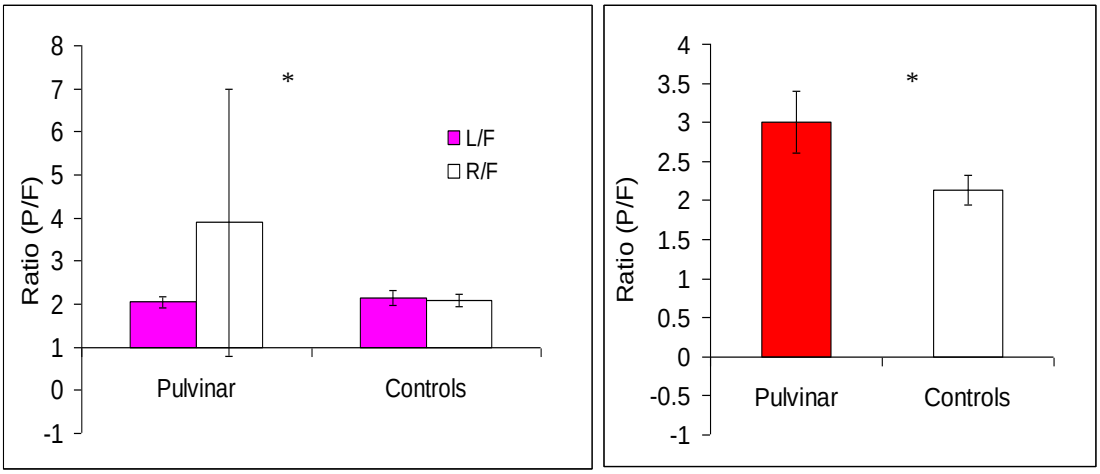


Figure 40a/b. Cpd in perceptual sensitivity for pulvinar patients and healthy age-matched controls calculated as a ratio periphery (at 13 degrees eccentricity) divided by fovea (ratio P/F). a) Lateralization effects. Left visual field cpd in pulvinar patients is significantly elevated when compared with healthy controls (p=.017). b) Cpd averaged over both visual fields is significantly elevated in pulvinar patients when compared with healthy controls (p=.016).

6 Discussion

Due to ocular anchoring by foveal stimuli reported in earlier studies (Rafal et al., 2004), increased cpd was hypothesized in pulvinar patients. Accordingly, elevated cpd has been found in four pulvinar patients tested. Additionally, lateralization effects for cpd increase were found in this study. Pulvinar patients seemed to show slightly elevated perceptual sensitivity in all three retinal loci tested, however perceptual sensitivity in the right visual field was highly impaired resulting in higher cpd ratios.

However, high interindividual differences were prominent for the pulvinar patient group tested. Some of the patients showed improved foveal processing and less impaired peripheral processing, other patients showed the opposite. However, the patients were of 2 age cohorts and showed differently lateralized lesions (2 were of left pulvinar damage, one of right pulvinar damage and one of bilateral pulvinar damage), which might have contributed to differences in lateralization of perceptual sensitivity. For instance, the young patient C.R. showed high cpd which was strikingly lateralised towards contralesional visual hemifield impairment. Other patients did not show clear contralesional effects. Previous studies with patient C.R. reported foveally tested temporal binding deficit (Arend et al. 2008) and when tested parafoveally (4 visual angles eccentricity) minor contralesional deficit in contrast processing. High deficits in contrast processing were reported only in the presence of visual distracters at 4 visual degrees in periphery and suggest visual filtering deficits (Snow et al., 2009). However, stimulus parameter employed in Snow et al., 2009 were different to those applied here. Stimulus duration of vertical Gabor patches was of 500 ms, while Gabor patches in this work were of 40ms presentation duration. Additionally, patients were tested at higher visual eccentricity (13 visual angle) than in Snow et al., (4 visual angle).

For future, it would be of interest to examine the entire visual field of pulvinar patients to examine exactly their patterns of perceptual sensitivity which might differ between different eccentricities. Additionally, an increased number of testing trials and increased number of pulvinar patients with homogenous pulvinar lesions should be tested to avoid or to examine interindividual differences.

CHAPTER 5

EXPERIMENTS 5 and 6

CPD AND COVERT ATTENTION AFTER FEF AND PULVINAR DAMAGE

1 Rationale

"Although there are a number of empirical approaches to the study of detection, most have not clearly separated between attentional factors and sensory factors and are thus incapable of providing an analysis of the relationship between the two. " (Posner, 1980)

Ruff et al., (2006) considered top-down control of covert attention as a possible explanation for outcomes of his FEF TMS stimulation on centre-periphery difference in contrast sensitivity. More studies have provided theoretical and empirical support for this assumption (Corbetta and Shulman, 1998, 2000: Kayser and Logothetis, 2006; Bender et al., 2008). There is strongly empirical evidence in humans suggesting that covert spatial attention can modulate neural sensitivity to peripheral stimuli behaviorally and at the neurophysiological level directly (Nobre et al., 1997). Additionally, studies in monkeys provided consistent evidence that FEF electrical stimulation changes performance in luminance discrimination tasks (Moore and Fallah, 2001, 2003, 2004). Complementary, psychophysical studies in humans indicate attentional influence on contrast perception (Hawkins et al., 1990; Handy at al., 1996; Muller and Humphreys, 1991; Sumner et al., 2006). This was often shown with visuospatial cues combining the features top-down and bottom-up manipulation of covert and overt attention (Posner, 1980; Müller and Rabbitt, 1989a; Smith et al., 2005, 2009; Carrasco et al., 2000; Carrasco et al., 2004; 2008, Pestilli and Carassco, 2005; Pestilli et al., 2007; Carrasco and Yeshurun, 1998; Yeshurun and Carrasco, 1998).

Although, Ruff et al., interpreted their results in the form of covert top-down attention, many studies suggest FEF involvement in bottom-up visuospatial processing (Corbetta and Shulman, 1998, 2000) and there is no direct evidence from the FEF TMS study of Ruff et al. that excludes bottom-up attentional processes on visual areas and on contrast perception. Therefore experiments in this chapter aimed to examine both: top-down and bottom-up covert attention manipulations and their influence on centre-periphery difference in contrast sensitivity. This has been investigated in patients with FEF and

contrasted with studies in patients with pulvinar lesions. The reason for this was that similar to FEF, the pulvinar were reported to be involved in both types of attentional control in monkeys (Robinson, 1993; Peterson et al. 1987; LaBerge and Buchsbaum, 1990; Grieve et al., 2000; Shipp, 2000; Weller et al. 2002; Chalupa et al., 1976; Bender, 1981; Beneveto and Miller, 1981) and in humans (Ward et al., 2002; Danziger et al., 2004; Rafal et al., 2004; Snow et al., 2009).

2 Scientific Background

Brain imaging, TMS and behavioural studies suggested strong links of the FEF area and effects of covert attention on oculomotor and low-level visual processing. However, patient studies seem to diverge as not reporting strong cueing effects on saccadic latencies, RT's or FOE (fixation-off-set effect) with chronic FEF damage. Attentional effects were tested in conjunction with oculomotor behaviour, measuring RT's or saccadic latencies and not visual perception in the form of perceptual thresholds. Therefore perceptual, attentional and oculomotor effects in FEF patients have not been differentiated (not disentangled). In pulvinar patients, contrast perception has been investigated recently (Snow et al., 2009). However, the experimental paradigm applied referred to perceptual filtering functions of the pulvinar. There is no study, which solely investigates visual properties in pulvinar patients or compared visual sensitivity between fovea and far periphery in pulvinar patients. The experiments presented here tested covert attention on contrast sensitivity without eye movements and examined sensitivity thresholds for the first time in FEF and pulvinar patients in fovea and in the periphery at 13 visual angles.

The paradigms applied were well established cueing paradigms (Posner, 1980; Carassco et al., 1998; Pestelli et al., 2007). In the top-down attentional paradigm, valid and neutral central arrows were applied, to consciously direct attention towards central or peripheral loci where Gabor patches occurred with 100% validity. In the bottom-up attention paradigm, valid and neutral peripheral cues (grey filled boxes) were displayed centrally and peripherally to summon attention also with 100% validity. This was done to simplify the task for patients and elderly controls. Contrast sensitivity thresholds were assessed by an orientation identification task (horizontal vs. vertical) using an adaptive staircase method as described in Chapters 2-4. Cueing effects were obtained as the ratio of contrast sensitivity of neutral (loci indifferent) versus cued trials.

3 Hypothesis

First, it was hypothesized that, if the attentional systems are well functioning in patients with FEF and pulvinar lesions, perceptual processing should be improved in both fovea and periphery. Second, if that is the case the deficits in contrast sensitivity measured in the previous chapters should also be made up for. Third, if the areas which are damaged play the same role in visuospatial attention control and perceptual processing, the perceptual deficits might not be made up for. Fourth, attentional effects could differ with damage of different brain areas. If the FEF area and the pulvinar belong to the same visuospatial covert attention functional network, damage of these areas might - when tested for perceptual processing - reveal how this area could co-work in this functional system.

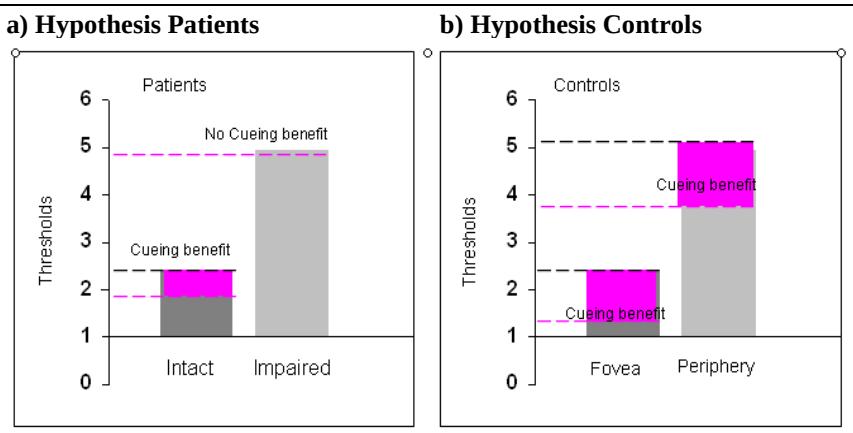


Figure 41a/b illustrates predictions of attentional effects on perceptual sensitivity thresholds. (a) in patients for intact and impaired retinal loci. Grey bars indicated assumed perceptual thresholds calculated as ratio (neutral/cued trials). Black dashed lines indicate thresholds obtained with neutral cues. The amount of attentional gain is indicated by the pink bar and pink dashed lines (which lower the visibility thresholds). (b) in healthy controls for fovea and periphery intact perceptual and attentional processing is expected in fovea and in periphery resulting in positive cueing effects at both retinal eccentricities.

Patient data indicates that contrary results might be expected in FEF patients when compared with pulvinar patients for foveal visual processing. While the FEF patients have shown deficient fixation abilities (which might be entirely oculomotor impairment) in previous studies, attentional cues could stabilize their vision resulting in increased perceptual sensitivity. On the contrary pulvinar patients have been reported to show "sticky" fixation (Watson et al., 1979; Ogren et al., 1984) which could already enhance perceptual sensitivity in the fovea, so that attentional cues would have a higher impact on perceptual sensitivity in the periphery than in the fovea. Both contrary results might have effects on peripheral processing, too.

Fig.41a/b illustrates possible impacts of attentional cueing in patients and in healthy controls, which might help to disentangle sensory from attentional impairments in theses patients. Perceptual sensitivity should increase in patients at the intact retinal loci (visual thresholds will decrease) when the attentional processing is applied. However, if the attentional processing is impaired as much as visual processing then no cueing benefits will occur at perceptually intact or perceptually impaired retinal loci. Note, it still remains unclear if attentional or perceptual processing is impaired if no attentional effects occur at perceptually impaired loci. This will be clarified however, when simultaneously perceptually intact retinal loci show cueing benefits.

4 Methods: Experiments 5 and 6

4.1 Set Up for Top-down and Bottom-up Deployment of Attention

The central cueing paradigm (i.e. deploying top-down attention) used central arrows to guide voluntary covert attentional shifts. Cues were 100% valid, and compared to a neutral condition in which all possible target locations were indicated. Targets could occur foveally or peripherally. Thus, a difference from the standard cueing paradigm was that the procedure included central targets as well as peripheral targets (both of which were cued centrally). In the second paradigm bottom-up cueing was applied. Stimuli near the location of a possible target flashed briefly just before target onset, to summon covert attention on the automatic level. In this paradigm there were also central and peripheral targets but the cues were central to central targets and peripheral cues were for peripheral targets. Two groups, patients with FEF and pulvinar lesions were tested and compared with age matched controls in exactly the same tasks.

4.2 Participants

The healthy control group consisted of two age cohorts to match the age of elderly and the young patient C.R. (age 20 years). The elderly age matched healthy control group was of mean age: 65, n=11 and the young age matched healthy control group was of mean age: 24, n=11, in top-down attentional paradigm. Additionally, exploratory 6 elderly (mean age: 66 years) and 4 young healthy controls (mean age: 21 years) have been tested in the bottom-up attentional paradigm. All participants gave informed consent in accordance with the local ethics committee before the study. Additionally, a fourth FEF patient, patient C.W, was available for attentional cueing experiments. Multiple slices of C.W are included in the appendix figure 1a (p. 204).

Patient C.W: The 60-year-old (at the time of testing) male stroke patient C.W. showed on an MRI scan a large infarction involving much of the right frontal and parietal lobes, indicating an infarct. Time from infarct was 11 years at the time of testing. Patient showed contralesional motor impairments with no functional use of the left hand.

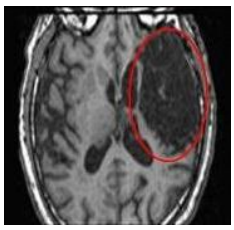


Figure 42. Patient C.W. MR scans which shows frontal right hemispherical lesion extending into parietal areas. For multiple slices see appendix figure 1a (p. 204).

4.3 Stimuli

Gabor patches of vertical and horizontal orientation as described in Chapter 2 were applied. A black dot was used as a fixation point in the following experiments and stimulus presentation was randomised. Prior to target presentation, cues were displayed.

4.4 Procedures

Cueing Paradigms

Top-Down Control of Attention: Red arrows placed in the center of the screen were employed to manipulate top-down covert attention and indicated left, right or central location of a subsequent Gabor patch. For the neutral condition, three joined centrally placed red arrows were displayed, each indicating different locations (Fig.43a).

Stimulus-Driven Control of Attention: In the bottom-up paradigm rectangular boxes of grey colour (mean luminance 25 cd/m^2) and size of 2x1cm, were displayed for 100ms. The bottom-up cues were placed just above the location where the subsequent Gabor patch was to be shown (Fig.43b).

Trial Sequence

The core presentation sequence in all attentional manipulation experiments consisted of a fixation point, which remained until stable fixation was achieved by a patient, followed by the display of a Gabor Patch for 40ms (Fig.43a/b). A trial sequence was

composed of a fixation point, a cue, and a target followed by a blank screen (Fig.43a/b). Each trial of fixation point-target sequence or of the cue-target sequence was initiated by a button-press by the experimenters, triggering a display of a fixation point till the participant fixated, followed by manual initialisation of a target/cue display, which was then proceeded by an interval of blank screen till participants verbal report. For peripheral trials, the clearly visible fixation point in the centre disappeared with the cue onset. The experimenter controlled the experimental flow in accordance with the patient's fixation abilities and readiness state. Such a procedure allowed for maximal adaptation to elderly participants' and to patients answers, behaviour and their resting needs. In order to counter balance for potential order confounds, adaptation or strategic eye movement shifts, cues and target locations as well as target orientation were presented randomly (as generated by the computer).

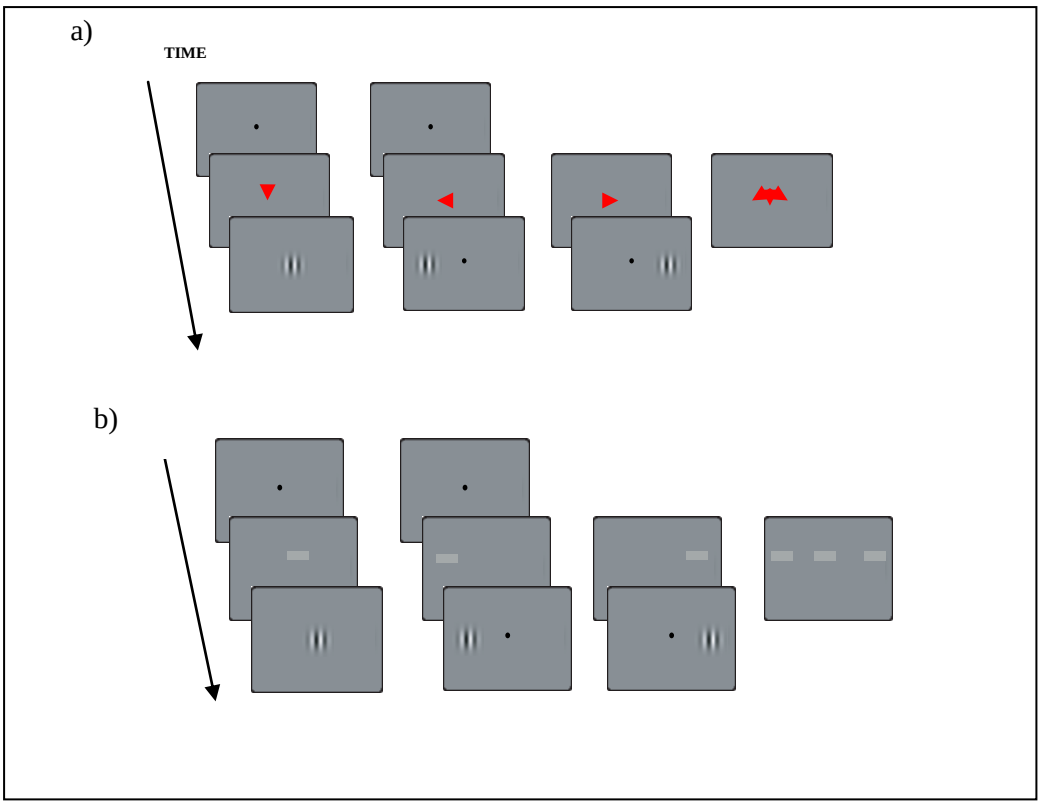


Figure 43a/b. Paradigms used to manipulate covert visuospatial attention: (a) top-down control of attentional shifts; (b) bottom-up control of attentional shifts. The stimulus sequence started with a fixation point and the stimulus sequence was triggered by the experimenter during stable fixation. This was monitored online using an eye tracker. In (a) red arrows placed vertically slightly off center were displayed and when fixation was stabilized in patients the target display triggered. The targets – horizontally or vertically oriented Gabor patches were displayed for 40 ms. In (b) the same parameters were applied but the cue was displayed for 40 ms only. The time parameter differences were necessary in order to avoid reversed effects during (b) such as inhibition of return.

Cueing Effects Estimation

Cueing effects were obtained by a forced-choice verbal response task within 120 trials per participant in one session. The experimental session duration was of ca. 40 minutes. A demonstration phase and a training sequence of 20 trials preceded the testing phase for each participant. The first block consisted of 60 trials; following blocks consisted of 120 trials. The first block implemented a bigger step size (1.4) and served the estimation of approximate threshold as well as a training phase. Participants were instructed to maintain fixation on the central fixation point during the trial sequence and to report the orientation of targets seen - without moving their eyes towards the peripheral targets. Participants were instructed to focus on the cue, which indicated the location of a proceeding target, as well as to be attentive to the expected location. Participants were reminded not to move their eyes towards the side of the expected direction of the target display. Stimulus initialization was during stable fixation and verbal responses were coded by the experimenter with key-presses accordingly, while the fixation was monitored online.

5 Analysis

Reversal values were obtained from all blocks to estimate the mean threshold value for each location tested at neutral (uncued) and cued trials. Ratios were calculated from reversal values uncued/cued. For comparison between neurological patients and healthy participants t-tests or non-parametric tests have been applied using SPSS19.

6 Results and Discussion

This results section is composed of three sections of which each is followed by a separate discussion. Section 1 describes and discusses results obtained from neutrally cued trials in the top-down cueing paradigm. Section 2 describes and discusses top-down cueing effects obtained in the same experiment. Section 3 describes and discusses bottom-up cueing effects and compares them with top-down cueing effects. Note that effects found for bottom-up attention and the comparisons made with results obtained in the top-down paradigm as well as the conclusions driven are preliminary due to small number of trials and controls tested in the bottom-up paradigm. Future studies should examine in more detail the patterns found here.

6.1. Perceptual Sensitivity obtained from Neutral Cues in Top-down Paradigm

Experiment 5a

6.1.1 Results: Centre-periphery Difference

Controls

Centre-periphery difference in perceptual sensitivity as revealed in top-down attentional paradigm has been calculated for healthy young controls (n=10) (M= 2.1, SME= 0.3) and healthy elderly controls (n=11) (M=1.8, SME=0.1). Two-sample t-test revealed non significant differences between the two age cohorts (two-tailed, $p > .05$). Therefore controls' data has been pooled together to be compared with patient groups. The combined healthy control group (n=21) showed significant differences for contrast sensitivity between fovea and periphery (left and right combined) (two-sample t-test (two-tailed), t=5.451, df=20, p=.001).

Patients

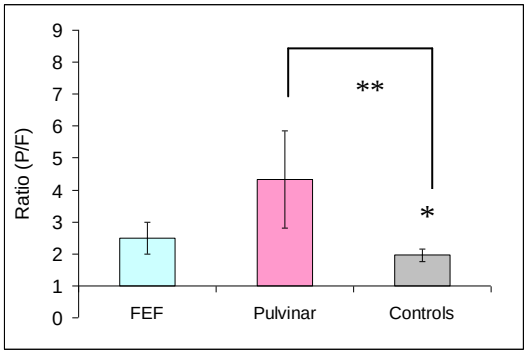
Centre-periphery difference was elevated in both patient groups but was however significantly elevated only for the pulvinar patient group (Md=21.75) when compared with healthy controls (Md=11.98) (non parametric Mann-Whitney U Test, Z = - 2. 605, two-tailed, p=.009). Centre-periphery difference in the FEF patient group (Md=18.33) did not reach significance level when compared with controls (Md=11.98) nor with the pulvinar patient group (non parametric Mann-Whitney U Test, two tailed, p>.05) (Fig.44a and Table 5a-c in appendix).

6.1.2 Results: Perceptual Sensitivity

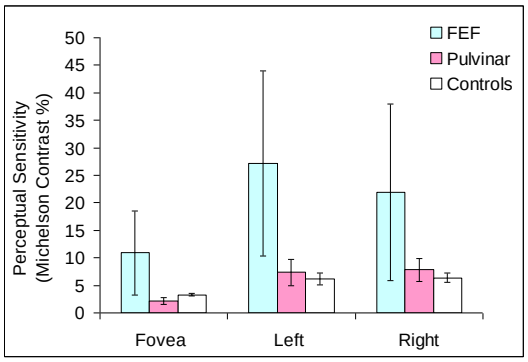
As shown in Fig. 44b. and Table 5a-c (appendix) for each patient group contrast sensitivity thresholds when compared between fovea (FEF M=10; Pulvinar M=2.2) periphery left (FEF M=27.2; Pulvinar M=7.4) or periphery right (FEF M=21.9; Pulvinar M=7.9) did not reach significance levels (non parametric Wilcoxon Sign Rank, p>.05) although contrast sensitivity thresholds for both patient groups did show descriptively a prominent elevation and the p-value was approximately 0.07 in most of

the fovea-periphery comparisons. In healthy controls, as expected, contrast sensitivity thresholds were lower in fovea (M=3.3, SEM=0.2) than in periphery left (M=6.2, SEM=0.45) or right (M=6.3, SEM=0.57) (left periphery: paired sample t-test, (two-tailed), t=-6.524, df=20, p=.00; right periphery (paired sample t-test, (two-tailed), t=-5.263, df=20, p=.00), and no significant difference was shown between both peripheral loci (paired sample t-test, (two-tailed), p>.05).

a) Cpd for FEF, pulvinar and controls



b) Contrast thresholds at three retinal loci



c) Cpd differences between FEF and Pulvinar

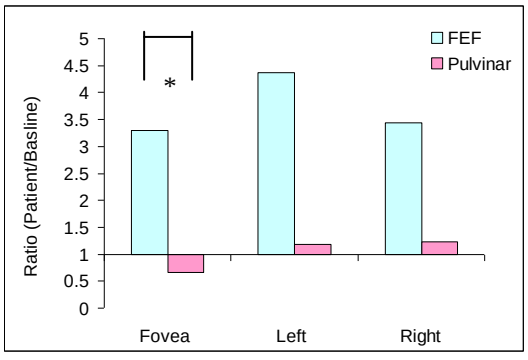


Figure 44a/b/c. Centre-periphery difference obtained in neutral trials for FEF and pulvinar patients, and controls (in top-down attentional trials). (a) Cpd in each group tested, calculated as a ratio from perceptual thresholds in periphery (left and right combined) and divided by perceptual thresholds in fovea (P/F). Cpd is highest in pulvinar patients and differs significantly from healthy controls as indicated by double asterix. Single asterix indicates the significant cpd within the control group (b) perceptual sensitivity thresholds calculated as Michelson Contrast in % for each retinal locus tested. FEF patients showed extremely increased perceptual thresholds in comparison to pulvinar patient group and healthy controls. This indicates high perceptual impairment in all retinal loci tested, with highest impairment in the contralesional visual field. However, there was extreme intra group variability in the FEF patient group resulting in high standard errors (indicated by error bars). Pulvinar patients have shown a decreased perceptual threshold in the visual centre while increased in the periphery left and right when compared with healthy controls, no consistent pattern of lateralization effects show up in the group analysis. (c) The cpd ratio has been calculated for perceptual thresholds in FEF and pulvinar group separately each divided by perceptual thresholds obtained from the control group (baseline) for each retinal locus tested. Cpd differed significantly between FEF and pulvinar patients for fovea.

As shown in Fig.44c and in Table 5a-c (appendix) when patient groups were tested for contrast sensitivity differences for each location divided by contrast sensitivity values

obtained from controls (baseline), contrast sensitivity was significantly different in fovea for FEF patients (Md=6.25) as compared with the pulvinar patient group (Md=2.75) (non parametric Mann-Whitney U Test, Z = -2. 071, (two-tailed), p=0.38) but the differences for peripheral loci were not significant (non parametric Mann-Whitney U Test, p >.05).

6.1.2 Discussion: Contrast Sensitivity obtained from Neutral Cues in Top-Down Paradigm (Experiment 5a)

In the next section contrast sensitivity results from the neutral cueing condition will be discussed, interpreted and compared with results obtained from contrast thresholds estimation procedures described in Chapters 3 and 4. Finally, a conclusion about a possible indication for the fronto-pulvinar-occipital network will be proposed.

FEF Patients

FEF patients did not show significantly elevated centre-periphery difference when compared with healthy controls. Nonetheless, the trend in the data indicates towards smaller cpd than the pulvinar patients, but higher than cpd in healthy controls. On the other hand within group contrast sensitivity between fovea and periphery did not differ significantly. This is expected when FEF TMS acted as a lesion. However, the thresholds were elevated in both fovea and periphery in FEF patients and differed again as in Chapter 3 within the patient group. The extremely high signal to noise ratio which is evident in FEF group lowers the effects which then do not reach a significant level. This could be reduced via three methods: (a) collapsing the results from Chapters 3 and 5, if cpd in contrast thresholds do not differ significantly between the two experimental sessions, (b) the FEF patient group should be enlarged in future and (c) patients only with focal right FEF lesions should be tested. Interestingly, the FEF patients showed in both testing sessions (Chapter 3 and here) a tendency to contralesional deficits in contrast sensitivity, which indicates a small but robust pattern, which is consistent with other occulomotor and perceptual effects reported in FEF patients in earlier studies (Rafal et al., 2004). The contralesional elevation of perceptual thresholds in FEF patients would partly allow an explanation of FEF TMS results (Ruff et al., 2006) predicting that TMS acted on FEF in a subthreshold manner. However, if the results with a focused and enlarged group of right FEF lesioned patients remain with no difference in contrast sensitivity between fovea and periphery, this could be a clear indication for FEF TMS acting as a lesion. Thus, in conclusion the data presented here is too vague to draw final conclusions about the FEF TMS. However, a third

interpretation of the data is possible, which simply suggests that chronic FEF lesions are not comparable with transient FEF TMS effects. Therefore, both methods should be applied complementarily to deliver a better understanding of complex brain mechanisms and to illuminate functions of singular brain areas in the human brain.

Pulvinar Patients

Centre-periphery difference was significantly elevated for the pulvinar patient group when compared with healthy controls, which is consistent with results in Chapter 4. In the experimental session described in this chapter the pulvinar patient group showed high intra-group variability as it did in the lateralization of lesions. No consistent effects were found between perceptual impairment and the lateralization of lesions within the pulvinar patient group and between the testing sessions of contrast sensitivity (Chapter 4 and Chapter 5), which seems different from the very consistent results in the FEF patient group. Also previous studies (Snow et al., 2009; Ward et al., 2001, Arend et al., 2008; Rafal et al., 2004) found rather systematic contralesional effects. However, the tasks applied in this work investigated contrast perception at different eccentricities and the paradigm used was measuring thresholds at simple perceptual level (no saccadic or attentional aspects like filtering functions) were involved – contrary to earlier studies of pulvinar and thalamic patients.

Fronto-pulvinar-occipital Network

More importantly, for the understanding of the fronto-pulvinar-occipital network for visuospatial processing in humans the comparison of the two patient groups is indicative. By taking the robust contrast sensitivity thresholds obtained from 21 healthy participants as a baseline value the contrast sensitivity thresholds in pulvinar and FEF patients have been compared. The results of this comparison help to differentiate the roles of FEF and pulvinar in visuospatial processing network. The FEF patients were found to show impaired perceptual sensitivity in fovea while pulvinar patients have shown enhanced perceptual sensitivity in fovea. Both results are consistent with the hypothesis derived from previous occulomotor and attentional studies of these patients that longer fixation times can lead to better perceptual performance in pulvinar patients in the fovea while the opposite should happen with jiggling fixation in FEF patients. This suggests possible complementary functions of fixation/ fixation release neurons in the FEF area and the thalamic pulvinar, which further suggests that these areas indeed work within one functional network crucial for visuo-spatial processing.

For peripheral processing these two brain areas seem to show parallel than complementary effects. Impairment of both, FEF or pulvinar, resulted in the tendency towards impaired peripheral visual processing in the form of elevated contrast thresholds in the periphery. However, the cpd in pulvinar patients seems to be produced by improved foveal contrast processing with impaired peripheral processing. FEF patients showed in average extremely impaired contrast processing in both fovea and periphery – resulting in overall cpd increase which however did not reach significance level. FEF patients show small but consistent contralesional peripheral impairments in perceptual sensitivity which was not evident in pulvinar patients.

The presented behavioral results allow distinguishing the two brain areas in their impact for visuospatial processing within possibly one or two neural circuits. For future it still remains to answer if neural populations within and between both areas act separately or in synchrony to form two visuospatial processing streams, one involved in foveal and the other involved more in peripheral visual processing. The data presented here requires further support from increased number of patients tested.

6.2 Perceptual Sensitivity Gain with Top-Down Attentional Cueing (Experiment 5b)

6.2.1 Results

Fig.45a/b illustrates systematic differences in top-down cueing between and within patient groups and controls tested.

a) Cueing effects FEF, pulvinar, controls **b) Cueing effects ratio FEF/Pulvinar**

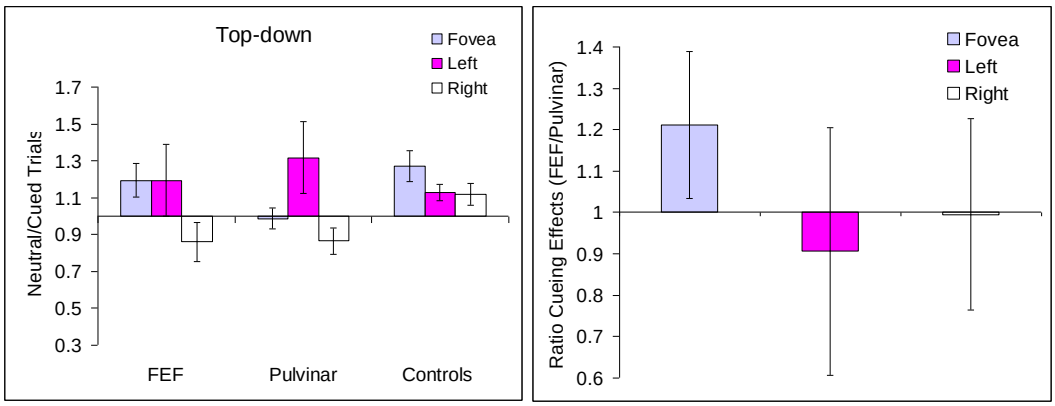


Figure 45a/b. Top-down cueing effects in FEF and pulvinar patients and age matched controls. (a) Calculated as ratio between visual thresholds obtained in neutral divided by threshold values obtained in cued trials. (b) Cueing effects ratio obtained from cueing values in the FEF patient group divided by cueing values obtained in the pulvinar patient group for each retinal locus. Values above ratio 1 indicate that cueing effects were bigger in FEF patients, while values below ratio 1 indicate that the cueing effects were bigger in pulvinar patients. Note that the axis in b) is stretched (ratio values 0.6-1.4) in order to provide a clear image of extremely small differences. None of the differences illustrated here were significant ($p>.05$).

As Fig. 45a shows healthy age matched controls show in average very small but positive cueing effects for all loci tested (fovea (M=1.2, SEM=0.1), periphery left (M=1.1, SEM=0.1), periphery right (M=1.1, SEM=0.1). FEF patients benefited from cueing effects in fovea (M=1.19, SEM=0.09) while pulvinar patients seem not to benefit much from foveal cueing (M=1.04, SEM=0.03) (Table 6 in appendix). Lateralization effects occurred in top-down cueing in both patient groups. Both the FEF and the pulvinar patient groups showed perceptual benefits with attentional top-down cuing effects in the left visual field (FEF periphery left (M=1.19, SEM=0.2); Pulvinar periphery left: (M=1.44, SEM=0.21) while cueing costs appeared in the right visual field in both (FEF periphery right (M=0.86, SEM=0.11); Pulvinar periphery right (M=0.81, SEM=0.07). This pattern is also illustrated in Fig.45b which shows cueing effects ratio obtained from cueing values in the FEF patient group divided by cueing values obtained in the pulvinar patient group for each retinal locus. Ratio values above 1 show that FEF patients benefited more from top-down cuing in fovea than the pulvinar patients (FEF/Pulvinar ratio in fovea (M=1.21, SEM=0.2)). Ratio values below 1 show that pulvinar patients benefited more from top-down cuing in the left visual field than the FEF patients as group (FEF/Pulvinar ratio periphery left (M=0.91, SEM=0.3)). Cueing costs in the right visual field did not differ much between both patient groups (FEF/Pulvinar ratio periphery right (M=0.99, SEM=0.2)).

Controls

Top-down cueing effects for young and elderly controls were not found to differ significantly (young controls: (fovea (M=1.15, SEM=0.9), periphery left (M=1.2, SEM=0.07), periphery right (M=1.15, SEM=0.1)), elderly controls: (fovea (M=1.41, SEM=0.13), periphery left (M=1.05, SEM=0.06), periphery right (M=1.07, SEM=0.06)) (two-sample t-test (two-tailed), $p > .05$) and were collapsed for further comparisons with patients (Table 6 in appendix).

Patients

Although there are interesting patterns in top-down cueing effects, they did not differ significantly between the loci tested in any of the patient groups when compared with healthy controls or between the FEF and pulvinar patient groups (non parametric Mann-Whitney U Test, two-tailed, $p>.05$). However, it might be useful to mention for purposes of future studies that the trends described above and illustrated by Fig.45a/b show a trend towards significance. These were the top-down cueing difference between

left and right visual fields in the FEF patients (non parametric Wilcoxon Sign Rank, p>.05) and between the FEF and the pulvinar patients for fovea (non parametric Mann-Whitney U Test, Z = -1. 845, (two-tailed), p=0.65) as well as top-down cueing effects in the right visual field when pulvinar patients were compared with the healthy control group (non parametric Mann-Whitney U Test, Z = -1. 071, (two-tailed), p=0.62).

6.2.2 Discussion

Top-down cueing effects show a distinct pattern in FEF and pulvinar patients, which however did not reach significance levels. The pattern of top-down cueing effects however seem to be consistent overall with results obtained in contrast perception without attentional cueing. Firstly, FEF patients show higher attentional cueing benefits in the fovea than the pulvinar patients. Perceptual sensitivity was extremely lowered in the FEF patient group according to Experiment 3 in Chapter 3 and thresholds obtained in the neutral cueing condition in Experiment 5 described in this chapter. However, on average the FEF patients seemed to be able to compensate for this when directional attention cues were applied in a top-down manner. FEF patients seem also to be able to compensate for contralesional deficits in the periphery and surprisingly show cueing deficits in the less impaired visual field (ipsilesional). Thus, FEF patients are able to benefit from top-down processing over most loci of their visual filed no matter how much impaired and independent from lateralization of the FEF damage.

Pulvinar patients have shown deficits in top-down cueing benefits in the right visual field similar to that of FEF patients and contrary to FEF patients also deficits in fovea. Pulvinar patients have shown less perceptual impairment in the periphery and improved perceptual sensitivity in the fovea when compared with FEF patients in previous experiments (Experiment 3 in Chapter 3 and in neutral cueing trials in Experiment 5). It seems that with maximum perceptual processing in the fovea, pulvinar patients do not benefit from top-down processing, which leads back to prolonged fixation in pulvinar patients (Rafal et al., 2004). It seems however, that pulvinar patients benefit from top-down cueing only in one peripheral visual field, the left visual field. Experiment 4 in Chapter 4 showed higher perceptual impairments in the right visual field. Pulvinar patients seem not to be able to compensate for perceptual deficits via top-down directed attention, which is contrary to FEF patients. However, pulvinar patients seem to be able to apply top-down directed attention in the less perceptually impaired visual field. It is however important to mention that none of the described effects reach significance level. Additionally, it is surprising that the right visual field did not benefit in either of

the patient groups. A replication of the experiment could cast light on how robust these results are.

It remains therefore to speculate if attentional and perceptual functions are to be disentangled in both of these patient groups. The rather inconsistent attentional benefits however could indicate a possible disentanglement of visual and attentional effects in visual hemifields in FEF patients which should be investigated in more detail in future. Interestingly, cueing effects in FEF patients for fovea and left visual field (contralesional) were the same. This could indicate equalization of attentional benefits for fovea and periphery left in FEF patients. This however does not lead to an equalization of perceptual sensitivity (foveal perceptual sensitivity in FEF patients was better than the periphery originally, thus top-down attention did not equalize the cpd difference in FEF patients). Overall it seems that top-down attention can be disentangled from perceptual sensitivity in FEF patients and in pulvinar patients too.

6.3 Perceptual Sensitivity Gain with Bottom-up Attentional Cueing (Experiment 6)

6.3.1 Results

Fig.46a/b and Table 7a-b in appendix illustrate bottom-up cueing effects (a) between and (b) within tested patient groups.

a) Cueing effects, FEF, pulvinar, controls **b) Cueing effects ratio FFF/Pulvinar**

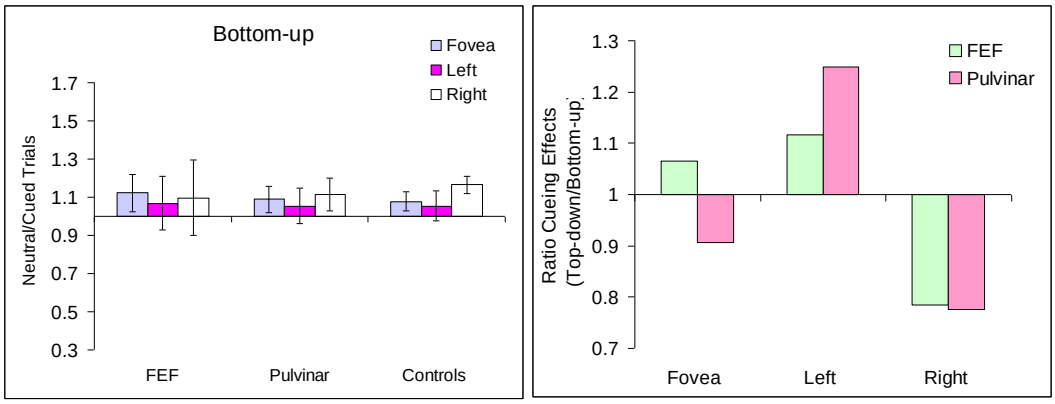


Figure 46a/b. Bottom-up attentional effects as a ratio between top-down cueing effects divided by bottom-up cueing effects. (a) Small but positive bottom-up cueing effects were evident in both patient groups and in healthy age-matched controls. (b) Top-down and bottom-up cueing effects were contrasted in FEF and pulvinar damage for three retinal loci tested. Note that the axis in b) is stretched (ratio values 0.7-1.3) in order to provide a clear image of the extremely small differences. None of the differences however were significant ($p>.05$) and illustrate only effects which can be seen only as hints for future studies.

Controls

Top-down cueing effects for young and elderly controls were found not to differ significantly (young controls: (fovea (M=0.99, SEM=0.5), periphery left (M=1.13, SEM=0.12), periphery right (M=1.28, SEM=0.04)), elderly controls: ((fovea (M=1.17, SEM=0.05), periphery left (M=0.98, SEM=0.05), periphery right (M=1.05, SEM=0.04)) (two-sample t-test (two-tailed), p >.05) and were collapsed for further comparisons with patients.

Patients

Bottom-up cueing effects on perceptual sensitivity did not differ significantly between the loci tested in any of the patient groups when compared with healthy controls or when compared between the FEF and pulvinar patient groups only (non parametric Mann-Whitney U Test, two-tailed, p>.05). In general, all groups benefited more from central cues than the peripheral; in particular sensitivity thresholds were improved in the right visual field in healthy controls and in patients.

6.3.2 Discussion

Bottom-up Cueing Effects

Bottom-up attentional effects seem not to be affected by any of the lesions examined. In fact both, FEF and pulvinar patients show slightly more foveal than peripheral cueing gain, of which the right visual field shows best cueing benefits. This is somehow surprising as it was expected that bottom-up attentional control would be impaired at least in pulvinar patients and perhaps in FEF patients, too. Previous brain imaging and monkey studies indicated involvement of these brain areas in visual saliency and bottom-up visual processing. Interestingly, some advantage in the right visual field has been shown in all groups which is in accordance with studies reporting RVF advantage for attentional effects. However, the bottom-up cuing effects were extremely small. Firstly, the task was extremely difficult for patients and would require more trials to learn it and to show consistent effects. Cueing effects to visibility thresholds have been reported rarely and are usually very small possibly due to the nature of the task in general. Signal-to-noise ratio could be increased by increasing a) amount of trials and training b) the sample size of patients.

Comparison of Bottom-up and Top-Down Cueing Effects

The comparison of top-down cueing effects with bottom-up cuing effects have shown differences in foveal processing but not peripheral processing between both patient groups. Cueing effects differed for fovea, small but positive perceptual sensitivity gain with top-down cueing was observed in FEF patients, while small perceptual costs were observed in pulvinar patients with top-down cueing (and perceptual sensitivity benefits with bottom-up cueing). However, there are some lateralization differences in cueing benefits when compared for left and right visual fields. Both, damage to FEF and pulvinar resulted in positive perceptual gain in the left visual field when the top-down cueing paradigm was used; while for right visual field bottom-up cueing resulted in perceptual sensitivity benefits. Thus, it can be assumed that FEF and pulvinar provide opposite mechanisms for fixation in the fovea, but seem not be distinguishable for cuing effects and mechanisms in the periphery left or right. It is however, somehow surprising that bottom-up and top-down attentional gain was different between the peripheral loci and not between the sites of the damage. The results could be explained by lateralization effects for healthy participants that indicate right visual field advantage for attentional effects, and left visual field advantage for visual perception (bottom-up saliency). Therefore, top down attentional control would be more impaired in the right visual field while bottom-up attentional control would be more impaired in the left visual field. Both brain areas, FEF and pulvinar could be passively passing such signals for left or right visual field without modifications (for example inhibitory effects) so that damage to both areas results in exactly the same effects for each visual field. However, these are only speculations as none of the results presented here reached significance levels. Only a replication study with increased number of patients and trials could reveal if these patterns are meaningful.

CHAPTER 6

EXPERIMENTS 7-9

CPD IN SENSORIMOTOR PROCESSES I

1 General Introduction to Chapter 6 and Chapter 7

1.1 Qualitative or Quantitative Differences between Foveal and Peripheral Visuomotor Processing

In line with experiments described in Chapters 2-5 it becomes evident that the fundamentals of human visual perception such as cpd in visual sensitivity shape complex brain mechanisms to ensure successful human-environment interactions. Chapters 2-5 were concerned with one of these processes – the top-down control of visuospatial processing and attention which examined, to what extent two brain areas are involved in these processes. The top-down control of covert visuospatial attention shifts can be considered as a visuo-motor control mechanism which increases visual sensitivity in the periphery but is not based on eye movements. Another control mechanism for visuo-motor processing in the brain has been reported to be influenced by cpd in visual sensitivity (Schlaghecken and Eimer, 2000). The cpd in visual sensitivity has been considered to have an impact on subconscious control mechanisms. This resulted in a proposal for a qualitative difference in foveal and peripheral sensorimotor processes.

Accordingly and initially, it was proposed that cpd in masked priming is closely linked to retinal sensitivity (Schlaghecken and Eimer; 2000); in other words, that NCE occurrence would depend on the strength of sensory traces elicited by mask primes and that perceptually strong primes were able to trigger activation and inhibition mechanisms in the motor system (Schlaghecken and Eimer; 2002). And so with larger peripheral stimuli, NCEs have been detected in the periphery. Thus it became accepted that no fundamental cpd for NCE remain when cortical magnification is controlled for (Lingnau and Vorberg, 2005). However, none of these studies provided evidence for NCE at extended retinal eccentricities. More importantly, it has not been tested whether the central and peripheral stimuli were equated in perceptual salience. Therefore the key prediction of the perceptual sensitivity hypothesis for the cpd in

priming has never been correctly tested. Consequently the following hypothesis will be tested in experiments described below. If foveal and peripheral primes are equated objectively (using threshold measurements), then the NCE/PCE should be identical for centre and periphery. The set of experiments introduced in Chapters 6 and 7 tested this prediction directly and also employed further eccentricities than Schlagecken and Eimer (2000) and Lingnau and Vorberg (2005). Additionally, the proposal is examined using a precise psychophysical method – which is a modified version of the visual thresholds estimation paradigm originally applied in Chapters 2-5.

1.2 Overview of Chapter 6 and Chapter 7

Chapter 6 describes 4 experiments concerned with the question of whether cpd in visual sensitivity is sufficient to account for visuo-motor priming differences between centre and periphery. Chapter 7 describes 3 experiments which examined aspects beyond cpd's visual sensitivity equation and succeeded in determination of the crucial aspect to obtain visuo-motor links originating in fovea and in the periphery.

2 General Methods

For all experiments described in Chapters 6 and 7, the procedure of prime equalization (Fig.47a) and priming effects (Fig.47b) were identical unless otherwise stated. The method is described in detail below and departures from this protocol are explained for subsequent experiments. All stimuli were displayed in three retinal positions: retinal centre, periphery left and right (6 degrees of visual angle) horizontally.

2.1 Apparatus

The stimuli were displayed in a dark room, on a Sony Triniton 19 inch GDM-F400T9 monitor, driven by a Cambridge Research Systems (CRS) ViSaGe graphics board at 100 Hz, which was calibrated with a CRS ColorCal and associated software. Viewing distance was 72 cm. Manual responses were made using a CRS CB6 button box. The subject's head was stabilised by a chin rest and a head rest. Stimulus control was provided by Matlab7.3. Eye tracking analysis was performed online; fixation was monitored by CRS high-speed video eye tracker. Trials on which saccades or blinks occurred and the eyes deviated outside a 1.5 degree window from fixation were discarded

2.2 Stimuli

Primes and targets were Gabor patches: phase-randomized sinusoidal gratings of 2 cycles per degree either vertical (90 degrees) or horizontal (180 degrees) orientation, presented within a sinusoidal envelope with a SD of 0.5 degrees for all three retinal locations tested. All stimuli were presented against a grey background of a luminance of 55 cd/m^2. Target presentation time for subliminal prime threshold estimation procedure was 40 ms and the starting contrast was set by the threshold procedure for each participant individually as described below. Masks were squared stimuli used to render Gabor patches invisible, e.g. to create subliminal primes. Masks consisted of an array of small squares and were of the same size as the Gabors. A constant total mask contrast (luminance amplitude) of 5 cd/m^2 was displayed and mask presentation time was 100 ms for all experiments, mask mean luminance was 55 cd/m^2. A mask was presented according to the retinal locus of the preceding Gabor.

2.3 Procedures

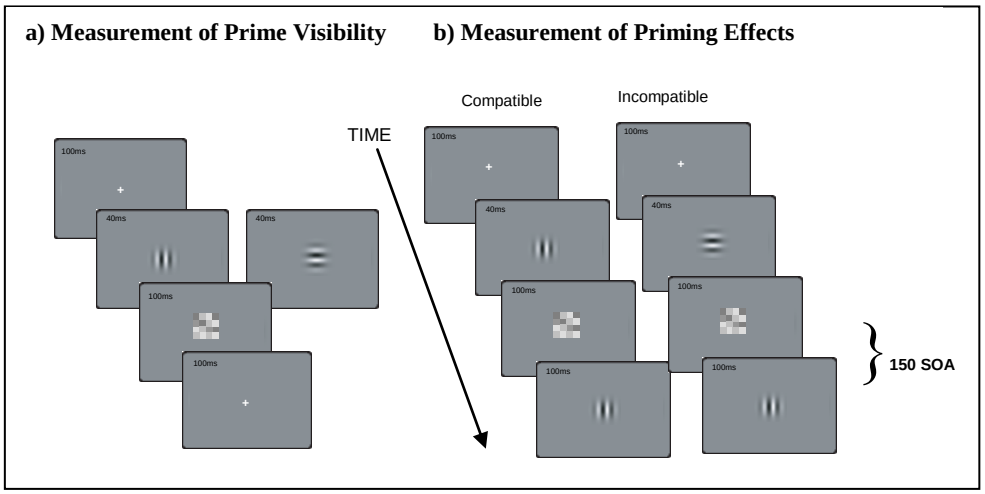


Figure 47a/b. Trial sequences applied to test (a) cpd in contrast sensitivity to subconscious primes and (b) cpd in visuo-motor priming. a) threshold measurement b) priming effects estimation procedure. Note that blank displays (fixation-prime interval, prime-mask interval and in (b) also mask onset-target-onset interval (SOA) are not shown in this schema in form of grey display as presented to participants – this is for simplification of the illustration). The sequence started with presentation of fixation cross for 100ms followed by prime display of 40ms, of which orientation – vertical or horizontal were randomly varied to match or not match the orientation of the target (compatible or incompatible trials). A square composed of small squares of varying luminance from trial to trial (maintaining constant mean luminance) rendered the prime invisible and was displayed for 100 ms. (Prime mask interval was 3 ms at which the observer saw a briefly displayed grey background). The mask target interval was displayed as grey background for 50 ms, while the target was displayed for 100 ms. This composed a SOA (stimulus onset asynchrony) or mask offset-target onset interval of 150 ms which is usually ideal to obtain NCE in fovea (Schlaghecken and Eimer, 1998).

In the experiments each participant took part in three identical sessions, each of which contained threshold measurements followed by priming estimation. Each session was ca. 20-30 minutes.

2.3.1 Threshold Measurement

Participants were required to identify the orientation (horizontal or vertical) of the masked Gabor patches in a two-alternative forced-choice task (2AFC) (Fig.47a). Each trial was self-initiated by a button-press, triggering a brief display of a fixation cross of 500 ms, an interval display of 300 ms, followed by a Gabor patch display of 40 ms followed by an interval display of 50 ms, after which the mask was displayed for 100 ms duration. Participants pressed one of two keys with the index- and middle finger of their right hand to indicate the orientation of a displayed masked Gabor patch. Index finger (left key on the response box) was for vertical orientation whereas the middle finger (right key on the response box) indicated the horizontally oriented Gabor patch, equivalently for all three retinal loci tested.

Threshold search started above threshold. The initial luminance amplitude of the Gabor was 5 cd/m^2 (9% contrast) for the foveal position or 10 cd/m^2 (18.2 % contrast) for the peripheral positions, and this value was decreased by a ratio of 1.2 if participants gave 3 correct responses in a row, while it was increased by the same ratio for a single incorrect response (a three-down, one-up staircase procedure). A reversal on the track occurred after one negative response. This procedure converges on a performance level of 79% correct (Levitt et al. 1971). The prime-mask sequence was presented in three retinal loci either in a randomised order (i.e. the staircases for each were interleaved) or blocked, depending on whether the masked prime procedure was to be randomised or blocked (see below). Generally, participants performed more than one block of the threshold measuring procedure and the starting contrast in the second or third block was set by an estimate of the threshold from the previous block. Trials on which blinks or saccades occurred (where the eyes deviated outside a 1.5 degree window from fixation) were discarded and the trial was repeated the next time that location was randomly selected.

2.3.2 Estimation of Priming Effects

Fig.47b shows the stimulus sequence for the estimation of priming effects. For central and the peripheral retinal locations, each trial sequence consisted of a fixation cross, a prime, a mask and a target with blank intervals in-between. Except for the target, the stimuli were identical to those used in the threshold measurement procedure. After the mask there was a blank interval of 50 ms, and then the target was presented for 100 ms in the same location as the prime and mask. For peripheral presentations, the fixation cross appeared again with prime onset and remained until target offset. Participants performed force-choice reaction task orientation identification. Participants were instructed to respond as quickly and accurately as possible to targets and to ignore stimuli preceding the target. Incompatible trials were obtained from trials when the prime and the target differed in orientation. Compatible trials were obtained from trials when the prime and the target were of identical orientation.

3 General Analysis

3.1 Thresholds

All data analysis was performed in Matlab7.3, Excel, WindowsXP 2006 and SPSS 16. The mean value of a visibility threshold (in cd/m^2) was obtained by averaging reversal values (direction reversals) for each of the retinal loci. Differences between the right vs. left visual field and fovea vs. periphery were tested using stats toolbox, Matlab07 or SPSS16. The levels at the last 5 direction reversals in the adaptive track (i.e. the turnaraound points) were averaged for each participant. This threshold value was lowerd by 10% in order to provide a contrast value for the primes in the priming task that would be likely to produce NCEs (e.g. Boy and Sumner, 2010).

3.2 Priming Effects

Reaction times (RT's) below 200ms and above 800ms were considered anticipations of errors, respectivly, and automaticlly deleted. Error Responses were removed from RT analysis. For each participant, mean RT's were obtained and combined respectivly into compatible and incompatible conditions for each retinal location. Since there was no

significant difference in performance between the left and right hemifield, the mean RT and compatibility effects for left and right for each participant were combined.

4 Experiments 7-9

Three experiments are described in this chapter. Experiments 7-8 are exploratory experiments (P1, P2) which examined the novel paradigm to establish parameters for robust NCE in the fovea first. In particular it was important to ensure that an abstract link between the direction of the orientation of a Gabor patch and the reaction to it could produce priming effects and see if such priming effects depend on the mask employed (P1 and P2). In all previous studies of the NCE, arrows or other simple stimuli have been used, normally with masks constructed with overlapping lines. We chose to use Gabors in order to have precise control over visibility thresholds. This meant that we had to design new masks to render the primes invisible since overlapping line masks were insufficient to do so. Therefore, it was important to first check that the basic NCE effect was present with these stimuli. Experiment 9a/b is the main experiment testing the cpd in NCE with perceptually equated primes in fovea and periphery. It incorporated the insights for best paradigm parameters shown in piloting experiments and also tested the potential attentional impact on the cpdp.

5 Experiment 7 (P1): The most efficient Mask for NCE in Fovea

5.1 Rationale

The first exploratory experiment examined the influence of shared visual features in primes and masks on NCE's in fovea only. The aim was to optimise the paradigm to obtain NCE in fovea before carrying on with testing in the periphery. As numerous studies indicated that when the mask and prime are sharing the same visual features the priming effects occur more easily (Jaskowski and Przekoracka-Krawczyk, 2005; Verleger et al., 2004, Sumner et al., 2008). However, providing proof for one of the hypothesis which explain how NCE emerges was out of scope and aim of this experiment. Nonetheless, the theories are introduced here to understand the deeper dilemmas of the topic and to reason on the paradigm applied here. Once the NCE in the fovea has been established the main question of the experiments was to explore NCE differences between periphery and fovea and to find more clues of how those are

interlinked with the assumed motor inhibition processes (Boy et al., 2008; Sumner, 2008).

5.2 Introduction

For the stimuli used in the series of experiments here, the orientation of the Gabors was the task relevant feature. Therefore it was of interest also to examine the influence on NCE of orientation features of the mask. In particular, the influence of iso-orientation (Saarela et al., 2008) for mask and prime/target was of interest. The features of the mask may have two roles. First, for feature relevance theory in triggering inhibition and second, in the ability of the mask to modulate the visibility of the prime (Sumner, 2008). There are indications from earlier literature that lateral inhibition in visual cortex acts for successively displayed stimuli with isofeatures. For instance, in primates Knierim and Van Essen (1992) showed that when a bar in the contextual field had the same orientation as the central bar, the cells' response was more strongly suppressed than when they had a contrasting orientation. Authors interpreted this as a neural correlate of the perceptual salience of feature singletons. Perceptual salience, in particular "subliminal perceptual salience" was of particular interest in this work, and this will be described later. In the following experiment, the emphasis was on examining the iso-orientation influence for prime/target and mask and their implications for manifestation of NCE.

5.3 Methods and Analysis

Participants

5 paid naive volunteers, 3 female and 2 male with normal or corrected to normal vision were tested. All participants were right-handed and of academic background, aged between 20 and 26 years (mean: 23 years). None had a history of neurological or psychiatric disorders or any sign of colour blindness or visual field defects. All gave informed consent in accordance with local ethics commiteee before the study.

Procedures and Analysis

The procedures followed are described in the general methods except as mentioned below. Two different types of masks were applied; i) masks were build from luminance

squares arranged in horizontal-vertical orientation or ii) in diagonal orientation. Primes and targets consisted of horizontally or vertically orientated Gabors. The mask orientations were applied in different blocks, thus two conditions were compared in a within-subject design. For each condition 4 blocks of 40 trials were performed. The results reported for the fourth block in each condition, to allow for practice effects (Boy and Sumner 2010). Prior to priming estimation, visibility thresholds were obtained for each type of mask.

5.4 Results

Thresholds

The results are shown in Table 8a in appendix. Thresholds obtained with diagonal oriented masks (M = 4 cd/m^2, SEM = 1.8) vs. horizontal oriented masks (M = 3.5 cd/m^2, SEM = 1.1) did not differ significantly (one-tailed, t = .29, df = 4, p = .79).

Priming Effects

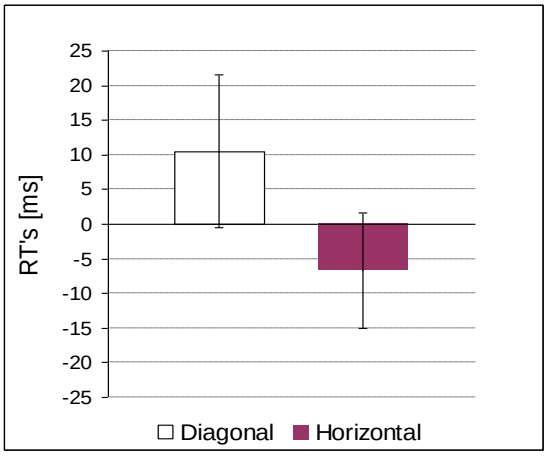


Figure 48. Experiment 7 (P1). Impact of shared visual features in prime and mask for priming effects in fovea. Mean priming effects with iso-oriented (horizontal) and an-iso-oriented (diagonal) mask-prime conditions calculated as RT's in ms for incompatible minus compatible trials. NCE were obtained in the iso-oriented prime-mask condition, i.e. when the orientation was horizontal in both the mask and the prime. Note that the effect here was not significant possibly due to a small number of participants and due to a high standard error (p>.05). However, there is a trend in the illustrated data which is in accordance with previous studies suggesting mask features effects facilitating NCE. Based on the conform results from previous studies following experiments will be conducted using iso-oriented prime-mask conditions.

As shown in Fig.48 and in Table 8ab in appendix for diagonal oriented masks (un-iso-oriented prime-mask combination) participants showed a mean positive compatibility effect (PCE) of 10.5 ms (*M=10.5, SEM* = 11.5). For horizontal oriented masks (isoriented prime mask combinations) participants showed small mean NCE of -6.8 ms (*M=-6.8, SEM = 8.3*). Although neither of these effects was significantly different from zero, there is a suggestion in the trend of the data that the horizontal masks are more likely to produce NCEs than diagonal masks which is in line with prior studies.

5.5 Discussion

There is a trend in the data that provides support for both theories, the "object updating" theory and the "mask triggered inhibition" (MTI) (Jaskowski and Verleger, 2007). The features in the mask which contained the same orientatation as the primes called for activation of the opposite orientation and inhibition of the repeated orientation. There is strong evidence from prior studies using arrows as primes and masks which share arrow features (Jaskowski and Przekoracka-Krawczyk, 2005; Lleras and Enns, 2004, 2006; Verleger et al., 2004). Jaskowski and Przekoracka-Krawczyk (2005) reported for masks with non shared prime features PCE of 53ms while for masks with features shared with primes NCE of -44ms.

However, this study used abstract stimuli to generate direction specific manual responses (left or right) and the small NCE found in this experiment is entirely in line with prior studies which found small NCE with abstract stimuli (prime and mask) sharing similar visual features (Lingnau and Vorberg, 2005; Jaskowski and Przekoracka-Krawczyk, 2005; Jaskowski and Verleger, 2007; Jaskowski and Sosarek, 2007; Sumner et al., 2008). For instance Sumner (2008) found NCE with shared features however "with insufficient effect size to account for the entire NCE". Thus, abstract stimuli seem to produce less NCE. Additionally, more recently reported NCEs sizes are about -10ms (Schlaghecken and Eimer, 2006), so that the NCE found here is not really surprisingly small for abstract stimuli.

There are reasons for this, which also has been discussed by Jaskowsik and Verleger, 2007, such as learning of visuo-motor associations (default activation of motor responses by arrows but not by abstract stimuli) and experimental procedures (randomised vs. blocked presentation of compatible vs. incompatible priming sequences) and which will be examined in subsequent experiments here. In addition, the trend in the data reported here as statistically insignificant could be due to the

number of participants, which was kept small due to the exploratory nature of this experiment. In conclusion, the trend of the data in this experiment is strongly supported by results of prior studies, which provides a strong basis for application of masks with shared prime features in all subsequent experiments.

6 Experiment 8 (P2): Equation of Prime Strength for Fovea & Periphery

This second exploratory experiment (P2) examined if the new abstract stimuli applied in the paradigm, the Gabor patches of two orientations (and not arrows as it was applied in previous studies) can produce visuo-motor associations which result in NCE's not only in fovea but also in the periphery. In line with the hypothesis of Schlaghecken and Eimer (2000, 2002) and experimental results of Lingnau and Vorberg (2005), NCE's in the fovea but also in the periphery after perceptual strength adjustment were expected.

6.1 Methods and Analysis

6.1.1 Procedures

This experiment was conducted without eye fixation monitoring. All other procedures were the same as described above. All trial types were randomly intermixed (3 locations, 2 orientations, compatible or incompatible). Participants performed 6 blocks of masked priming in total, over 3 sessions, and each session began with two blocks of the thresholding procedure for prime contrast (120 and 90 trials). The total number of priming trials obtained per locus was 240, 40 trials per retinal locus in one block. Each block consisted of 120 trails. Thus each participant performed 720 trials in total.

Thresholds were obtained from the 5 last reversals of the second block and lowered by 10% of their value to produce the prime strength applied in the priming procedure. Priming effects were calculated for the performance in the last block which was from 600th to 720th trials. The first blocks were for training purposes during which the visuo-motor association was established, thus allowing the assumed inhibition process gradually to build up and give the optimal chance of detecting an NCE in both periphery and fovea (Boy and Sumner, 2009). Incompatible trials were averaged over horizontal and vertical orientation conditions and so were the compatible trials. Priming effects were calculated for incompatible minus compatible trails for each locus. All effects for the peripheral condition were averaged over left and right location if the

difference between left and right was not significant. Significance levels and values were calculated with two-paired t-test or repeated measures ANOVA in SPSS16. Where appropriate, Greenhouse-Geisser adjustments to the degrees of freedom were performed (indicated in the Results section by ε).

Participants

7 paid naive volunteers, 3 female and 4 male with normal or corrected to normal vision were tested. All participants were right-handed and of academic background, aged between 22 and 38 years (mean: 27 years). None had a history of neurological or psychiatric disorders or any sign of colour blindness or visual field defects. All gave informed consent in accordance with the local ethics commiteee before the study.

6.2 Results

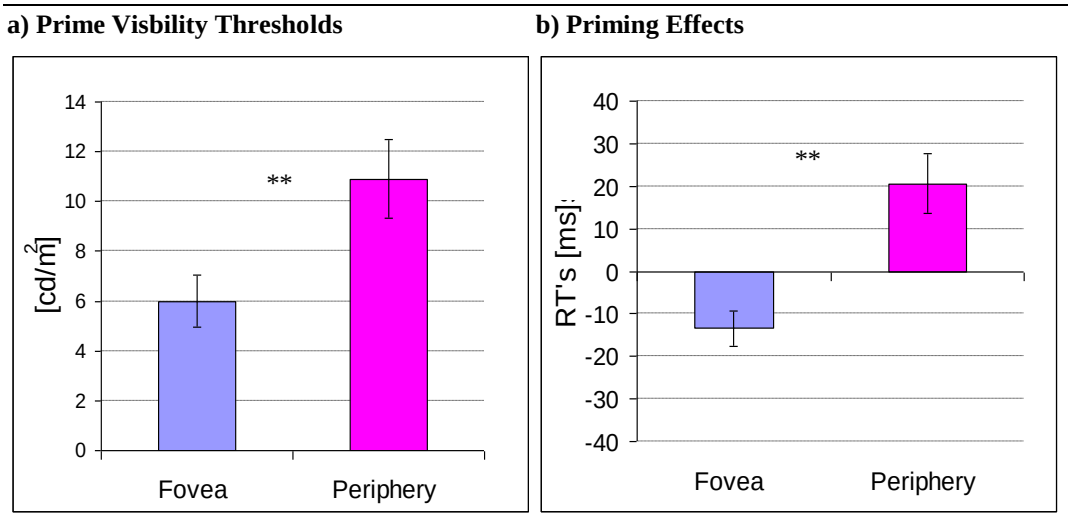


Figure 49a/b. Experimetnt 8 (P2). Cpd in visual sensitivity and in priming. Randomised trials procedure (no eye tracking). Means and standard mean errors for (a) Prime visibility thresholds, (b) Priming effects, both effects for fovea (blue) and periphery (magenta) (left and right combined (6 visual angles)). (a) calculated as luminance values in candela per square meter (cd/m^2) and (b) calculated as RT's in ms for incompatible minus compatible trials. Cpd in prime visibility thresholds was significant (t = -2.46, df = 6, p = .049) and the cpd for priming effects too (t = - 4.47, df = 6, p = .004). The obtained prime visibility thresholds were applied in the priming estimation. The prime strenght was equalised between fovea and periphery for each participant tested. In fovea NCE were found but in periphery only PCE were obtained. Therefore, the equation of prime strenght between fovea and periphery does not account for the lack of NCE in periphery.

Thresholds

As shown in Fig.49a and in Table 9a (appendix) thresholds obtained for fovea (M = 6 cd/m^2, SEM = 1.03) were, as expected, significantly lower than those obtained for peripheral locations (left and right combined) (M = 10.1 cd/m^2, SEM = 1.30, t = -2.46, df = 6, p = .049).

Priming Effects

As shown in Fig.49b and in Table 9b (appendix) for fovea, the mean negative compatibility effect (NCE) was -13.5 ms (SEM = 4.29) whereas for periphery there was a positive compatibility effect (PCE) of 20.6 ms (SEM = 7.12). The cpd for priming effects between the two locations was highly significant (t = - 4.47, df = 6, p = .004). The mean cpd for priming effects was ~ 34 ms.

6.3 Discussion

This experiment showed that with peripheral primes equated for perceptual strength with foveal primes, no NCE effects were found, even though a normal NCE appeared for the fovea. This is contrary to the hypothesis that the NCE in the center and periphery would be the same once perceptual sensitivity differences are taken into account.

However, in this experiment, there was an anomaly in the visibility threshold differences in primes measured for fovea and periphery. Two participants showed the reversed pattern, with better sensitivity in the periphery than in fovea. One of those participants reported astigmatism. It remains unclear if these two participants (or in fact, any other participants) did not follow the instruction not to move their eyes towards peripheral stimuli i.e. to maintain constant fixation on the center. Therefore, in all following experiments eye fixation was monitored with an eye-tracker and trials in which saccades towards the peripheral stimuli appeared were discharged from analysis.

7 Experiments 9a/b: Attentional Influence on CPDP

In the next section Experiments 9a and 9b are described, which are based on the parameter examination from the above described Experiments 1-2. Investigated are i) the cpd after the subliminal prime strength was adjusted and ii) attentional influences on cpd when the presentation of retinal loci was varied. Additionally, eye-movement monitoring was applied to ensure participants maintain fixation. In Experiment 9a, cpd was examined with a randomised presentation of retinal loci per block. In Experiment 9b retinal loci (center, periphery left, and periphery right) were presented in separated blocks.

7.1 Experiment 9a

7.1.1 Scientific Background

Studies on masked priming showed that focussing attention in time or space can modulate the effectiveness of invisible stimuli (Lachter et al., 2004; Schlaghecken and Eimer, 2000). Sumner et al., 2006 demonstrated that attention can directly enhance sensorimotor processes in a different manner to enhancing perceptual representation of stimuli (perceptual strength). In their study, the attentional manipulation did not mimic physical stimulus enhancement. Thus, attention can enhance unconscious sensorimotor processes directly and not via enhancement of perceptual strength. Attentional accounts for NCE were also considered in several other studies (Bavelier et al., 2000; Huber, 2008; Sohrabi and West, 2008). Sohrabi and West (2008) proposed in their model that NCE emerges due to an attentional refractory period which would act to slow the perceptual processing of the target in compatible trials.

Schlaghecken and Eimer (2000) tested if the cpd for NCE could be related to visual-spatial attention. Peripheral non-informative cues were used to summon attention to peripheral primes and targets. The results indicated that the cpd is independent of attentional factors but rather strongly related to the physiological inhomogenity of the retina. However it remains the case that previous experiments on the cpd may not have kept attentional factors the same for foveal and peripheral stimuli. Experiments 3a and 9b were designed to look at this in more detail. In particular, previous studies have presented fovea and periphery in different blocks, for the fovea there was only one

possible location, but for periphery there were two possible locations, right and left (Schlaghecken and Eimer, 2000)

In Experiment 9a attentional influences were modulated by randomised presentation of retinal loci for each of the experimental blocks. Participants fixated in the center, while stimuli were displayed in the fovea, right or left periphery in randomised order so that participants could not predict the location. In that way, participants had to attend to the entire visual field simultaneously and distribute their attentional resources over the entire visual filed. The randomisation procedure resembled the procedure Schlaghecken and Eimer (2000) applied for periphery.

In Experiment 9b participants were presented with each retinal locus in a separate block. Participants had to maintain fixation on the center again but were informed prior to the task where the stimuli would appear in the presented block. In that way, spatial uncertainty was reduced, which might have influenced the amount of NCE obtained. With attention covertly but focally focused on one retinal location, increased NCE are expected and therefore smaller periphery-fovea ratio for NCE (smaller cpd) were expected. The blocked procedure resembled the procedure Schlaghecken and Eimer (2000) applied for the fovea. Note that in the results section firstly priming effects will be introduced and illustrated for each of the experiments. Comparison between Experiment 9a and 9b i.e. for blocked vs. randomised paradigm will be illustrated in a later section of this chapter.

7.1.2 Methods

Participants

Eight paid naive volunteers, 1 female and 7 males with normal or corrected to normal vision were tested. All participants were right-handed and of academic background, aged between 20 and 35 years (mean: 26 years). None had a history of neurological or psychiatric disorders or any sign of colour blindness or visual field defects. All gave informed consent in accordance with the local ethics committee before the study.

Threshold Estimation

Participants performed 2 blocks of threshold measuring procedure, first of 120 trails and second of 90 trials duration. The prime-mask sequence was presented in three retinal loci in a randomised order.

Priming Estimation

Participants performed 6 blocks of priming measuring procedure, each 120 trails, 40 trials per retinal locus (3 x 40). Total number of trails per locus was 240 and total trials number was 720.

7.1.3 Analysis

Thresholds

Thresholds were obtained from 5 last reversals of the second block and lowered by 10% of their value to produce the prime strength applied in the priming estimation procedure. Significance levels and values for cpd were calculated using two-tailed, paired sample *t*-test in SPSS16.

Priming Effects

Reaction times (RT's) were calculated. The first blocks were for training purposes during which the visuo-motor association was established, thus allowing the assumed inhibition process to gradually build up (Boy and Sumner, 2009). Incompatible trials were averaged over horizontal and vertical orientation conditions and so were, the compatible trails. Priming effects were calculated for incompatible minus compatible trails for each condition. All effects for the peripheral condition were averaged over the left and right location if the difference between left and right was not significant. Significance levels and values were calculated with two-paired t-test or repeated measures ANOVA in SPSS16. Where appropriate, Greenhouse-Geisser adjustments to the degrees of freedom were performed (indicated in the Results section by ε).

7.1.4 Results

Thresholds

As shown in Table 10a in appendix visibility thresholds for foveally (M = 6.5 cd/m^2, SEM = 0.7) displayed masked Gabors were significantly lower than for peripherally (M = 13.0 cd/m^2, SEM = 1.6) displayed (left and right combined) (t = -4.554, df = 7, p = .003). Visibility thresholds for left (M = 13.2 cd/m^2, SEM = 2.2) and right (M = 12.8 cd/m^2, SEM = 1.9) peripheral location did not differ significantly (t =.188, df = 7, p = .85). The mean center-periphery ratio (ratio calculated as periphery/center) was 1.7 (SEM = 0.2).

Priming Effects

As shown in Fig. 50a and Table 10b (in appendix) for fovea on incompatible trials (M = 426.7 ms, SEM = 11.7) participants were faster than on compatible trials (M = 439.2 ms, SEM = 5.6) resulting in small negative compatibility effect (NCE) of -12.5 ms (SEM = 8.8). For peripheral condition (left and right combined) on incompatible trials (M = 459.4 ms, SEM = 14.8) participants were slower than on compatible trials (M = 428.5 ms, SEM = 9.7) resulting in positive compatibility effect (PCE) (M = 30.9 ms, SEM = 8.3). There was no main effect of locus or compatibility on reaction time, but a significant interaction locus x compatibility (F (1,7) = 1.9, p = .00, η_p^2= .96). Thus, priming effects for fovea were different from priming effects in periphery, with a very high effect size. This cpd for compatibility effects was in total ~43.5 ms.

7.1.5 Discussion

The above described experiment did not show NCE in the periphery but small NCE in fovea. The cpd was statistically significant, thus neither the attentional manipulation (randomised presentation of loci) nor the perceptual sensitivity adjustment for primes' visibility managed to evoke NCE's over the entire visual field.

Schlaghecken and Eimer (2002) obtained NCE in fovea but not in periphery when peripheral positions were randomly presented, while foveal condition was tested in separate blocks. Thus, all three locations were not randomised equally unlike in this experiment. It is possible that the small size of the NCE was due to randomised

presentation of loci in this experiment, which might have caused bigger decision and expectation uncertainty and therefore no reliability which might be necessary to establish a stable neural visuo-motor link resulting in the NCE.

Additionally, in particular the peripheral locations might have been affected by spatial uncertainty because spatial attentional resources needed to be spread over a greater visual field. Given the difficulty of the task, it remains possible that participants chose to attend more to the fovea region than the periphery. For this reason, we reduced attentional load in the next experiment by presenting each retinal locus in a separate condition.

7.2. Experiment 9b

A single locus presentation in one block should ensure that participants were able to focus covertly without eye movements comparably well in both the peripheral condition and the foveal condition.

7.2.1 Methods

In the blocked presentation of stimuli to counterbalance for order confounds stimuli were presented in the right or left periphery randomly according to the schema ABBA – BAAB and were preceded and followed by 2 blocks of central condition.

Participants

Eight paid naive volunteers, 2 females and 6 males with normal or corrected to normal vision were tested. All participants were right-handed and of academic background, aged between 19 and 25 years (mean: 22 years). None had a history of neurological or psychiatric disorders or any sign of colour blindness or visual field defects. All gave informed consent in accordance with local ethics committee before the study.

Thresholds Estimation

Masked Gabors' thresholds for each location were obtained in a blocked manner. Participants performed 2 blocks of threshold measuring procedure, first of 90 trails and second of 60 trials duration. The prime-mask sequence was presented in three retinal

loci in a blocked order. The trials number for threshold estimation was reduced to 60 and 40 trials per block as most of the participants participated in the prior experiment.

Priming Effect Estimation

In the priming estimation task participants performed 6 blocks, each of 40 trials, in 3 sessions. Total number of trails per locus was 240 and total trials number was 720.

7.2.2 Analysis

Thresholds

Thresholds were obtained from 5 last reversals of the second block and lowered by 10% of the obtained average value to construct the prime strength applied in the priming estimation procedure. Significance levels and values for cpd were calculated with two-paired t-test using SPSS16.

Priming Effects

Mean of last session was calculated. The first 2 sessions were considered as training sessions to establish the visuo-motor association and to allow for the inhibition process to gradually build up (Boy and Sumner, 2009). Compatibility effects and significance levels were calculated using repeated measurement ANOVA in SPSS16.

7.2.3 Results

Thresholds

As Table 11a in appendix shows, visibility thresholds for foveally (M = 5.5 cd/m^2, SEM = 0.7) displayed masked Gabors were significantly lower than for peripherally (M=9.2 cd/m^2, SEM=1.6) displayed (left and right combined) (t = -3.325, df = 7, p = .01). Visibility thresholds for left (M = 11.6 cd/m^2, SEM = 2.3) and right (M = 10.5 cd/m^2, SEM = 2.7) peripheral location did not differ significantly (t =.441, df = 7, p = .63). The mean center-periphery ratio (periphery/center) was 1.67 (SEM = 0.2).

Priming Effects

Fig.50b and Table 11b in appendix show for fovea on incompatible trials (*M* = 440.4 ms, *SEM* = 16.1) that participants were significantly faster than on compatible trials (*M* = 460.4 ms, *SEM* = 16.9) resulting in a mean NCE of 20 ms. For peripheral condition (left and right combined) on incompatible trials (*M* = 475.2 ms, *SEM* = 18.1) participants were slower than on compatible trials (*M* = 448.1 ms, *SEM* = 24.0) resulting in a mean PCE of 27 ms. There was no main effect of locus on reaction time and no main effect of compatibility. However, there was a highly significant interaction for locus x compatibility ($F(1,7) = 19.28$, $p=.003$, $\eta_p^2 = .73$). Thus, priming effects in fovea were highly significantly different from the priming effects in the periphery, with a high effect size. This cpd for compatibility effects was in total of ~47.5 ms.

a) Experiment 9a, randomised presentation **b) Experiment 9b, blocked presentation**

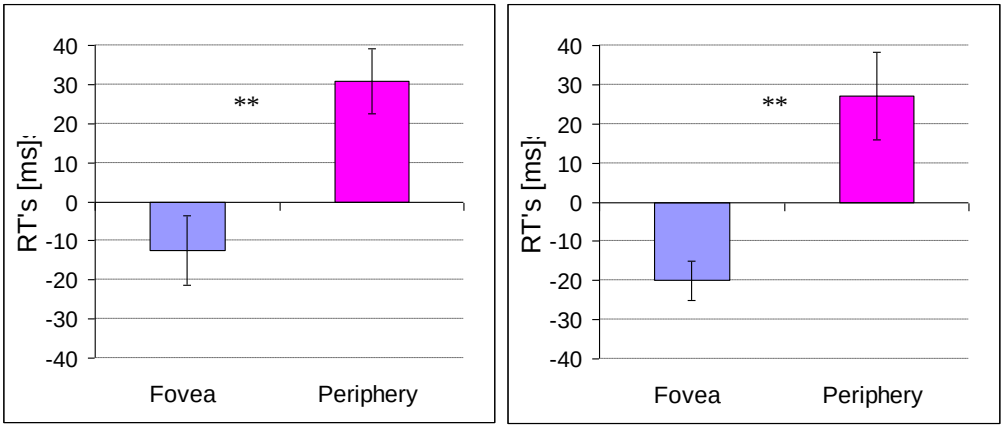


Figure 50a/b. Eperiment 9a/b. Attentional modulation of the cpd in NCE patterns. Mean of priming effects and standard mean errors calculated as RT's in ms for incompatible minus compatible trials in Experimetnt 3a and Expetriment 9b for fovea (blue) and periphery (magenta). a) Experiment 9a: randomised presentation of trials to the retinal loci (fovea, periphery left and periphery right). b) Experiment 3b: blocked presentation of trials to the retinal loci (fovea, periphery left and periphery right). Fig. a and b illustrate that the cpd for priming effects did not change significantly when prime-mask-target trials were presented in randomised or blocked manner. Negative numbers indicate NCE, positive numbers indicate PCE. In randomised presentation cpd for compatibility effects was in total of ~43.5 ms ($F(1,7) = 19.28$, $p=.003$, $\eta_p^2 = .73$). In blocked presentation cpd for compatibility effects was in total of ~47.5 ms ($F(1,7) = 1.9$, $p = .00$, $\eta_p^2 = .96$).

Thresholds and Training Effects

Thresholds

It was of interest to compare thresholds obtained with randomised vs. blocked paradigms. Fig.51 shows that in the blocked paradigm, thresholds in the peripheral condition were decreased (M=9.2 cd/m^2, SEM=1.6) when compared with the randomised paradigm (M = 13 cd/m^2, SEM = 1.6), resulting in a benefit on perceptual thresholds when spatial uncertainty is reduced. However this difference for periphery was n.s. (t =.-1.509, df = 7, p > 5). For foveal condition randomised (M = 6.5 cd/m^2, SEM = 0.7) vs. blocked (M = 5.5 cd/m^2, SEM = 0.7) presentation did not have much impact on the thresholds as expected. In total the periphery-center ratio was very similar, blocked (ratio=1.67, SEM = 0.2).vs. randomised (ratio=1.7, SEM = 0.2).

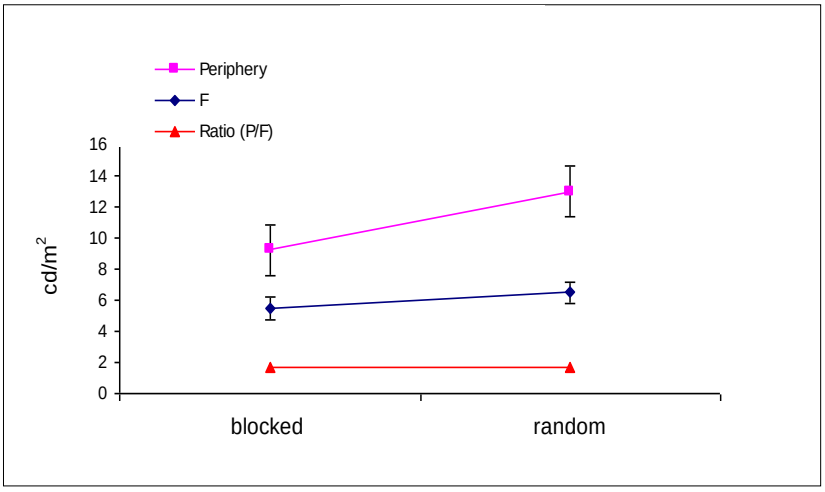


Figure 51. Experiment 9a/b. Attentional modulation of prime visibilty thresholds. Mean primes visibility thresholds and standard mean errors measured as luminance in candela per square meter (cd/m^2) for fovea (blue) and periphery (magenta) in randomised (Experiment 9a) or blocked (Experiment 9b) trial presentation. There was a minor threshold differnce between blocked and randomised trial presentation for peripheral loci and very minor difference for fovea, of which both were not significant, while the ratio between periphery and fovea remained unchanged in both paradigms.

Growing of Priming Effects with Training

Participants priming effects were measured in a high number of trials. This was necessary to establish a new visuo-motor association in participants. During the course of experiments it emerged that priming effects to a non-intuitive visuo-motor link such as right button-press to horizontal while left button press to vertical, require longer training to evoke the activation-inhibition process resulting in NCE. Thus, NCE (and PCE) increased with training as shown in Figure 52 and in Table 11c in appendix.

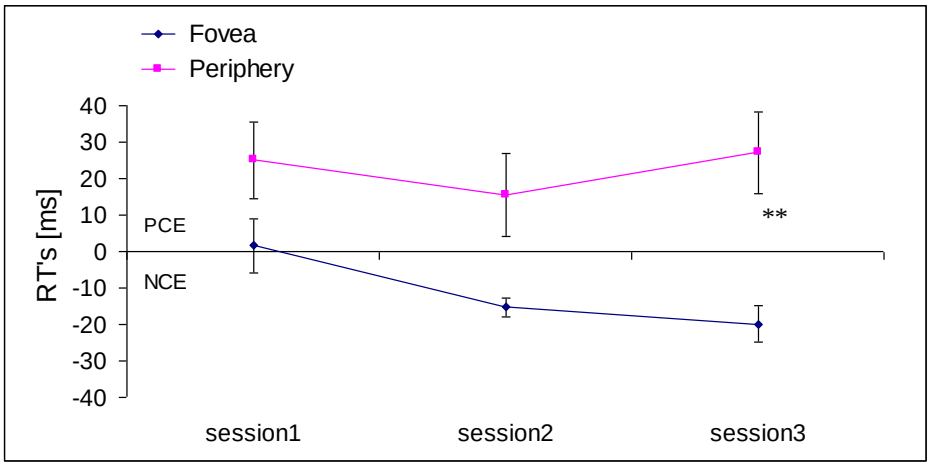


Figure 52. Experiment 9b. Grow of priming effects over 3 testing sessions (s1-s3) for periphery and fovea. Legend: Periphery: magenta, Fovea: blue. Priming effects measured as RT's in ms calculated for incompatible minus compatible trials. Both positive and negative priming effects seem to increase almost mirror-like with increasing practice. Priming effects in fovea grew increasingly negative while priming effects in periphery grew increasingly positive. Priming effects for fovea and periphery were significantly different in session 3 only (t = - 4.47, df = 7, p = .004) and the cpd was significantly different only between session one and session three (t = - 4.47, df = 7, p = .004).

As shown in Fig.52 and in Table 11c in appendix, the cpd for priming effects changed with the number of practice sessions. However, while in session 2-3 NCE was established for fovea, no NCE occured in periphery, on the contrary PCE grew with each session for periphery as the NCE grew with each training session for fovea. For fovea in session 1 PCE of 1.61 ms (*SEM* = 7.32) occurred, in session 2 NCE of -15.34 ms (*SEM* = 2.69) and in session 3 again NCE of -19.89 ms (*SEM* = 4.96). For periphery on the contrary only PCE occurred in session 1-3: in session 1 mean PCE of 25.08 ms (*SEM* = 10.59) occurred, in session 2 mean PCE of 15.56 ms (*SEM* = 11.45) occurred and in session 3 again mean PCE of -27.14 ms (*SEM* = 11.15) occurred. Accordingly,

the difference in priming effects for fovea and periphery calculated as RT's in periphery minus RT's in fovea were not significant for session 1 (t =.-2.051, df = 7, p > 5) but for session 2 (t =.-2.865, df = 7, p = .024) and highly significant for session 3 (t = - 4.394, df = 7, p = .003). The difference in priming effects between fovea and periphery in session there was of mean 47.03ms (*SEM* =10.72). Cpd in session one which was of mean 23.47 ms (*SEM* =11.44) when compared with cpd in session three, 47.03ms (*SEM* =10.72) was of a significant difference (t = - 2.476, df = 7, p = .042), while the cpd in session 1 when compared with cpd in session 2 (t = - .716, df = 7, p > 5), or compared with session 2 with session 3 were not significantly different (t =.-1.564, df = 7, p > 5).

7.2.4 Discussion

Experiment 9b showed that perceptual sensitivity adjustment did not produce NCE in the periphery. The cpd was statistically significant. The increase in the NCE for the fovea compared with Experiment 9a is consistent with results of Sumner et al., 2006 that attentional focus can indeed enhance directly the sensory-motor processes. However, interestingly a corresponding increase in the PCE did not occur for the peripheral results, potentially contradicting Sumner et al., 2006. This data might indicate that sensory-motor processes in the periphery are differently influenced or not influenced at all by attentional processes. For exact description of the attentional influence on priming effects in the periphery a replication of experiments analogous to Sumner et al., 2006 would be interesting for future experiments. The essential result here, however, is that neither the blocking nor randomisation procedure is responsible for the centre-periphery difference in priming effects. This difference remained robust whether locations were blocked or randomised.

The development of NCE over the time course of training in subliminal reaction task was described by Boy et al., 2008. Positive priming has been found to be influenced by training when new and arbitrary links between stimulus and responses are learned (Boy and Sumner, 2009). A stimulus-response (S-R) association is required to be strong enough to be activated by very weak subliminal primes. Mirroring the training effect of PCE, the NCE has been found to increase over the time course of training (Boy and Sumner, 2009). This dependency was not evident in previous studies in which well established stimulus-response associations such as right-pointing arrows for right button response etc. were applied (Jaskowski and Slosarek, 2007). Such established S-R associations would if at all show a very steep learning curve and have little impact on

the time point of NCE occurrence. However, there are previous studies indicating that practice is necessary to obtain robust priming effects (Klapp and Hinkley, 2002; Schlaghecken et al., 2007; Sumner, 2008). The "building up" of the visuo-motor link was monitored over several sessions, and the PCE and NCE development was traced in more detail for fovea and periphery in this experiment. The most important point is that the cpd cannot be explained by insufficient training for foveal or peripheral stimuli (e.g. different rates of learning for periphery compared to fovea) since the cpd appears to grow, not decrease, with training.

3.5 General Discussion (Experiments 7-9)

In all experiments described in this chapter, cpdp were investigated under conditions when primes were equalized in their perceptual strength for the centre and periphery. It was assumed, that with sufficiently strong primes NCE should occur and according to the motor-inhibition hypothesis (Schlaghecken and Eimer, 2000) the theoretical inhibitory threshold should be overcome by peripheral primes with strong representations. However, no NCE's were found with strong subliminal primes in periphery in all three experiments, while robust NCE's were traced at equivalent perceptual levels in the fovea. Therefore, it is concluded that the equalization of perceptual strength of primes for periphery and fovea is insufficient to equalize the priming effects measured for these locations.

This then raises the question of whether perceptual strength – as measured by threshold tasks, is of direct causal importance for priming tasks. Strong representations might be interpreted not only at the stage of perceptual activation but in terms of strong visuo-motor links; which is in accordance with the assumption of continuous flow of information from sensory to motor systems (Coles et al., 1985). It is possible that primes in the periphery require longer time intervals to initiate or establish visuo-motor links and equivalently longer time intervals to initiate motor inhibition. NCE's were reported when each of those timing parameters (inter-stimulus interval (ITS) prime-mask and mask-target interval (SOA)) were prolonged (Schlagheacken and Eimer, 2002; Lingnau and Vorberg, 2005). Thus, in the next series of experiments introduced in chapter 7 timing parameters were manipulated to investigate NCE in the periphery.

CHAPTER 7

EXPERIMENTS 10-12

CPD IN SENSORIMOTOR PROCESSES II

1. Introduction and Rationale

In Chapter 6, Experiments 7-9 investigated whether the perceptual sensitivity decrease in periphery can account for lack of negative compatibility effects for sensorimotor processing. It was found that objectively equating prime visibility did not succeed in generating NCE for periphery. However, very few previous studies indicate that visual stimuli presented in retinal periphery might take longer and follow time courses that are shifted (onsets delayed) or stretched (longer SOA's). Therefore, this chapter describes three experiments in which the SOA between prime and target was extended in an attempt to find an NCE in periphery.

As mentioned above, NCEs in fovea have been reported for longer between the prime-mask intervals (ISI) and longer mask-target interval (SOA) than the ones employed in Chapter 6. In combination with changes to prime size when ISI and SOA were prolonged, NCE were reported in para-foveal retinal loci up to 4.4 visual angles (Schlaghecken and Eimer, 1999; Schlaghecken and Eimer, 2000). This is based on the idea that prime-mask interval presents the amount of motor activation until the mask arrives whereas the mask-target SOA would determine the time available for motor inhibition process to develop (Lingnau and Vorberg, 2005). Since within the brain, there is cascaded processing and the mask does not simply shut off prime related activity, the prime-mask interval may have a similar effect to increasing the contrast of the prime – both make the prime more powerful. Given that the paradigm used here already manipulates prime contrast to equate visibility between fovea and periphery, the more critical interval for investigation is the mask-target interval, in which the inhibition causing the NCE is supposed to occur.

In Experiment 10a/b priming effects were systematically tested at different durations of mask-target SOA. Again abstract contrast stimuli were applied for primes and tested at further eccentricity left and right (6°). Visibility thresholds for peripheral primes were estimated, to ensure there was sufficient prime strength to elicit the motor activation phase. In Experiment 10b thresholds were tested prior and post priming task in three

sessions to trace the course of threshold change. Having found some evidence for an NCE in periphery in Experiment 10, Experiment 12 then examined different levels of prime visibility, to test whether prime visibility levels producing optimal NCEs were similar for periphery and fovea. This was an extension of an Experiment 11 which was an exploratory experiment and reported as P3, which showed that at very weak prime stimuli no NCE in fovea were found.

2. Experiments 10a/b: Influence of SOA on CPDP

In order to investigate whether NCEs appear in the periphery at longer time delays, the duration of the time interval between mask and target (SOA) were varied. Experiment 10a/b tested NCE in periphery only. In Experiment 10a priming effects were investigated at two different SOA durations. There were four separate sessions of testing, and thresholds were measured prior- and post- priming procedure in each of the first three sessions to examine if thresholds changed over the time of testing (training effects). In Experiment 10b five of the same participants took part and priming effects were investigated again at two different SOA durations.

2.1 Experiment 10a

2.1.1 Participants

Eight paid naive volunteers, 3 female and 5 male with normal or corrected to normal vision were tested. All participants were right-handed and of academic background, aged between 19 and 31 years (mean: 25 years). None had a history of neurological or psychiatric disorders or any sign of colour blindness or visual field defects. All gave informed consent in accordance with the local ethics committee before the study.

2.1.2 Methods

Threshold estimation

In each of the 3 sessions all eight participants performed 1 block of threshold measuring procedure prior and post priming task, each of 60 trials duration. The prime-mask sequence was presented in two peripheral loci at 6 visual angle left and right.

Priming estimation

In the priming estimation task participants performed 8 blocks of SOA 350 and 8 blocks of SOA 450, thus 4 blocks for each of the two peripheral loci tested for each of the SOA. Each block was of 40 trials. Blocks have been varied in the ABBA-AB or BAAB-BA manner. In sessions 1 and 2 participants performed 6 blocks each while in the final session 4 blocks, as calculated together for each SOA and peripheral locus. Total number of trails per SOA and per locus was 160 and total number of trials performed was 640.

2.1.3 Analysis

Thresholds

Thresholds were obtained from 5 last reversals in each block prior and post priming task in each of three sessions. Significance levels and values were calculated with two-paired t-test using SPSS16.

Priming Estimation

The experiments were carried for equal number for each peripheral loci. Priming effects were estimated for each SOA and collapsed over left and right peripheral location. Priming effects were calculated from RT's in incompatible minus compatible trails for each condition. Compatibility effects and significance levels were calculated using repeated measures ANOVA in SPSS16. The within subjects, repeated measures ANOVA was calculated from effects obtained in all 4 blocks. At the fourth block with a trial number of 640 no NCE occurred and the testing had to stop after block 4 due to increasing drop-outs of participants with increasing number of testing sessions. This is also evident in participant number in the next experiments where only 5 remaining participants (n=5) carried on to participate in the experiments.

2.1.4 Results

Thresholds

Fig.53 and Table 12 in appendix show mean threshold values for masked Gabors as obtained in pre- and post- measurement to priming task (all 8 participants are included). Thresholds were compared over 3 sessions. Since prime contrast values were set by the pre-test in each session, the important result is that the post test shows no reduction in threshold over the course of any session (Pre-Post main effect was not significant, $F(1,7) = 1.7$, $p = .23$, $\eta_p^2 = .19$). Therefore we can assume that primes did not become more visible during each session. The apparent slight reduction over the sessions is also not significant. For Session and the interaction Pre-Post x Session, Mauchly's test indicated that assumption of sphericity was violated; Session ($\chi^2(2) = 7.7$, $p > .05$, $\varepsilon = 58$), Pre-Post x Session ($\chi^2(2) = 7.9$, $p > .05$, $\varepsilon = 58$), therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity for Session ($F(1.2,8.2) = 3.8$, $p = .23$, $\eta_p^2 = .35$) and for Pre-Post x Session ($F(1.2,14) = 1.5$, $p = .45$, $\eta_p^2 = .02$)

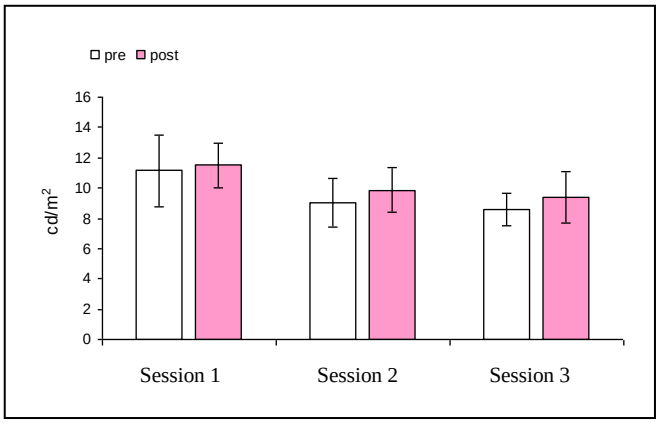


Figure 53. Mean primes visibility thresholds and standard mean errors obtained in three pre- & post testing sessions (s1-s3) measured as luminance in candela per square meter (cd/m^2) Before priming effects were tested visibility thresholds of primes were acquired and applied in the subsequent priming sequence. After that again visibility thresholds were measured to examine if the priming procedure itself would affect the visual sensitivity for invisible primes. This procedure has been repeated for each participant tested in three separate sessions (on separate days). Although the figure shows that there was a general decrease of thresholds over 3 testing sessions the effects were not significant in any of the combinations tested – within session or between sessions for pre or post tests.

For comparison reasons with results obtained in Experiment 10b in which 3 participants dropped out, priming results for Experiment 10a will be shown for the 5 participants who completed Experiment 10b. Table 13a (in appendix) shows results of all 8 participants in Experiment 10a while Table 13b (in appendix) for 5 participants, as shown in Fig.54a/b. Fig.54b shows that for SOA 450 in the periphery (left and right combined) participants were faster on compatible (M = 455.26 ms, SEM = 18.77) than on incompatible trials (M = 465.05 ms, SEM = 21.35), resulting in PCE of 9.78 ms as shown in Table 13d (in appendix). For SOA 350 in the periphery (left and right combined) on compatible (M = 420.6 ms, SEM = 15.59) were faster than on incompatible trails (M = 423.05 ms, SEM = 13.38), resulting in PCE of ~ 2.5 ms. ANOVA on RT's showed non significant effects for SOA ($F(1,7) = 1.8$, $p > .05$, $\eta_p^2 = .21$), significant effects for compability ($F(1,7) = 9.9$, $p = .02$, $\eta_p^2 = .59$) and no significant interaction for SOA x compability ($F(1,7) = .06$, $p > .05$, $\eta_p^2 = .01$). Additionally, as the figures show, there was no clear sign of any developing NCE over the four blocks.

Priming Effects

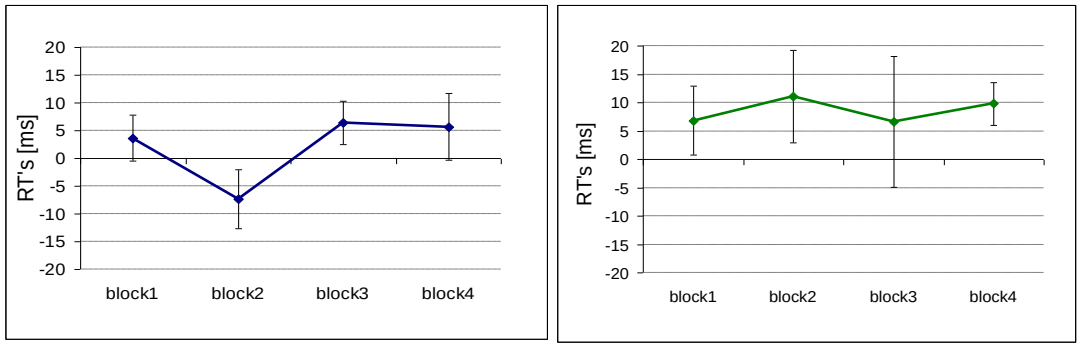


Figure 54a/b. Development of priming effects over the time course of testing (block 1-4) as calculated from RT's in incompatible minus compatible trials for periphery only (at 6 visual angle). (a) Mean reaction times: Mean reaction times at stimulus onset synchrony between mask and target of 350 ms (b) Mean reaction times and standard mean errors at stimulus onset asynchrony between mask and target of 450 ms. Even after the fourth practice block no NCE occurred at any of the SOA's.

2.1.5 Discussion

Previous research showed that there can be threshold decline which means perceptual performance improvement during psychometric measurements (Carasco et al.,

2002; Saarela et al., 2008). However, in this study after initial and extensive training thresholds stabilised or improved only slightly. Thus, thresholds were measured precisely enough to equate for perceptual sensitivity decrease from fovea to periphery. Peripherally displayed prime-mask-target sequences at two prolonged SOA's did not produce NCE's. However, since the eccentricity was only 6 visual angles into retinal periphery, a shorter SOA duration could be required (Lingnau and Vorberg, 2005; Schlagheacken and Eimer, 2002).

2.2 Experiment 10b

In fovea mask-target onset interval (SOA) around 60-100 ms were found to produce NCE's, however not shorter or longer SOA's (Schlaghecken and Eimer, 2000; Sumner and Brandwood, 2007). Thus, a "SOA - time window" might be appropriate for certain eccentricities to allow for visuo-motor inhibitory processes to emerge. Shorter SOA's than 350 ms and 450 ms could be sufficient for 6 visual angles in periphery to obtain NCE's. In this experiment priming effects were examined in periphery at SOA of 250ms duration and contrasted with retest at SOA of 450 ms duration; thus exploring the "time window" appropriate to initialise motor inhibition at 6 visual angles eccentricity.

2.2.1 Methods and Analysis

Participants

5 paid volunteers, 1 female and 4 male with normal or corrected to normal vision were tested. All participants were right-handed and of academic background, aged between 25 and 31 years (mean: 29 years). None had a history of neurological or psychiatric disorders or any sign of colour blindness or visual field defects. All gave informed consent in accordance with local ethics committee before the study. The aim was to test all the same participants as in experiment 1a for direct comparison, but 3 dropped out during the course of studies (each experiment had 4 blocks of up to an hour each). However, the results of 5 participants are traced continually.

Thresholds Estimation

All participants performed 1 block of threshold measuring procedure prior to the priming task, each of 60 trials duration. The prime-mask sequence was presented in two peripheral locations 6 visual angles left and right, in a blocked manner. A reduced number of trials were sufficient to estimate thresholds as most of the participants participated in previous experiments.

Priming Effects

Identical procedures were applied for priming effects estimation as described in Experiment 10a.

2.2.2 Results

Priming Effects

As shown in Fig.55a/b and in Table 13c (in appendix) for SOA 250 in the final block, on compatible trials (M = 429.34 ms, SEM = 15.08), RT's were found to be longer than on incompatible trails (M = 419.1 ms, SEM = 15.82), resulting in NCE of -9.64 ms. Individual data are shown in Fig.55b and in Table 13c in appendix. As appendix figure 3 (p. 218) illustrates that three participants showed a steady development towards NCE in block 4 whereas two participants showed a varied pattern of PCE-NCE which established with an NCE in block 4. Results for SOA 450r were similar to those in Experiment 10a, resulting in a small PCE even after 8 blocks of training (when calculated for Experiment 10a and this Experiment) and can be found in Table 13d in appendix. ANOVA was calculated for block 4 only as the preceding 3 blocks were training sessions in accordance with earlier experiments (Experiment 10b in this thesis) and studies by Boy et al., 2008. Boy and Sumner, 2009 have shown that training in high number of trials is required to obtain NCE. In this experiment ANOVA on RT's showed non significant effects for SOA ($F(2,8) = 3.4$, $p > .05$, $\eta_p^2 = .08$), and non significant effects for compability ($F(1,4) = 9.9$, $p > .05$, $\eta_p^2 = .16$) but significant interaction for SOA x compability ($F(2,8) = 6.7$, $p = .02$, $\eta_p^2 = .62$). Thus, at SOA 250 NCE started to appear after ca. 500 trials (block 3 and block 4) while at SOA 350 trials in Experiment 10a even after 560 trials (block 3 and block 4) no NCE

occurred, and no NCE occurred at SOA of 450 after the double amount of trials (over 1000 trials). However, to prove the stability of NCE at SOA 250 in periphery and to prove if the results are replicable another experiment was designed as described in the last section of this chapter.

a) Mask-Target SOA 250 **b) Mask-Target SOA 450**

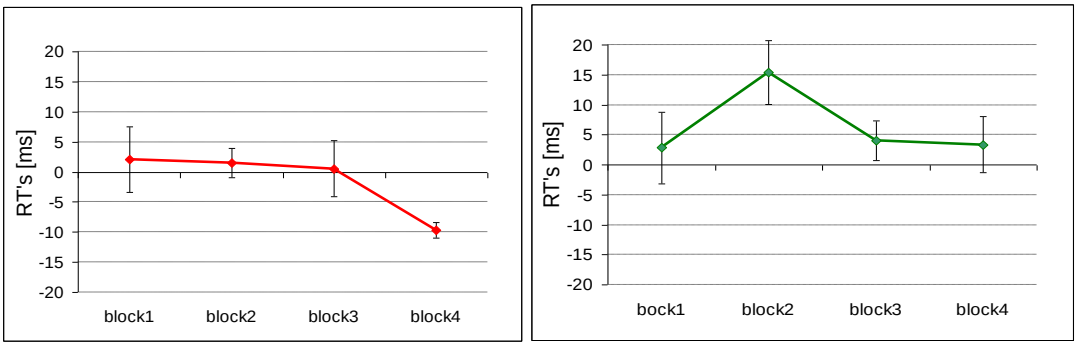


Figure 55a/b. Development of priming effects over the time course of testing (block 1-4) calculated as RT's in incompatible – compatible trials for periphery only (at 6 visual angle). (a) Mean reaction times: Mean reaction times at stimulus onset synchrony between mask and target of 250 ms (b) Mean reaction times and standard mean errors at stimulus onset asynchrony between mask and target of 450 ms repeated (450ms SOA has been tested against 350ms SOA firstly). In the fourth practice block NCE occurred at 250 ms SOA but no NCE occurred at repeated 450 SOA's (so after a double number of trials as for 250).

2.2.3 Discussion

An NCE was found in the peripheral locations at 6° with SOA of 250 ms. This supports the theory that allocating more time to the processing of subconscious peripheral primes can facilitate motor inhibition. Additionally, our results indicate that there might exist a preferable "time window" for inhibitory processes which increases with ascending eccentricity in retina. Another question emerges if in previous experiments the adjustment of thresholds for peripheral primes' strength was performed with enough precision. 90% of the obtained threshold value was applied in prime test to ensure the perceptual threshold is not visible to participants. However, although this value for prime contrast was known from previous experiments to be adequate to produce NCEs, the results from Chapter 7 clearly show it was not adequate to produce NCEs in periphery. Now that it has been found that the optimal timing parameters differ between fovea and periphery, the next question to ask in the final study is what the optimal visibility level is for primes presented at SOA 250 ms in the periphery for producing NCEs. The SOA of 250 ms will be applied also in the

next experiment – therefore it will be proved again if NCE can be obtained under this condition in the periphery as compared with fovea.

2.2.4 Conclusion

In Experiment 1b compability effects in periphery at SOA of 250 ms duration was contrasted with SOA of 450 ms which at last was tested with prolonged training (after it had been tested in this experiment first) and showed that not the training but the SOA duration is the critical factor for NCE in the periphery.

2.3 Experiment 11 (P3): Piloting Perceptually Weak Stimuli

2.3.1 Scientific Background and Rationale

Schlaghecken and Eimer (2002) found that when stimuli, reduced in their perceptual strength by random dot noise were applied in fovea, no NCE's occurred. For peripheral retinal locations when perceptual strength was increased (longer inter-stimulus interval between prime and mask), NCE were evident. Deducting from these results, Schlaghecken and Eimer (2002) suggested a threshold mechanism for triggering motor inhibition in a low-level motor control model (explained below). This model has been recently updated and supported by additional studies (Bowman et al., 2006). Thus it was of interest to examine cpd in NCE for very weak subliminal primes. In the previous experiments of Chapters 7 and 8, priming effects were estimated using subliminal luminance values which were 90% of the luminance value obtained from the threshold procedure. In this experiment, perceptually very weak subliminal primes of 50% of the threshold value obtained were applied. Before presenting this experiment the original model (Schlaghecken and Eimer, 2002) will be explained in the next section.

Functional Model of Early Motor Control

Schlaghecken and Eimer (2000, 2002) developed a simple functional model of early motor control (i.e. model of automatic inhibition), in which thresholds would trigger prime processes. This model (shown in Chapter 1) consists of an early sensory processing

subsystem, a motor control subsystem and a response execution stage. In the motor control system, activation (M+) and inhibition (M-) modules are assumed to receive a common input specific for their acting direction (- or +) from the early perceptual processing stage. The modules are interconnected in an asymmetric activation/inhibition loop; i.e. M+ is assumed to activate M- continuously, while M- was proposed to inhibit M+ only if the activation level (from M+) exceeded a criterion value (the inhibition threshold). Execution of an overt motor response would be initiated only if M+ activation exceeded a motor output threshold. An above-threshold activation of M- should be possible only if a strong perceptual input is subsequently masked. Therefore just as there is a time window (SOA window) for measuring the NCE, there should be a "prime-strength window" for measuring the NCE. Primes that are either too strong or too weak could cause some positive priming, but no NCE.

2.3.2 Methods, Procedures and Analysis

Participants

Eight paid naive volunteers, 3 female and 4 male with normal or corrected to normal vision were tested. All participants were right-handed and of academic background, aged between 20 and 32 years (mean: 26 years). None had a history of neurological or psychiatric disorders or any sign of colour blindness or visual field defects. All gave informed consent in accordance with the local ethics committee before the study.

Procedures

All procedures described in Experiment 7 (Chapter 6) were applied in this experiment. Primes and targets were horizontally or vertically orientated Gabor patches, masks were iso-oriented. Thresholds were measured prior to priming task. In both, the priming and the thresholds estimation procedure, retinal loci were displayed randomly within one block. In total there were four blocks of 120 trails displayed to a participant. After obtaining thresholds from applied staircase method the thresholds were lowered by half of their values, theoretically creating thresholds below chance level. Thus, they were never visible to participants.

2.3.3 Results

Thresholds

As shown in Fig.56a and in Table 14a in appendix visibility thresholds for foveally displayed masked Gabors were significantly lower (M = 7.2 cd/m^2, SEM = 0.65) than for peripherally displayed (left and right combined) (M = 12.9 cd/m^2, SEM = 1.1) (t = -4.6, df = 7, p = .002). Visibility thresholds for left (M = 11.8 cd/m^2, SEM = 1.1) and right (M = 12.9 cd/m^2, SEM = 1.8) peripheral location did not differ significantly (t = -.41, df = 7, p = .69). The mean center-periphery ratio (periphery/center) was 1.8 (SEM = 0.2).

Priming Effects

a) Prime Visibility Thresholds **b) Priming Effects**

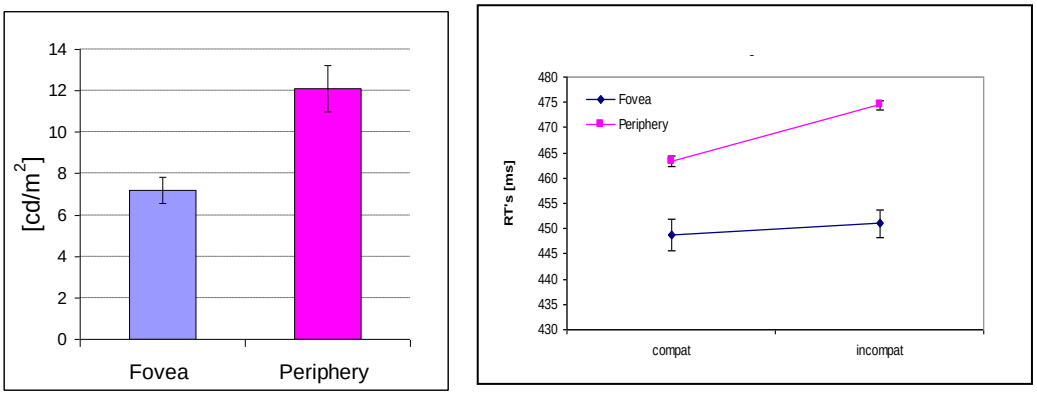


Figure 56a/b. Cpd and priming effects in experiment 12 (P3). a) Mean prime visibility theresholds and standard mean errors for fovea and periphery calculated as luminance in candela per square meter (cd/m2) b) Mean priming effects and standard mean errors for fovea and periphery calculated as reaction times for compatible and incompatible trials.

As shown in Fig.56b and in Table 14b in appendix, for fovea on compatible trials (M = 448.7 ms, SEM = 11.1) participants were numerically slightly faster than on incompatible trials (M = 451 ms, SEM = 5.5) resulting in minor PCE of 2.3 ms. For peripheral condition (left and right combined) on incompatible trials (M = 474.5 ms, SEM = 1.8) participants were numerically slower than on compatible trials (M = 463.3 ms, SEM = 2.1) resulting in PCE of 11.2 ms. However, the difference for compatibility effects was not significant (F(1,7) = 14.1, p > .05, η_p^2= .67). The difference for the locus condition (periphery vs. fovea) was not significant (F(1,7) = 9.3, p > .05, η_p^2= .57). The Cpd for priming effects

was numerically ~8.9 ms, with higher PCE in periphery than in fovea, however this difference was not significant (ANOVA on RT's, interaction locus x compability ($F(1,7) = 4.2$, $p > .05$, $\eta_p^2 = .38$).

2.3.4 Discussion

The exploratory experiment showed that extremely weak subliminal primes do not produce NCE in the fovea or in the periphery. Thus it was of interest to determine the exact threshold levels of prime's strength can produce NCE in fovea and in the periphery. This could describe also the perceptual threshold for the activation-inhibition pattern in the motor system.

2.4 Experiment 12. The Optimal Perceptual Threshold for 250ms SOA to obtain NCE in Periphery

2.4.1 Rationale

In Experiments 7-9 introduced in Chapter 6 and in Experiments 10a/b described in this chapter, visibility thresholds were estimated and this value was lowered by 10% for periphery and fovea respectively before being applied as primes in the priming task. However, it remains open if such procedure produces subliminal primes of enough and of absolutely equivalent strength for fovea and for periphery. The exploratory experiment showed that primes at very low visibility (low prime strength) do not elicit NCE in fovea and in periphery. Therefore it is crucial to apply primes of optimal strength even subliminally to obtain NCE. Such optimal visibility for subliminal primes might be different for center than for periphery. To test this, thresholds were re-measured using a psychometric procedure, the constant stimuli method, and full psychometric functions were fitted, which allowed accessing the exact contrast values for chosen performance levels. Luminance values for masked Gabors at 55%, 65% and 75%, correct discrimination performance levels were obtained individually and applied in the priming task. Priming effects were tested at the SOA of 250 ms duration for both the central and for left peripheral condition to replicate the findings from Experiment 1b; the occurrence of NCE at this particular SOA in the periphery.

2.4.2 Methods and Analysis

Participants

A psychometric approach was applied with 4 paid participants, 1 female and 3 male with normal or corrected to normal vision were tested. All participants were right-handed and of academic background, aged between 25 and 32 years (mean: 29 years). None had a history of neurological or psychiatric disorders or any sign of colour blindness or visual field defects. All gave informed consent in accordance with the local ethics committee before the study.

Threshold Estimation

Method of constant stimuli was applied in this experiment to measure performance on masked Gabors' orientation discrimination. Based on threshold values for masked Gabors obtained with adaptive staircase procedure in previous experiments, four luminance values distributed equally around the original value (two above and two below) were defined. In that way, the big disadvantage of constant stimuli method was reduced; i.e. the uncertainty was reduced to which mean threshold value to choose. All five values were randomly displayed at foveal or at the peripheral location at 6 visual angle. To reduce experimental impact on participants' drop out, periphery was tested only in the left hemifield. It was possible to do so as previous experiments showed no differences between thresholds obtained for left and right. Periphery and fovea were tested in separate blocks. Participants reported via key presses if the stimulus was of vertical or horizontal orientation. Prime's perceptual thresholds were estimated based on five luminance values displayed. Psychometric functions were fitted for foveal and peripheral condition for each of the four participants tested which precisely described the subliminal prime's strength obtained at 55%, 65% and 75% performance accuracy, which then were employed in priming task.

Priming Estimation

Priming effects were obtained in 4 blocks each of 60 trials, for the three performance levels estimated for periphery and fovea. Per condition there were 240 trials and in total 720 trials per retinal locus. Priming effects were calculated from RT's in incompatible minus compatible trails for each subliminal prime's strength level and for each retinal locus.

2.4.3 Results

Thresholds

Fig.57 shows psychometric functions for prime discrimination performance presented to fovea or to periphery as averaged over four participants tested (Tab.12a and figure 2 (p.218) in appendix). Mean priming values were obtained at 55%, 65% and 75% performance accuracy. Individual data for each of the participants is shown in Tables 12a and Fig.3a/b/c/d in appendix.

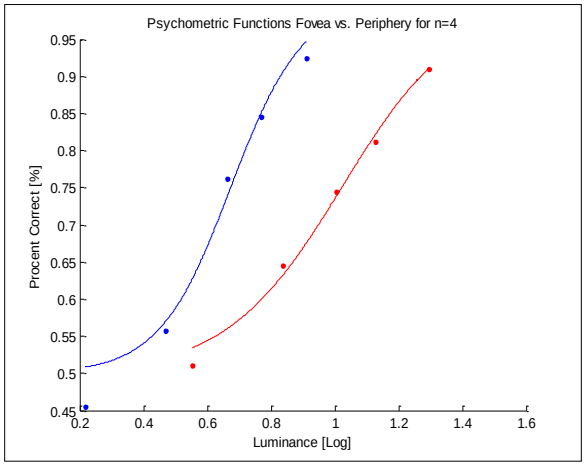


Figure 57. Psychometric functions for orientation discrimination accuracy in % with increasing contrast of Gabors as averaged over four participants and fitted for fovea and periphery. Luminace is described on a logarithmic scale on the x-axis. The probability to accurately discriminate the orientation at given luminance level of the Gabor is described in % (y-axis).

Priming Effects

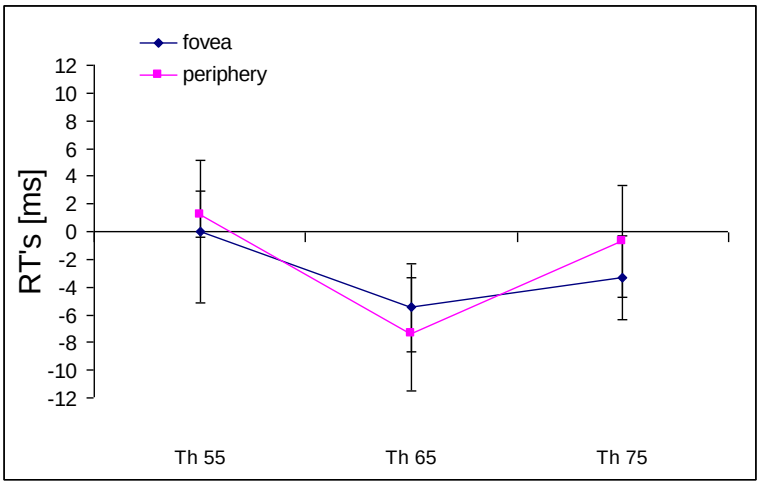


Figure 58. Priming effects calculated as RT's for compatible minus incompatible trials (y-axis) obtained at three different prime strength's (x-axis) for fovea and periphery and averaged over four participants tested.

Well-trained participants (Pb.T and Pb.J) showed almost disappearing differences in psychometric functions between periphery and fovea, resulting in small center-periphery ratios. These two participants show some threshold change, but the slope change dominated. The less experienced participants (Pb.K and Pb.U) showed bigger cpd in psychometric functions than the trained participants (right lateral shift on the x-axis), indicating a threshold change. In average there was a clear visual threshold difference between fovea and periphery.

Fig.58 demonstrates a clear trend for the NCE to be maximal for 65% prime discrimination performance as averaged over four participants. Three out of four participants showed for both fovea and periphery, peak effect of NCE at 65% threshold (Fovea: *M* = -5.5 ms, *SEM* = 3.3, Periphery: *M* = -7.4 ms, *SEM* = 4.1) (Table 15b in appendix). Not all participants would be expected to show exactly the same results, but there is a clear trend for the NCE to be maximal for 65% discrimination performance of the prime. Fig.58 demonstrates that NCE for periphery was similar to fovea when averaged for all participants.

2.4.4 Discussion

Firstly, for both the peripherally and the centrally tested primes, the highest NCEs tended to be found at 65% performance accuracy. The NCE's for fovea were, if anything, found to be slightly smaller than in periphery under these conditions. This suggests that 250ms SOA would not be an optimal timing for motor inhibition to central primes. This is consistent with previous research that has found 150 ms or 200 ms to be the optimal SOA for foveal primes (e.g. Brandwood and Sumner, 2008; Sumner et al., 2007).

At this experimental stage, we can conclude that the center-periphery dichotomy for visuo-motor processing is rather of quantitative than qualitative nature. Future experiments should focus on examination of further eccentricities to examine the link between eccentricity and the amount of time necessary to obtain motor inhibition from peripheral subconscious visual primes.

4 Conclusions

The main interest in Chapter 6 and Chapter 7 was to examine if and to what extent visuo-motor processes are dependent on the difference between foveal and peripheral visual processing – in particular the perceptual sensitivity drop off with increasing retinal eccentricity. In a set of experiments the lack of NCE from peripherally displayed subliminal primes was investigated. Various aspects of the priming paradigm were manipulated while perceptual visibility of primes was equalized between fovea and periphery. Contrary to previous theories the NCE in the periphery remained absent even when prime visibility was equated. It also remained absent when attentional aspects were manipulated. The crucial condition for NCE occurrence was the time interval between mask onset and target onset – a time window which is believed to be crucial for motor inhibitory processes to kick in. A "SOA time window" for foveal and para-foveal stimuli was found in previous literature; however it was not described for further eccentricities, nor were perceptual and timing properties investigated in separation or in such precision as it has been done here (Schlaghecken and Eimer, 1998, 2000, 2002; Lingnau and Vorberg, 2005).

5 General Discussion (Chapter 6-7)

There is converging evidence that visual information processing is already divided at early stage of visual processing as in the retina with a dominance of certain size of cell types in fovea vs. periphery (Wiesel and Hubel, 1966; De Monastario & Gouras, 1975; Heeger et al., 1996). The differences in cell size were suggested to imply differences in conduction velocities (Enroth-Cugell and Robson, 1966), which again might result in different onset latencies of brain areas involved (Nowak et al., 1997; Nowak et al., 1995; Mitzdorf and Singer; 1978, 1979). This indicates that at the perceptual level there will be differences between fovea and peripheral processing of stimuli – sub- or supra-consciously. However, for subliminal or unconscious visual processing as obtained in back-ward masking paradigms different neural routes and rules might apply. According to Lamme and Roelfsema (2000), Roelfsema et al., 2000; Ekstrom et al., 2008 response inhibition should critically depend on both prime-mask and mask-target SOA's.

Thus, results of this study are consistent with previous theoretical models on sensorimotor processes and suggest that inhibitory processes evolved firstly through conscious-visuo motor routes and can be revealed by subliminal primes in backward masking paradigms when sufficient processing time is provided. On the other hand, Vorberg et al., 1998, 2000 and Klapp and Hinkley (2002) found that response inhibition can also be traced with fully visible primes i.e. when pseudo-masks (masks which do not obliterate the prime stimulus) or blank interval replaced the mask. However, the onset delay was found to be longer for conscious primes than with invisible primes to reveal response inhibition, suggesting different processes for conscious and subliminally triggered motor processes. Thus, subliminal stimuli when applied as primes can elicit motor responses and activation in motor system perhaps even on a direct route which disengages from conscious processes of visual input.

When looking into cpd on visuo-motor processing from subliminal primes, one needs to consider the influence of mask on visual processing before understanding the motor activation processes. Traditional models of perceptuo-motor interactions suggested that visual perception and a motor response process construct discrete stages, activated successively (Sander, 1980). However, models that are more recent assume a continuous flow of information from sensory to motor systems, thus making it possible that a motor

response is conducted before perceptual analysis is finished (Coles et al., 1985). Research into backward masking showed that the masked stimulus evokes initial transients at low-level and at high-level visual areas (Rolls et al. 1999). A mask cannot catch up with very fast feedforward activation of visual areas but it can still influence the response, which is in a transient state at that time. Another suggestion is that the mask would disrupt recurrent interactions and the feed-back information would clash with mismatching feed-forward information from the mask in the low-level areas (Corthout et al., 2001).

However, such processes cannot explain prolonged SOA's for center and in particular for periphery required to elicit motor inhibition. Prolonged SOA might not be an indication of fast or slow cellular processing on visual feed-back level but rather on the level of visuo-motor connections after V1 (V1-motor cortex route, not retina-visual cortex route) and so the motor inhibitory process might be independent from visual entities. Thus, the initially believed quantitative difference for visuo-motor processing between fovea and periphery turns into a qualitative one with adjusted perceptual and neural timing parameters. Origin of the cpd might come from the fact that periphery usually is used to notice some visual input which then activated eye movement processing rather than manual processing, the first route might be fast and efficient as it ensures evolutionary advantage, the second route is usually less used and needs to be categorized into procedural motor learning, which takes longer to be established in terms of neural links (Wolfe et al., 1998).

In sum, the data suggest that there are no discrete stages for visuo-motor processing once a link has been established and that there are subconscious visuo-motor routes and mechanisms linking visual input from periphery to motor areas independent from conscious processing. On the perceptual level data showed that threshold differences disappear as the motor system takes over the task and stable visuo-motor links have been established. Therefore, the visual threshold does not "matter" anymore, the response above chance happens on a level, which is subconscious to visual perception (Sanders et al., 1974; Huxlin et al., 2009; Leh et al., 2010; Cowey, 2010; Kentridge 1999ab, 2004). This is in line with the theory of continuous visuo-motor processing. However, it remains a good question for future studies to answer to which extent the perceptual threshold on the one hand and the motor threshold on the other contribute to the NCE's phenomenon (Schlaghecken and Eimer, 2000).

5 General Summary

The synthesis of results obtained from 8 experiments as described in Chapters 6 and 7 suggests that perceptual sensitivity is not a sufficient explanation for the cpd in masked priming. Dissociation between prime discrimination performance and the magnitude of the NCE for foveally presented stimuli reported in previous studies was reported in earlier studies (Schlaghecken et al., 2002; Hermens et al., 2010). The equation for perceptual differences between fovea and periphery is not equivalent to equation of sensorimotor impact originating at the center or in the periphery of the retina. A distinction between *perceptual* sensitivity and *sensorimotor* sensitivity can be suggested to explain the NCE occurrence in periphery with prolongation of time which is needed for motor inhibitory processes to emerge. Data presented here imply that the sensorimotor link might be slightly slower for peripheral stimuli, so it takes 100 ms longer for the NCE to become established.

In sum, the accepted explanation for cpd in masked priming as accounted for by differences in perceptual sensitivity seems a rather premature suggestion. It is important to draw a distinction between *perceptual* and *sensorimotor* sensitivity, which can differ for center and periphery for various anatomical, neural and behavioural reasons– suggesting a higher motor inhibition threshold in periphery than in fovea.

Response inhibition was initially investigated with supraliminal primes in tasks like go/nogo where a conscious voluntary stop action is required. Recent studies provide evidence for subconscious inhibitory processes from subliminal primes. This subliminal inhibitory response was concluded from a reversed pattern of compability effects with subliminal primes presented in the center of visual field when delaying the time point of target display i.e. at longer mask-target stimulus onset asynchrony (SOA) (Schlaghecken et al., 1998). These results suggested that at a certain critical time after prime onset, the response to the target stimulus is selected during an inhibitory phase and therefore the response mapped to the prime is under inhibition, which is reflected in faster response on incompatible trials as compared to compatible trials (the NCE).

However, when the same primes were presented to the near periphery (peripheral primes) at 2.8 ° above or below fixation – initially no NCEs were reported (Schlaghecken and Eimer, 1997, 2000) for any type of response, including manual, saccadic eye movements

and vocal responses (Eimer and Schlaghecken, 2001). With masked primes at increasing retinal eccentricity, the NCE gradually turned into a PCE, and this effect was called the "*center-periphery asymmetry*" (Schlaghecken and Eimer, 2000), referred to here as "Center-periphery Difference" (cpd). Electrophysiological recordings in motor cortex revealed distinctive modulation of LRP waveforms for periphery and fovea. With longer SOA's activation-inhibition pattern occurred with foveal primes but activation only with peripheral primes (Eimer and Schlaghecken, 2003).

CHAPTER 8

GENERAL DISCUSSION

The discussion chapter is divided into several separate modules, a short theoretical introduction and integration followed by a summary and discussion of results and future directions for a) FEF patient studies (Chapters 3 and 5), followed by b) pulvinar patient studies (Chapters 4 and 5) and c) visuo-motor priming studies (Chapters 6 and 7). Visuo-motor priming studies have been discussed in detail in Chapter 7. Here an overview of all results is given with the emphasis to integrate data from all experiments (patients and priming) into a comprehensive model of foveal and peripheral routes belonging to the visuo-motor control circuits. A circuits model of integrated visuo-motor systems is proposed; i) the visuospatial attentional/ oculomotor, peripheral system composed of a network of occipital areas, the FEF and the pulvinar (mostly operating on the unconscious level, but influenced by conscious top-down processes) and ii) the foveal processing route which activate supra- and subliminally the manual visuo-motor control system composed of a network of brain areas such as the preSMA (and other motor, frontal and parietal areas). Finally, discussion of methods and theoretical integration of results of this work into current models of visual processing such as that of Milner and Goodale, 1992 and that of Ungerleider and Mishkin, 1982 will follow.

8.1 Theoretical Introduction and Integration

The present work contributes towards understanding of neural pathways and networks subservient to the integrated functions of vision and action (Sumner et al., 2004, Chambers et al. 2004, Anderson et al., 2007) and supramodal mechanisms (Hodgson et al., 1999) and extends beyond current theories of vision and action (Millner and Goodale, 1992; Ungerleider and Mishkin, 1989).

First, it has been proposed that several visuo-motor systems have evolved for different kinds of behavior as relatively independent functional modules (Goodale, 1996; Milner and Goodale, 2006). For instance in vertebrates the visuo-motor circuits for grasping vs. identification of visual targets are transmitted in separate pathways (Goodale, 1996). In humans, Hodgson et al., 1999, found “dissociations between saccadic and simple manual

responses", which however seem to operate within one supramodal attentional system for visual space.

Second, in humans, visuo-motor processes need to be processed in flexible circuits. Thus, in addition to the rather rigid subcortically regulated and separated visuo-motor systems, cortically controlled circuits in the human brain developed, to meet the demands of complex human-environment interactions (Milner and Goodale 1993, Goodale and Milner, 1992; Sumner et al., 2008). To such control mechanisms belong not only conscious top-down processes controlling all sorts of visuo-motor processes but also automatic and unconscious control mechanisms (e.g. in sensorimotor areas (Schlagecken and Eimer, 2002)). Such cortical conscious and unconscious control mechanisms involve processes which are inhibitory and excitatory to integrate visual, motor and visuo-motor (sensorimotor) systems and regulate them. However, there is still a gap in our understanding of how these complex control mechanisms interact with specific entities of the visual system, such as the central and peripheral processing in the retina. This work aimed to examine visuo-motor systems from this perspective.

Interestingly, although fovea processes conscious perception it can also trigger visuo-motor control mechanisms at the subliminal subconscious level, while the periphery which is considered to trigger eye movements unconsciously cannot get easy access to subconscious visuo-motor processing of manual actions. This way, these functionally distinct retinal areas seem to provide starting points of two separated visuo-motor control systems, one manual, the other oculomotor, which however, as shown in Chapter 7 can be linked and integrated via independent visuo-motor representations. There is a possibility that the attentional system does influence subconsciously manual visuo-motor control mechanisms. This has been shown by Sumner at al., 2008, which however could not be replicated with a simple and possibly too weak attentional manipulation in the experiment described in Chapter 6.

In Chapter 2, a paradigm to test centre-periphery difference in vision contrast sensitivity thresholds have been measured and then applied in all experiments. The aim was to measure cpd in contrast sensitivity in FEF (Chapter 3) and in pulvinar patients (Chapter 4) to access the roles and a possible co-work of these two brain areas for viusospatial processing. The cpd in contrast sensitivity should indicate their specific mechanisms for top-down control of covert visuospatial attention (Chapter 5), which successfully links vision and motor functions

in the brain (Millner and Goodale, 1992). Oculomotor functions and covert attentional shifts are usually understood as an automatic (subconscious) component of visuospatial processing , which has been tested too in the form of bottom-up control of covert visuospatial attention after FEF and pulvinar damage (Chapter 5).

Investigation of automatic links between visual and motor processes continues in Chapter 6 and Chapter 7, leaving aside patient studies and the investigation of brain damage and turning toward precise experiments in healthy participants. Chapter 6 and 7 deals with the visuo-motor system in the brain related to manual responses which is important for grasping and motor action in visual space (Millner and Goodale, 1992). Also for this kind of visuo-motor links cpd has been reported (Schlaghecken and Eimer, 1998). Chapters 6 and 7 contain a series of experiments designed to pin down the differences between fovea and periphery on the visual level (Ungerleider and Mishkin, 1982) and then on the visuo-motor control level (Milner and Goodale, 1992; Schlagheacken and Eimer, 1998; Lingnau and Vorberg, 2005).

8.2 Summary of Results, Interpretation and Future Directions

8.2.1 Cpd in Contrast Sensitivity in FEF Patients

Centre-periphery difference in visual sensitivity was measured in two brain areas, the FEF and the subcortical pulvinar to examine their involvement in visuospatial processing in humans. The approach was to test patients with damage to these areas and to examine their visual sensitivity and their ability to shift covert attention across the visual field. Based on previous TMS and imaging studies the difference in contrast perception between fovea and periphery was of particular interest. It has been shown in Chapters 3 and 5 that right FEF damage show impaired visual sensitivity in both fovea and periphery, in particular showing higher impairments to the contralesional side peripherally. This pattern indicates that transient TMS FEF effects in healthy participants (Ruff et al., 2006) are different to the effects of chronic lesions in FEF. TMS FEF has been assumed by Ruff et al., to act as a subthreshold activation not as a virtual lesion (Ruff et al., 2006). Cpd in contrast sensitivity after real lesions in FEF seem to support this assumption. This indicates that FEF is important for contrast sensitivity as suggested by Ruff et al., 2006 and Taylor et al., 2007.

However, tested FEF patients show a wide range of contrast sensitivity impairments, with the bilaterally damaged patients not showing any contrast sensitivity impairments but some variations in attentional modulation, while a patient with included right parietal damage (C.W) showed big lateralization effects. Thus a possible confound from lesions overlap, in patient C.W and in patient L.B (includes the DLPFC) might have had influences on their results.

8.2.2 Lesion Overlap – DLPFC and Parietal Areas

DLPFC has been found to be visuotopically organized (Sereno et al., 2005) and is known to be involved in visuospatial working memory, attentional and executive control (Miller and Cohen, 2001) (for more detail see Chapter 1). Vanni and Uutela (2000) found that the right precentral cortex (PrCeS) close to the FEF is sensitive to stimuli in all parts of the visual field. Other research suggests a complex integration of DLPC into visuospatial processing (Smith et al., 1996). However, PFC lesions have showed no apparent deficits in sensory discrimination or motor performance (Duncan et al., 1996). On the other hand, Corbetta et al. (1998 a,b,c) found activations during eye movements and covert attentional shifts in the whole PrCeS. It has been suggested that this increase of spatial tuning is equivalent to that found with higher visual areas during spatial attention tasks (Luck et al., 1997). Thus, DLPFC is a serious confound in the work presented here, however this is most evident only in the patient with bilateral FEF lesions.

It was reported that during suppression of eye movements FEF neurons, which are placed closely to the PrCeS encoding targets increased activity while activity declined in the movement-related cells in FEF. Thus, a damage of FEF might have consequences for fixation abilities. Another lesion overlap confound in the cpd examination in the FEF patient group might take origin in parietal areas, which are well known from neglect studies to be crucial for visuospatial attention and result in contralesional attentional deficits. Therefore, in future it is strongly suggested to test such patient groups separately, FEF, DLPFC, PrCeS and parietal lesions to examine functions and links of each of these brain areas in Visuospatial processing.

Interestingly, the size of lesions and deficits in contrast perception did not correlate (Chapter 3). Thus, the general processing capacity which is deficient after extensive brain damage found in stroke patients seems not to have affected visuospatial processing in patients tested.

Another important aspect which should be accounted for in studies with chronic lesions is that there is a considerable amount of plasticity and reorganisation in the human brain. This could explain why transient TMS FEF effects are different to visual impairments found after chronic FEF damage. This will be discussed in the methods section below.

8.2.3 Top-down Control of Covert Attention

Ruff et al., suggested that equalization of cpd in contrast sensitivity was a result of top-down covert attention. Therefore in Chapter 5, top-down control on attentional shifts was examined in FEF patients. Attentional shifts in FEF patients as averaged resulted in benefits in fovea and in the contralesional visual field (left periphery) while ipsilesional visual field seemed to be top-down control deficient (right periphery). FEF patients seem to benefit from attentional shifts in their previously reported perceptually deficient visual field. These results show that specific perceptual deficiencies after FEF lesions can be compensated and therefore it can be assumed that visual processing or top-down attentional control is not restricted to the FEF area only. This is consistent with brain system models of visuospatial attention (Corbetta and Shulman, 1998; Corbetta, et al., 2000; Kastner and Ungerleider, 2000; Kundsen, 2007). However, bilateral lesions of FEF extending to prefrontal areas seem to show impaired attentional abilities.

8.2.4 Bottom-up Control of Covert Attention

The results of bottom-up summoned attentional shifts differed from top-down cueing effects in the FEF patient group. In average patients with FEF damage have shown small attentional benefits to automatically summoned targets in fovea and in periphery. It therefore seems that automatic covert attention shifts are intact in FEF patients, while top-down control was unilaterally deficient. For the ipsilesional visual field top-down deficits were shown while bottom-up seems intact. Although again no significant meaning can be claimed one might speculate why this difference showed up. One explanation is the right visual field (RVF) advantage for attentional effects while left visual field (LVF) advantage exists for visual processing. If top-down attention is particularly affected in the right visual field, this will be consistent with observations in healthy participants, while visual processing and bottom-up summoned covert attention shows deficits in the left visual field. Left visual field has also

been more impaired in contrast sensitivity. This has been interpreted as contralesional deficit; however it could have been independent from the side of the lesion. Although some detailed explanations of the attentional results are provided, this is mainly to inspire future research, as the attentional results described in Chapter 5 did not reach any significance level.

8.2.5 Summary FEF Patient Studies

In summary, results from patients with chronic FEF lesions are in accordance with brain imaging studies which reported that FEF is a brain area which is engaged in visuosptial processing and in both types of attentional control (Corbetta and Shulman, 1998; Corbetta, et al., 2000; Kastner and Ungerleider, 2000; Kundsen, 2007). This however needs to be proved in bigger patient samples in the future.

8.3 Cpd in Contrast Sensitivity in Pulvinar Patients - Indications for a Fixation Network between FEF and Pulvinar?

Cpd in visual processing was increased in pulvinar patients when compared with FEF and healthy controls. Pulvinar patients have shown impairments in peripheral visual fields and improvement in fovea, which means the cpd was extended in both directions (Chapter 4 and Chapter 5). Pulvinar patients' improvement in visual processing in the fovea is consistent with "sticky" fixation found during saccades in humans after pulvinar damage (Watson et al., 1979; Ogren et al., 1984; Rafal et al., 2004). This is opposite to the mechanism which was shown in the fovea after FEF damage. Therefore, that author proposes that, FEF and pulvinar contribute to visuospatial processing and cooperate within a fixation network integrating mechanisms of fixation and release. This is consistent with previous research in monkeys and in humans. It strongly suggests that the pulvinar is an important part of visuospatial processing and is tightly integrated in corticothalamic transmission of visual signals in visuotopic manner (Stepniewska and Kaas, 1997; Shipp et al., 2003; Adams et al., 2000; Lyon and Kaas, 2007; Logothetis et al., 2010; Berman and Wurtz, 2008; 2010; 2011; Rafal and Posner, 1987; Snow et al., 2009; Arend et al., 2008; Leh et al., 2007)

8.3.1 Top-down Control of Covert Attention in Pulvinar Patients

When tested for top-down attention pulvinar patients have shown a pattern of attentional benefits in the left visual field and attentional costs in the right visual field similar to FEF patients. This can again be explained with sticky fixation directed to the central arrow (placed slightly above the target) while the release of fixation towards the target was impaired in pulvinar patients particularly in one direction. However, it is difficult to explain why pulvinar patients have shown peripheral impairment independent of their contralesional side.

8.3.2 Bottom-up Control of Covert Attention in Pulvinar Patients

Bottom-up attentional benefits in pulvinar patients were small but positive and did not differ much from those found in FEF patients. This seems surprising in respect to previous studies which assumed that pulvinar is a structure coordinating bottom-up visual processing. However, due to the limited number of testing trials bottom-up attentional effects need to be interpreted with caution.

8.3.3 Summary Pulvinar Patient Studies

At the current stage of results, it can be assumed that the FEF and the pulvinar have complementary neural functions for fixation properties, which might work together when passing visual and attentional signals in the periphery. Due to increased cpd after pulvinar lesions it might be interesting to consider if the pulvinar could work not only as a driver but even as amplifier of visuospatial signal transmission .However, such speculation might be far fetched given the current results, and would need a back up from literature.

8.3.4 Future Outlook for Fronto-pulvinar-occipital Network

Secondly, we still do not know enough about the foveal FEF-pulvinar-occipital route itself. While there is convincing evidence form monkey studies about visuospatial processing in the pulvinar, there is a huge gap in the understanding of how the pulvinar coordinates visual signals in the human brain. Pulvinar patient studies in this work provid the first hint on the importance of this structure for visual processing in humans. In future, signal processing in

the pulvinar between FEF and occipital areas could be investigated in humans via application of theta burst TMS over the FEF and occipital areas while pulvinar activity in fMRI post TMS could be measured. Secondly, with the application of fMRI at high resolution and higher magnetic fields (7 Tesla magnetic strength) (Windischberger et al., 2010) retinotopic maps in the human pulvinar should be detectable by established retinotopic mapping tools (Sereno et al., 1998). Secondly, this work would benefit from further examination of visuospatial attention in FEF and pulvinar patients and as mentioned above in a carful separation in lesion studies of other brain areas such as DLPFC, PrCeS and the parietal lobe which all belong to the functional networks for visuospatial processing and attentional control (Corbetta and Shulman, 1998; Corbetta, et al., 2000; Kastner and Ungerleider, 2000; Kundsen, 2007).

8.4 Cpd in Visuo-Motor Associations (Sensorimotor Processes)

While visual attention can be summoned by stimuli revealing an automatic control mechanism, manual actions to visual stimuli can be triggered without conscious decisions too. Subliminal visual primes have been found to evoke visuo-motor processes which are different when presented in fovea or in the periphery of the visual field (Schlaghecken and Eimer, 1998; Eimer and Schlaghecken 2000, 2002; Vorberg, 2000; Klapp and Hinkley, 2002; Lingnau and Vorberg, 2005; Sumner et al., 2008; Boy et al., 2010a/b). During compatible prime-target trials presented to fovea there is a speed up of reaction times to targets. This is however only evident at short delays between the mask onset and target onset (stimulus onset asynchrony or SOA). With prolonged SOA's RT´s in compatible trials were found to reverse from positive compatibility effects (PCE) to negative compatibility effects (NCE). However, when presented in the periphery, only PCE at longer SOA's were found. This has been explained by a model of partial activation and inhibition in a visuo-motor system with peripheral stimuli having higher activation thresholds (Eimer and Schlaghecken 2000, 2002).

However, the visual strength of the primes has not been equated for fovea and periphery in previous studies in the form of precisely measured prime visibility thresholds (Schlaghecken and Eimer, 2000, 2001; Eimer and Schlaghecken 2000, 2002; Lignau and Vorberg, 2005; Schlaghecken and Eimer, 2006). Visibility thresholds were therefore measured carefully using orientation discrimination and masked primes for three retinal loci. As expected

visibility thresholds were significantly higher in periphery than in fovea. Once the visual cpd has been measured, a series of experiments investigated successively several factors which could have determined cpd in visuo-motor priming. Experiments in Chapter 6 have shown a trend which is in accordance with object update theories (Lleras and Enns, 2004; Verleger et al., 2004; Sumner et al., 2007; Jaskowski and Przekoracka-Krawczyk, 2005; Jaskowski et al., 2007; Jaskowski, 2008) suggesting that a mask of similar visual features as the prime will facilitate NCE. The mask which showed that trend in the first experiment has been adapted for all following experiments.

Then, influences of attention on NCE were investigated (Macaluso et al., 2003; Eimer et al., 2010). In that context it is interesting to consider if and to what extent visuo-motor associations belong to a bigger control system including visuo-spatial attention directed by voluntary control mechanisms and if visuo-motor representations can be influenced by attention (Kundsen, 2007). Although some studies have shown attentional influences on priming effects directly (Sumner et al., 2006; Bavelier et al., 2000; Huber, 2008; Sohrabi and West, 2008) the randomization versus blocked presentation paradigm did not change the cpd pattern. The next crucial factor was the amount of training participants received to establish the novel and abstract visuo-motor association. With increased practice NCE occurred in fovea, but not in the periphery. This ruled out that cpd in visuo-motor priming is dependent on visual strength of the primes, as these have been equalised and tested over a series of experiments, without producing NCE in the periphery.

In Chapter 7, different SOA's have been applied to test thresholds in the periphery. Only SOA at 250 ms produced reliable NCE in the periphery after 3 testing sessions. SOA at 250 ms has been in fovea and again periphery. Peripheral NCE were slightly higher than NCE obtained in the fovea under the same conditions. It can therefore be concluded that at 10 visual degrees peripheral eccentricity, at least one time window exists, that of 250 ms which allows sensorimotor processes to be controled via periphery. This on the other hand, suggests that there is no cpd in visuo-motor processing once the correct determinants have been applied. Experiments in Chapter 7 are in line with Lingnau and Vorberg, 2005 and show that visuo-motor plans on a manual level can be accessed through the periphery when the requirements of neural peripheral processing: prime strength in combination with prolonged SOA is met. Visuo-motor representation could be triggered across retinotopic space (further periphery) only if the signal has been strong (meaningful) and frequent (relevant) enough.

8.5 Theoretical Integration of Top-down and Sensorimotor Processes

8.5.1 Model of Integrated Visuo-Motor Systems

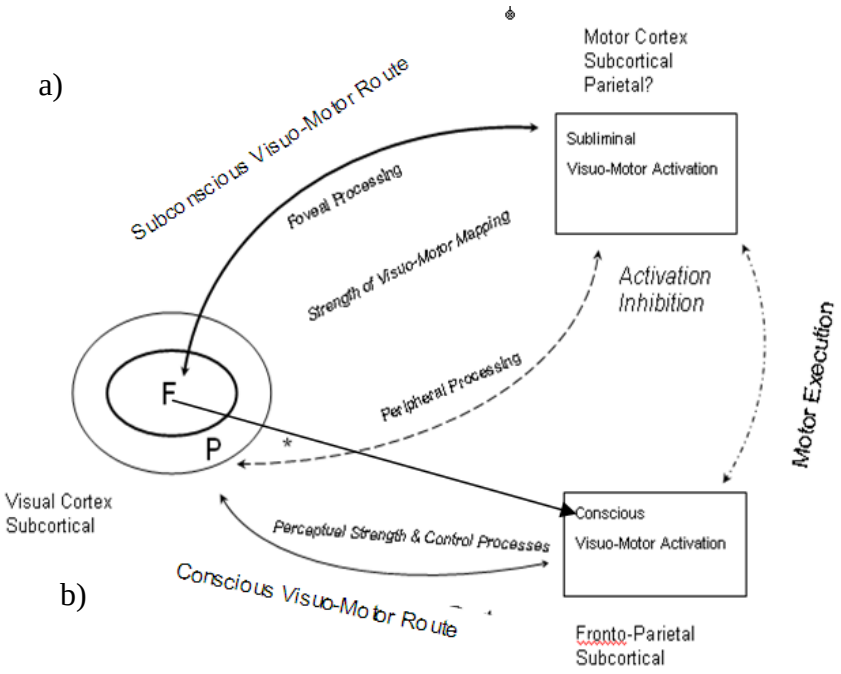


Figure 59. A model for neural circuits for visuo-motor processing in the human brain (separate but integrated visuo-motor systems) as accessed through the fovea (F) or the periphery (P) of the visual field. The model draws from previous literature indicating brain areas involved in specific functions and integrates the results of this work. **Legend:** Solid lines indicate the strength of links: dashed lines: weaker processing route, not prioritised link in the processing system, e.g. the peripheral route to visuo-motor representations processing brain areas; the thicker the line the stronger the link: e.g the link for subconscious visuo-motor processing between fovea and motor brain areas, which facilitates visuo-motor activation and inhibition processes. a) motor brain areas (motor cortex (preSMA), subcortical areas and parietal lobe) as regulated via the fovea preferably when conscious percepts initiate motor actions b) attentional and oculomotor control areas (FEF, puvinar and parietal lobe) accessible through the periphery preferably initiating eye movements and attentional shifts (preferably on unconscious level), which in turn facilitate conscious visuospatial processing in fovea. At this point both distinct visuo-motor systems meet and both can have an effect on motor manual execution as found in chapter 7. Both the subconscious and the conscious loop shown in the model are proposed to be involved in motor execution based on subconscious activation and inhibition of visuo-motor neural representations (visuo motor associations). The strength of visuo-motor processing is high between fovea and motor areas but weak between periphery and some motor areas. This however might be different for the conscious visuo-motor route between fovea and fronto-pulvinar-parietal network where perceptual strength and control processes play an important role, this is indicated by a straight line from fovea to the frontoparietal motor network at the conscious level. There is another link between periphery (occipital cortex) and oculomotor fronto-subcortical-parietal network (Corbetta and Shulman, 1998; Corbetta, et al., 2000; Kastner and Ungerleider, 2000; Kundsen, 2007) which is thought of as a subconscious rout and involves some connections to the subconscious visuo-motor processing areas, which is not indicated in this graph. On the conscious level perceptual strength matters as well as conscious top-down processes are involved.

Separate but integrated visuo-motor systems has been proposed by Goodale, 2010 and Sumner et al., 2008. The author suggest the following three semi-independent visuo-motor systems a) the subconscious visuo-motor control system concerned with manual responses and b) the conscious top-down motor control system and c) the subconscious oculomotor - attentional system. Fig. 59 shows a thought model integrating these functional systems. Firstly, this model emphasizes the role and the differences between inputs conveyed through periphery versus fovea. Secondly, this model tries to integrate conscious and subconscious visuo-motor processing. The model is explained in detail in the text below Figure 59.

8.5.2 Is Vision-Action Model of Millner and Goodale (1992) - accurate?

The experiments and results of this work allow discussion of how much the proposal of Milner and Goodale (1992) to divide vision and action in separate functional systems is still relevant and if it does need updating at all (Kundsen, 2007). Accordingly previous studies indicate that there is reasonable crosstalk between both pathways (Wolfensteller et al., 2004) and it is possible that a motor response is conducted before perceptual analysis is finished, and therefore not necessarily requiring full conscious visual analysis (Coles et al. 1985, Schmidt et al., 2007).

There is also a wide body of research generated within the research groups of Millner and Goodale themselves providing evidence that the vision-action pathways model is too simplistic and requires refinement if not complete rejection (Schlaghecken et al, 2003, 2007; Broogard, 2011; Rice et al., 2007; Milner and Goodale, 2008; Goodale et al., 2005; Schenk et al., 2005, 2006; Goodale and Westwood, 2004; Goodale et al., 2004). On the other hand this model is a backbone for understanding of brain networks and provides the first systematic approach to visuo-motor processes. Finally, it is important to mention that Goodale and Millner do not deny integration of visuo-motor control systems at different stages of visual and motor processing.

In conclusion, at the stage of current evidence the author of this work proposes, that while fovea is preferably used for conscious processing with two purposes: conscious recognition and manual action to visual objects in the center of vision, the periphery is an important signalling center triggering eye movements and attention and is less suited to trigger manual actions (to blurred objects).

In that way, however both parts of the retina are engaged in visuo-motor processing (or action pathway according to Milner and Goodale, 1992) – but within partly separated visuo-motor systems. Periphery would control attention and eye movements via a functional network of FEF – subcortical-occipital – parietal areas, while fovea would trigger the manual route via temporal-occipital-parietal–premotor–motor – orbito-frontal areas as illustrated in Fig.59, of which the orbitofrontal areas for planning and anticipation have not been investigated in this work and should be considered for future studies on cpd in manual visuo-motor control mechanisms.

8.5.3 Integrative Visuo-motor Ventral and Dorsal Pathways?

Finally, the understanding of both foveal and peripheral pathways in the form of visuo-motor systems has consequences for another important model of visual perception proposed by Ungerleider and Miskin (1982) – the where and what pathways. Fovea was supposed to process identity of visual targets while periphery has to localise them. It is a definition of visuospatial processing and only implicitly suggests the integration of manual or oculomotor actions of the system. Therefore, the author proposes that both foveal and peripheral processing are tightly connected to visuo-motor functions. However, it is important to have the separation in ventral and dorsal systems to emphasise the differently specialised visuo-motor control systems in the human brain – the ventral for manual visuomotor functions and the dorsal for attentional/oculomotor functions.

8.5.4 Integration and Differentiation of Top-down Processes

Initially response inhibition has been investigated with supraliminal primes in tasks like go/nogo where a conscious voluntary stop action is required. The NCE experiments have shown that response inhibition also exists at the automatic level, suggesting that top-down is not equivalent with conscious processing. Accordingly, top-down processes are suggested to exist at the micro-level (for instance within one multisensory brain area) and at the macro-level (between brain areas) and can be facilitatory or inhibitory. Working memory has been suggested to be distributed in the network of areas and might be effector/ function specific. Thus, top-down processes might not be localized in the PFC only, which is unlikely to store the automatic "visuo-motor representation". This is in line with studies which found PFC to be less engaged in a task with performance becoming automatic (Fuster et al., 2000). Thus, top-down mechanisms can develop and be independent from PFC and be "localized" as

independent effector specific micro-circuits, for example in FEF. Another candidate area for such visuo-motor micro-circuit might be the preSMA (Sumner et al., 2008) or at the macro-level the fronto-pulvinar-occipital network.

8.7 Discussion of Methods

This work has been using two contrary methods. Usually complex behavioural and brain imaging studies dominate the investigation of impact of lesions on behaviour in patients, from which most evidence for the perception-action model of Millner and Goodale, 1992 has been generated. Tests of optic ataxia, visual agnosia, apraxia and neglect provided exciting insights (and some misguidance) to the concepts and underatanding of brain networks. Psychophysical methods on the other hand, are routinely used in healthy participants while in patients, with rare exceptions (Snow et al., 2009). Very often data from psychophysical studies in healthy humans does not support experimental findings in patients. While there is high reliability but poor external validity in psychophysical experiments, patient studies can be unreliable and or the opposite extremely devoted. Due to the low number of focal lesions available, plasticity and reorganisation processes, or due to the loss of concentration capacities, motor or verbalisation skills, it becomes a challenge to obtain meaningfull data from patients. Finally mood disorders in patients and (depression or lack of emotional control) can negatively influence performance in experiments.

With the knowledge of the down-sides of lesion studies in humans (as discussed in detail in Chapter 1), it was of particular interest to validate these against TMS studies in healthy participants. The aim of this work was to precisely describe visuospatial processing without confounds from decision, verbal or motor functions. Nonetheless, some kind of decision processes will be involved in an orientation discrimination paradigm; however it is a relatively simple task when compared with other cognitive paradigms used in experiments with patients (Ward et al., 2001). As in all patient studies, this work suffers from insufficient access to a bigger patient group with focal lesions. New statistical methods for a reliable lesion-symptom mapping also require bigger groups of patients and allow for more extended lesions to be tolerated.

8.8 Conclusions

In conclusion results of this work allow new insights to visuo-motor functions and neural networks in the human brain. First, results obtained from brain damaged patients have shown that the FEF area and the subcortical pulvinar contribute to visuospatial processing and are very likely to cooperate in a functional fixation network coordinating neural mechanisms of fixation and release. Secondly, the comparison of real lesions in FEF patients, with transient TMS FEF in healthy participants showed that both methods produce distinct results for centre-periphery differences in visual processing and that there is some indication of contralesional perceptual deficit in FEF patients. Thirdly, top-down control of attention is impaired after FEF and pulvinar damage in the right visual field in both patient groups and this pattern seems distinct in comparison to small but positive gain in perception after bottom-up attentional control. This suggests that both the FEF area and the pulvinar are involved in top-down control of visuospatial attention; however, this effect did not reach significance level and requires replication. This was out of scope of this project and patients were not available for further testing. However, the proposal of fronto-pulvinar-occipital network could prove a valuable proposal for future investigations.

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APPENDIX

Chapter 2

Table 1. Experiment 1. Cpd calculated as periphery/centre ratio for visibility thresholds in two different psychometric methods

	Ratio Periphery/Fovea	
Pb #	Orientation Discrimination	Point of Subjective Equality
Pb1	1.9	1.5
Pb2	1.7	1.2
Pb3	2.2	1.4
P4	1.6	1.2
Pb5	1.1	0.9
Pb6	1.6	1.1
Pb7	2.2	1.5
M	1.7	1.2
SEM	0.15	0.08

Table 2. Experiment 2b. Perceptual sensitivity thresholds in luminance (candela/m2) at short and long target durations in N=10.

	40ms target duration			120ms target duration		
	Centre	Periphery		Centre	Periphery	
Pb #	Fovea	Left	Right	Fovea	Left	Right
Pb1	3.86	7.75	7.66	0.78	0.73	1.09
Pb2	2.61	7.15	7.91	1.05	1.46	1.51
Pb3	3.97	7.57	5.93	1.13	1.84	0.70
Pb4	3.10	6.69	5.80	0.86	0.77	0.89
Pb5	3.37	13.34	16.41	1.07	0.88	1.19
Pb6	4.64	6.55	5.28	1.00	0.78	1.07
Pb7	3.19	7.32	4.62	1.41	0.74	1.00
Pb8	3.63	4.50	4.71	0.79	1.11	1.01
Pb9	3.06	6.12	6.33	0.95	0.96	0.78
Pb10	3.83	6.21	7.74	1.18	0.85	1.22
M	3.53	7.32	7.24	1.02	1.01	1.05
SEM	0.18	0.73	1.09	0.06	0.12	0.07

Chapter 3

Appendix Figure 1a shows a multi-slice view on lesion extent in each FEF patient tested (Experiment 3, Eperiments 5 and 6). All slices have been acquired under supervision of Prof. Robert Rafal at the Wolfson Institute for Cognitive Neuroscience, UK.

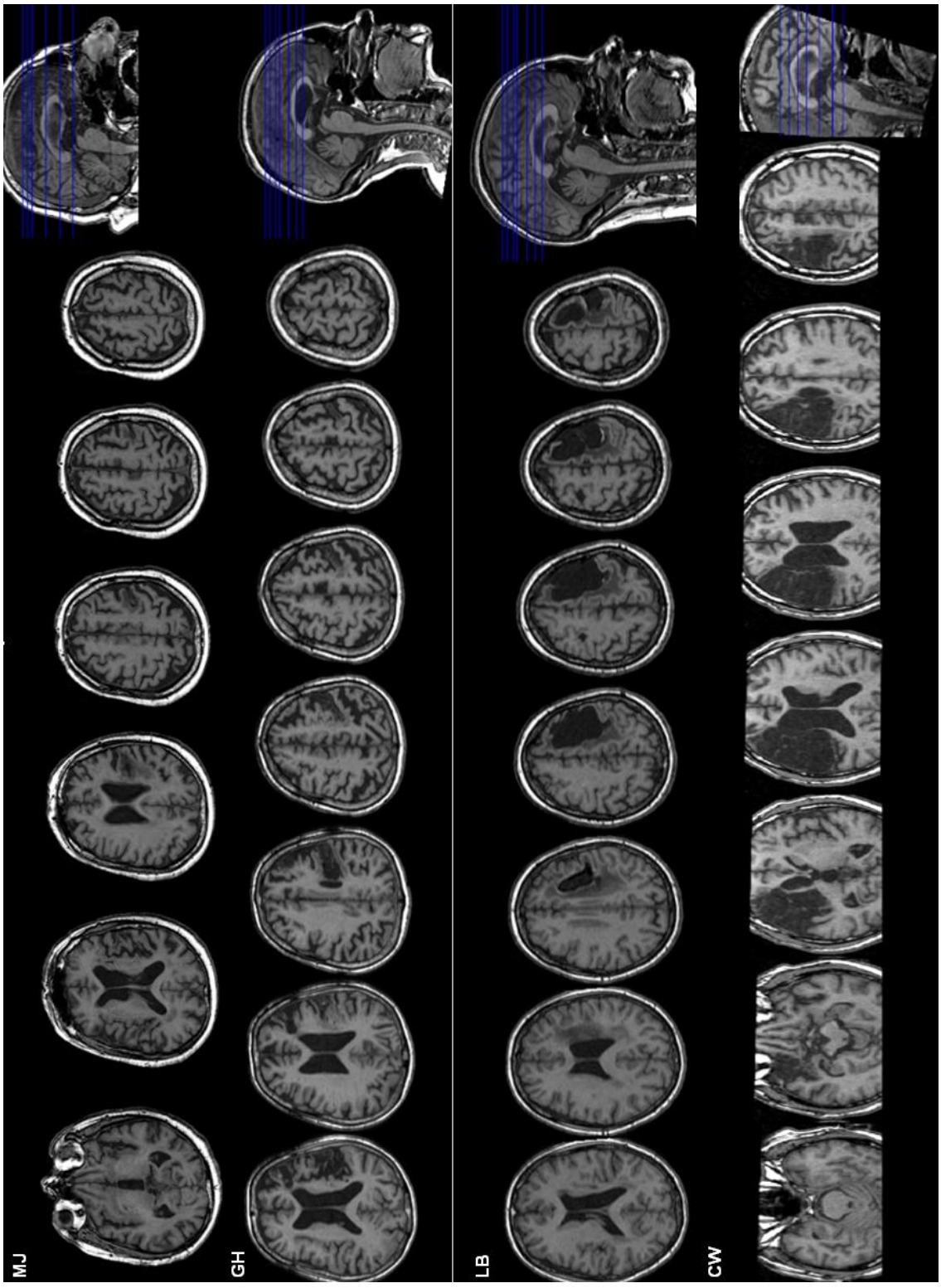


Table 3a. Experiment 3. Contrast perception thresholds as calculated in Michelson contrast shown in % for FEF patients (N=3) and age-matched controls (N=8) and centre-periphery ratios calculated for left periphery divided by fovea (L/F), right periphery divided by fovea (L/F), right and left periphery averaged (L&R) divided by fovea (P/F). M=Arithmetic Mean, SEM=Standard Error Mean.

	Contrast Sensitivity Thresholds in Michelson Contrast %				Centre-Periphery Differences as Periphery/Centre Ratios		
FEF Patients	Centre Fovea	Periphery Left	Periphery Right	Left&Right	L/F	R/F	P/F
MJ (R)	27.3	88.6	61.4	75	3.3	2.3	2.8
GH (L)	33.6	77.3	79.5	78.9	2.3	2.4	2.3
LB (Bi)	5.9	13.6	11.8	12.7	2.3	2	2.2
M	22.3	59.8	50.9	55.5	2.6	2.2	2.4
SEM	8.4	23.3	20.2	21.4	0.3	0.1	0.2

Table 3b Experiment 3	Contrast Sensitivity Thresholds in Michelson Contrast %				Centre-Periphery Differences as Periphery/Centre Ratios		
Controls Pb #	Center Fovea	Periphery Left	Periphery Right	Left &Right	L/F	R/F	P/F
Pb 1	10.8	20.6	28.4	24.5	1.9	2.6	2.3
Pb 2	4.2	12.1	6.1	9.1	2.9	1.5	2.2
Pb 3	12.1	24.6	31.7	28.1	2	2.6	2.3
Pb 4	5	10.6	10	10.3	2.1	2	2.1
Pb 5	9.6	27.3	18.8	23	2.9	2	2.4
Pb 6	6.5	13.5	15.1	14.3	2.1	2.3	2.2
Pb 7	4.9	8.3	9.5	8.9	1.7	1.9	1.8
Pb 8	10.3	16.5	17.6	17.1	1.6	1.7	1.7
M	7.9	16.7	17.1	16.9	2.1	2.1	2.1
SEM	1.1	2.4	3.2	2.7	0.2	0.1	0.1

Chapter 4

Appendix Figure 1b shows a multi-slice view on lesion extent in each pulvinar patient tested (Experiment 3, Eperiments 5 and 6). The multi slice image of patient CR included only 4 slices as the lesions was very focal while the lesion of patient JL required more slices to be shown accordingly. All slices have been adapted from the data bank of the Wolfson Institute for Cognitive Neuroscience in Bangor, UK.

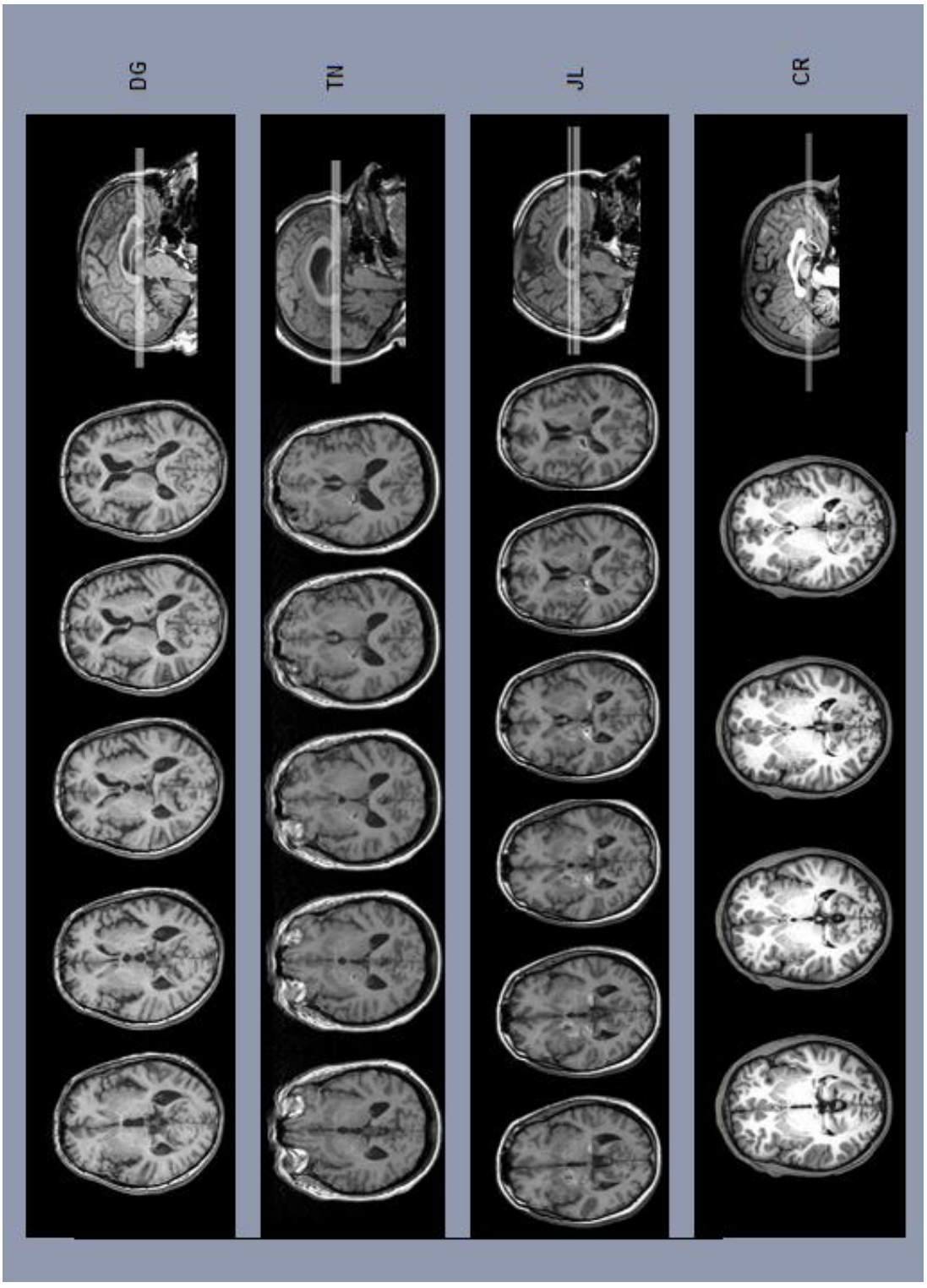


Table 4. Experiment 4. Contrast perception thresholds as calculated in Michelson contrast shown in % for pulvinar patients (N=4) and age-matched controls (N=8) and centre-periphery ratios calculated for left periphery divided by fovea (L/F), right periphery divided by fovea (L/F), right and left periphery averaged (L&R) divided by fovea (P/F). M=Arithmetic Mean, SEM=Standard Error Mean. R= lesion in the right hemisphere. L= lesion in the left hemisphere. Bi=bilateral, lesion in both hemispheres.

	Contrast Sensitivity Thresholds in Michelson Contrast %				Centre-Periphery Differences as Periphery/Centre Ratios		
Pulvinar Patients	Centre Fovea	Periphery Left	Periphery Right	Left &Right	L/F	R/F	P/F
DG (L)	9.4	23.4	24.0	23.7	2.5	2.5	2.5
TN (R)	8.0	17.0	32.1	24.6	2.1	4.0	3.1
CR (L)	6.1	10.3	38.6	24.5	1.7	6.3	4.0
JL (Bi)	16.0	30.7	42.9	36.8	1.9	2.7	2.3
M	9.9	20.4	34.4	27.4	2.1	3.9	3.0
SEM	2.1	4.4	4.1	3.1	0.2	0.9	0.4
Controls (N=8)	7.9	16.7	17.1	16.9	2.1	2.1	2.1

Chapter 5

Table 5a-c. Experiment 5a. Neutral cues results from top-down paradigm. Contrast perception thresholds as calculated in Michelson contrast shown in % for FEF patients (N=4), pulvinar patients (N=4) and all controls (N=21) and centre-periphery ratios calculated for left periphery divided by fovea (L/F), right periphery divided by fovea (L/F), right and left periphery averaged (L&R) divided by fovea (P/F). M=Arithmetic Mean, SEM=Standard Error Mean, L=left lesion, R= right lesion, Bi=bilateral lesion.

Table 5a Experiment 5a	Contrast Sensitivity Thresholds in Michelson Contrast %				Centre-Periphery Differences as Periphery/Centre Ratios		
Patients FEF	Center Fovea	Periphery Left	Periphery Right	L&R	L/F	R/F	P/F
MJ (R)	33.6	77.3	70	73.6	2.3	2.1	2.2
GH (R)	3.5	7.3	6.4	6.8	2.1	1.8	2
CW (R)	4.5	14.2	4.7	9.5	3.2	1	2.1
LB (Bi)	2.1	10	6.4	8.2	4.8	3	3.9
M	10.9	27.2	21.9	24.5	3.1	2	2.5
SEM	7.6	16.8	16.1	16.4	0.6	0.4	0.5
All Controls							
M	3.3	6.2	6.4	6.3	1.9	1.4	1.4
MSE	0.2	1.1	0.9	1.0	0.1	0.5	0.4

Table 5b **Experiment 5a**	Contrast Sensitivity Thresholds in Michelson Contrast %				Centre-Periphery Differences as Periphery/Centre Ratios		
Patients Pulvinar	Fovea	Left	Right	Left & Right	L/F	R/F	P/F
DG (L)	3.7	13.8	9.0	11.4	3.7	2.4	3.1
TN (R)	2.2	7.5	4.7	6.1	3.3	2.1	2.7
CR (L)	0.9	2.1	13.3	7.7	2.4	15.4	8.9
JL (Bi)	2.0	6.1	4.5	5.3	3.1	2.3	2.7
M	2.2	7.3	7.9	7.6	3.1	5.6	4.3
MSE	0.6	2.4	2.1	1.3	0.3	3.3	1.5

Table 5c **Experiment 5a**							
Control (Y)	Fovea	Left	Right	Left &Right	L/F	R/F	P/F
1	3.9	7.8	7.7	7.7	2.0	2.0	2.0
2	2.6	7.1	7.9	7.5	2.7	3.0	2.9
3	4.0	7.6	5.9	6.8	1.9	1.5	1.7
4	3.1	6.7	5.8	6.2	2.2	1.9	2.0
5	3.4	13.3	16.4	14.9	4.0	4.9	4.4
6	4.6	6.5	5.3	5.9	1.4	1.1	1.3
7	3.2	7.3	4.6	6.0	2.3	1.5	1.9
8	3.6	4.5	4.7	4.6	1.2	1.3	1.3
9	3.1	6.1	6.3	6.2	2.0	2.1	2.0
10	3.8	6.2	7.7	7.0	1.6	2.0	1.8
M	3.5	7.3	7.2	7.3	2.1	2.1	2.1
SEM	0.2	0.7	1.0	0.8	0.2	0.3	0.3
Controls (E)							
	Fovea	Left	Right	Left &Right	L/F	R/F	P/F
1	3.4	5.5	5	5.3	1.6	1.5	1.5
2	2.4	5.5	5	5.3	2.3	2	2.2
3	4.1	4.6	6.3	5.5	1.1	1.5	1.3
4	4.1	5.4	7	6.2	1.3	1.7	1.5
5	4.7	5.3	4.4	4.9	1.1	0.9	1
6	3.2	4.6	6.6	5.6	1.4	2	1.7
7	2.8	6.6	4.4	5.5	2.4	1.6	2
8	1.9	5	6.1	5.5	2.5	3.1	2.8
9	2.4	3.4	3.9	3.6	1.4	1.6	1.5
10	2.1	4.5	5.5	5	2.1	2.6	2.3
11	2.7	6	6.3	6.1	2.2	2.3	2.3
M	3.1	5.1	5.5	5.3	1.8	1.9	1.8
SEM	0.2	0.2	0.3	0.2	0.1	0.2	0.1

Table 6. Experiment 5b. Top-down cueing effects calculated as ratio in neutral/cued trials for FEF patients (N=4), pulvinar patients (N=4) and all controls (N=21). M=Arithmetic Mean, SEM=Standard Error Mean. L=left lesion, R= right lesion, Bi=bilateral lesion,Y=young controls, E=elderly controls

Pb #	Cueing Effects (Uncued/Cued Ratios)			
	Centre	Periphery		
FEF	Fovea	Left	Right	Left&Right
MJ (R)	1.19	0.98	0.86	0.92
GH (R)	1.36	1.01	1.05	1.03
CW (R)	0.92	0.81	0.81	0.81
LB (Bi)	1.01	1.47	1.67	1.57
M	1.12	1.07	1.1	1.08
SEM	0.1	0.14	0.2	0.17
Pulvinar	Fovea	Left	Right	Left&Right
DG (L)	1.08	0.83	1.16	0.86
TN (R)	1.29	1.27	1.1	1.06
CR (L)	0.98	1	0.89	0.95
JL (Bi)	1	1.11	1.3	1.36
M	1.12	1.07	1.19	1.09
SEM	0.09	0.13	0.06	0.15
Controls (Y)	Fovea	Left	Right	Left&Right
Pb1	1.04	1.42	1.36	1.39
Pb2	1.09	0.89	1.34	1.12
Pb3	0.84	1.2	1.25	1.22
Pb4	0.96	1.01	1.18	1.09
M	0.99	1.13	1.28	1.21
SEM	0.05	0.12	0.04	0.07
Controls (E)	Fovea	Left	Right	Left&Right
Pb1	1.12	0.86	1.03	0.95
Pb2	1.05	0.9	0.94	0.92
Pb3	1.37	0.96	1	0.98
Pb4	1.26	1.18	1.2	1.19
Pb5	1.13	0.95	0.94	0.95
Pb6	1.09	1.02	1.16	1.09
M	1.17	0.98	1.05	1.01
SEM	0.05	0.05	0.05	0.04
All Controls	Fovea	Left	Right	Left&Right
M	1.1	1.1	1.2	1.1
SEM	0.1	0.1	0.0	0.1

Table 7a. Experiment 6. Bottom-up cueing effects calculated as ratio in neutral/cued trials for FEF patients (N=4), pulvinar patients (N=4) and all controls (N=21). M=Arithmetic Mean, SEM=Standard Error Mean, L=left lesion, R= right lesion, Bi=bilateral lesion.

Pb #	Cueing Effects (Uncued/Cued Ratios)			
	Centre	Periphery		
FEF	Fovea	Left	Right	L&R
MJ (R)	1.05	0.85	0.82	0.83
GH (R)	1.16	0.87	0.85	0.86
CW (R)	1.46	1.49	0.62	1.06
LB (Bi)	1.1	1.58	1.14	1.36
M	1.19	1.19	0.86	1.03
SEM	0.09	0.2	0.11	0.12
Pulvinar				
DG (L)	1.08	1.57	0.88	1.23
TN (R)	0.98	1.73	0.88	1.31
CR (L)	0.83	0.94	1.02	0.98
JL (Bi)	1.05	1.03	0.67	0.85
M	1.04	1.44	0.81	1.09
SEM	0.03	0.21	0.07	0.15
All Controls				
M	1.2	1.1	1.1	1.1
MSE	0.1	0.1	0.1	0.1

Table 7b. Experiment 6. Bottom-up cueing effects calculated as ratio in neutral/cued trials for young controls (N=10). M=Arithmetic Mean, SEM=Standard Error Mean. Y=young controls.

Pb #	Cueing Effects (Uncued/Cued Ratios)			
	Centre	Periphery		
Controls (Y)	Fovea	Left	Right	L&R
Pb1	0.94	0.99	1.23	1.11
Pb2	1.22	1.6	1.02	1.31
Pb3	1.32	1.1	0.89	0.99
Pb4	1.03	1.3	1.03	1.17
Pb5	0.6	1.1	1.79	1.45
Pb6	1.56	1.04	0.99	1.01
Pb7	1.1	0.92	0.64	0.78
Pb8	1.38	1.24	1.2	1.22
Pb9	0.98	1.3	1.17	1.23
Pb10	1.42	1.42	1.53	1.47
M	1.15	1.2	1.15	1.17
SEM	0.09	0.07	0.1	0.07

Table 7c. Experiment 6. Bottom-up cueing effects calculated as ratio in neutral/cued trials for elderly controls (N=10). M=Arithmetic Mean, SEM=Standard Error Mean. E=elderly controls.

Pb #	Cueing Effects (Uncued/Cued Ratios)			
	Centre	Periphery		
Controls (E)	Fovea	Left	Right	L&R
Pb1	1.45	1.37	1.1	1.23
Pb2	1.76	0.92	1.31	1.11
Pb3	1.3	0.89	0.92	0.91
Pb4	1.44	1.04	0.98	1.01
Pb5	1.63	1.05	0.97	1.01
Pb6	0.89	0.83	1.44	1.13
Pb7	2.39	1.03	1.09	1.06
Pb8	1	1.07	1.25	1.16
Pb9	1.28	0.89	0.94	0.91
Pb10	0.94	1.4	0.72	1.06
Pb11	1.09	1.17	1.32	1.24
M	1.41	1.05	1.07	1.06
SEM	0.13	0.06	0.06	0.03

Chapter 6

Table 8a. Experiment 7 (P1). Masked prime visibility thresholds obtained for five participants (Pb) with iso-oriented primes and masks (both horizontal/vertical) and an-iso-oriented primes (horizontal/vertical) and masks (diagonal), M: Arithmetic Mean.

Pb #	An-iso-oriented Prime-Mask	Iso-oriented Prime-Mask
Pb1	11.0	5
Pb2	2.5	3
Pb3	1.2	1.4
Pb4	3.0	7
Pb5	2.5	1.4
M	4.0	3.6
SEM	1.8	1.1

Table 8b. Experiment 7 (P1). Priming effects obtained with masked primes with iso-oriented primes and masks (both horizontal/vertical) and an-iso-oriented primes (horizontal/ vertical) and masks (diagonal).

Pb #	An-iso-oriented Prime-Mask	Iso-oriented Prime-Mask
Pb1	61.3	9.7
Pb2	-3.4	-32.5
Pb3	-13.7	3.5
Pb4	-6.3	15.5
Pb5	14.5	-30
M	10.48	-6.76
SEM	11.0	8.3

Table 9a. Experiment 8 (P2). Primes visibility thresholds and ratios for periphery and fovea,(bocked?) trials procedure between foveal and peripheral loci. No eye tracking.

	Fovea	Periphery		Ratio	
Pb #	Fovea	Left	Right	Right &Left Combined	Periphery/Fovea
P1	5.5	16.5	14.0	15.3	2.8
P2	3.5	10.2	10.9	10.6	3.0
P3	8.2	7.6	6.2	6.2	0.8
P4	10.2	7.8	9.7	8.7	0.9
P5	7.6	14.6	14.1	14.3	1.9
P6	2.7	6.5	9.0	7.8	2.9
P7	4.4	9.6	6.5	8.0	1.8
M	6.0	10.9	10.0	10.45	2.0
SEM	1.03	1.59	1.21	1.30	0.35

Table 9b. Experiment 8a (P2). Priming effects obtained for fovea and periphery (left and right combined) with randomized trials presentation between fovea and periphery. No eye tracking.

	Priming Effects	
Pb #	Fovea	Periphery
P1	-16.4	38.0
P2	-13.7	28.8
P3	-10.0	6.9
P4	3.9	19.7
P5	-4.6	35.9
P6	-29.8	30.0
P7	-23.7	-14.8
M	-13.5	20.6
SEM	4.29	7.12

Table 10a. Experiment 9a. Primes visibility thresholds and ratios for periphery and fovea, randomized trials procedure between foveal and peripheral loci. P/F: ratio periphery divided by fovea. Ratio: P/F: ratio of periphery divided by fovea. L: trials presentation on the left in the periphery, R: trials presentation on the right in periphery, Fovea: trials presentation in the center, L&R combined: averaged over left and right peripheral trials.

	Prime Visibility Thresholds				Ratio
Pb #	Fovea	Left	Right	Left & Right combined	(P/F)
Pb1	6.0	10.5	24.0	17.3	2.3
Pb2	4.0	9.0	10.5	9.8	2.0
Pb3	7.0	14.0	11.0	12.5	1.5
Pb4	7.5	10.0	11.0	10.5	1.3
Pb5	5.6	7.3	8.0	7.7	1.2
Pb6	4.7	11.0	7.7	9.4	1.7
Pb7	10.0	18.0	14.0	16.0	1.4
Pb8	7.0	26.0	16.0	21.0	2.3
M	6.5	13.2	12.8	13.0	1.7
SEM	0.7	2.2	1.9	1.6	0.2

Table 10b. Experiment 9b. Compatability effects calculated as reaction times (RT's) and priming effects calculated as incompatible minus compatible trials in milliseconds obtained at randomized trials presentation for fovea and periphery (left and right combined). Comp: compatible prime target trials, Incomp: incompatible prime-target trials.

	Fovea		Periphery		Priming Effects	
Pb #	Comp	Incomp	Comp	Incomp	Fovea	Periphery
Pb1	458.3	475.0	450.4	498.4	16.6	48.0
Pb2	438.6	444.7	440.2	480.8	6.1	40.6
Pb3	443.0	406.1	429.6	429.6	-36.9	0.0
Pb4	447.4	429.2	430.8	467.0	-18.2	36.3
Pb5	406.0	372.7	374.3	382.5	-33.4	8.2
Pb6	428.8	424.1	406.0	450.4	-4.6	44.5
Pb7	450.3	459.9	461.9	515.9	9.7	54.0
Pb8	441.4	402.2	434.6	450.5	-39.2	15.9
M	439.2	426.7	428.5	459.4	-12.5	30.9
SEM	5.6	11.7	9.7	14.8	8.8	8.3

Table 11a Experiment 9b. Primes visibility thresholds and ratios for periphery and fovea, blocked trials procedure between foveal and peripheral loci. P/F: ratio periphery divided by fovea. Ratio: P/F: ratio of periphery divided by fovea. Left: trials presentation on the left in the periphery, Right: trials presentation on the right in periphery, Fovea: trials presentation in the center, Left & Right combined: averaged over left and right peripheral trials.

	Prime Visibility Thresholds				Ratio
Pb #	Fovea	Left Periphery	Right Periphery	L&R Combined Periphery	(P/F)
Pb1	8.0	13.0	13.0	11.3	1.4
Pb2	3.6	6.5	4.2	4.8	1.3
Pb3	4.5	4.6	6.2	5.1	1.1
Pb4	4.0	8.0	5.0	5.7	1.4
Pb5	8.0	13.0	26.0	15.7	2.0
Pb6	4.0	18.0	16.0	12.7	3.2
Pb7	8.0	23.0	9.0	13.3	1.7
Pb8	4.0	7.0	4.5	5.2	1.3
M	5.5	11.6	10.5	11.1	1.7
SEM	0.7	2.3	2.7	1.6	0.2

Table 11b. Experiment 9b. Compatibility effects calculated as reaction times (RT's) and priming effects calculated as incompatible minus compatible trials in milliseconds obtained at blocked trials presentation for fovea and periphery (left and right combined). P/F: ratio of periphery divided by fovea.

	RT's Fovea		RT's Periphery		Priming Effects	
Pb#	Comp	Incomp	Comp	Incomp	Fovea	Periphery
Pb1	538.8	519.7	532.7	524.1	-19.1	-8.6
Pb2	431.8	409.2	373.6	417.4	-22.6	43.8
Pb3	409.5	384.5	405.4	403.5	-24.9	-1.9
Pb4	485.6	467.0	514.1	517.3	-18.6	3.1
Pb5	492.8	469.0	470.1	483.7	-23.8	13.7
Pb6	438.4	401.9	389.8	456.7	-36.5	66.9
Pb7	485.6	459.6	518.6	544.6	-26.0	26.0
Pb8	400.6	412.5	380.5	454.7	11.9	74.2
M	460.4	440.4	448.1	475.2	-20.0	27.1
SEM	16.9	16.1	24.0	18.1	5.0	11.1

Table 11c. Experiment 9b. Summary of the growth of priming effects over three testing sessions. Negative numbers indicate NCE (negative compatibility effect) while positive numbers indicate PCE (positive compability effect). Cpd: center-periphery difference for priming effects.

N=8		Session 1	Session 2	Session 3
Fovea	*Mean*	1.61	-15.34	-19.89
	SEM	7.32	2.69	4.96
Periphery	*Mean*	25.08	15.56	27.14
	SEM	10.59	11.45	11.15
Cpd	*Mean*	23.47	30.90	47.03**
	SEM	11.44	10.79	10.72

Chapter 7

Table 12. Experiment 10a. Prime visibility thresholds obtained in three testing sessions, each twice. Pre-priming: before prime effects measurements, Post-priming: after prime effects measurements.

	Pre – priming			Post-priming		
Pb#	Session 1	Session 2	Session 3	Session 1	Session 2	Session 3
Pb1	9.5	6.9	5.5	7.5	10.0	7.4
Pb2	10.5	7.0	4.9	8.5	6.5	8.0
Pb3	9.0	4.9	4.7	6.5	4.4	5.0
Pb4	27.0	24.0	26.0	36.0	26.0	20.0
Pb5	7.4	6.0	5.9	5.4	7.0	9.2
Pb6	13.4	10.9	10.5	11.8	11.0	8.6
Pb7	6.8	6.1	4.6	8.0	7.1	9.8
Pb8	5.7	6.4	6.4	5.7	7.0	7.0
M	11.2	11.2	8.5	11.2	9.9	9.4
SEM	3.0	2.9	3.4	4.8	3.2	2.1

Table 13a. Experiment 10a. Priming Effects obtained at Stimulus Onset Asynchrony SOA 350 and SOA 450 at six visual degrees in periphery (left and right combined). Comp: compatible prime target trials, Incomp: incompatible prime-target trials.

	Compatibility Effects				Priming Effects	
	Reaction Times				Difference for	
	SOA 350		SOA 450		Incompat - Compat	
Pb#	Compat	Incompat	Compat	Incompat	SOA 350	SOA 450
Pb1	469.04	467.67	519.60	540.07	-1.37	20.47
Pb2	378.22	387.77	408.85	413.27	9.55	4.42
Pb3	397.71	407.28	469.88	476.56	9.57	6.68
Pb4	434.15	432.48	436.69	453.54	-1.67	16.85
Pb5	423.81	420.06	441.29	441.83	-3.75	0.54
Pb6	469.00	467.70	492.60	507.00	-1.30	14.40
Pb7	427.70	443.10	465.20	466.50	15.40	1.30
Pb8	397.70	407.30	402.80	400.10	9.60	-2.70
M	424.67	429.17	454.61	462.36	4.50	7.75
SEM	11.68	10.29	14.20	16.39	2.57	3.00

Table 13b. Experiment 10a. Reaction times obtained at SOA 350 and SOA 450 at six visual degrees in periphery (left and right combined) for five participants tested.

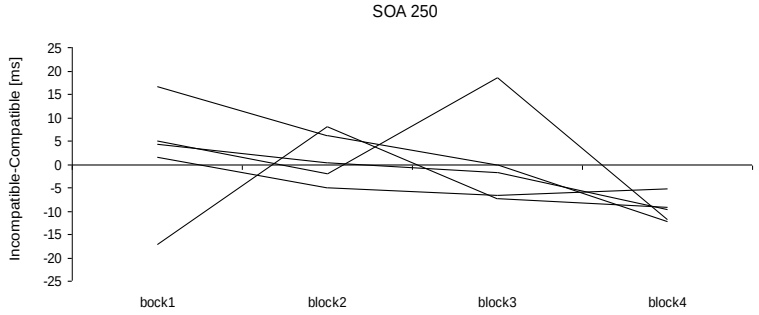
	Reaction Times			
	SOA 350		SOA 450	
Pb#	comp	incomp	comp	incomp
Pb1	397.71	407.28	469.88	476.56
Pb2	434.15	432.48	436.69	453.54
Pb3	378.22	387.77	408.85	413.27
Pb4	423.81	420.06	441.29	441.83
Pb5	469.04	467.67	519.60	540.07
M	420.59	423.05	455.26	465.05
SEM	15.59	13.38	18.77	21.35

Table 13c. Experiment 10b. Reaction times obtained at SOA 250 and SOA 450 repeated at six visual degrees in periphery (left and right combined) for five participants tested.

	Reaction Times			
	SOA 250		SOA 450r	
Pb#	comp	incomp	comp	incomp
Pb1	385.09	375.48	400.57	395.40
Pb2	401.05	388.77	425.47	432.68
Pb3	456.61	447.48	400.77	409.08
Pb4	418.61	413.43	446.30	448.47
Pb5	485.37	473.39	474.13	478.85
M	429.34	419.71	429.45	432.90
SEM	15.08	15.82	14.06	14.71

Table 13d. Experiment 10a/b. Priming effects obtained at SOA 250, 350, 450 and 450repetition at six visual degrees in periphery (left and right combined) for five participants tested.

	Priming Effects Stimulus Onset Asynchrony			
Pb#	250	350	450	450r
Pb1	-9.61	9.57	6.68	-5.17
Pb2	-9.12	-1.67	16.84	7.22
Pb3	-12.28	9.55	4.42	8.31
Pb4	-5.19	-3.75	0.53	2.17
Pb5	-11.98	-1.37	20.48	4.72
M	-9.64	2.47	9.78	3.45
SEM	1.46	2.92	3.80	2.40



Appendix Figure 2. (Experiment 10b). Development of priming effects over the time course of testing (block 1-4) as calculated from RT's in incompatible – compatible trials. (a) SOA 250

Table 14a. Experiment 11a (P3). Prime visibility thresholds.

Pb #	Fovea	Periphery	P/F
Pb1	9	11.0	1.2
Pb2	10	16.0	1.6
Pb3	7	12.5	1.8
Pb4	7.5	10.5	1.4
Pb5	6	17.3	2.9
Pb6	4	9.8	2.4
Pb7	7.5	10.5	1.4
Pb8	6.6	9.3	1.4
M	7.2	12.1	1.8
SEM	0.65	1.1	0.2

Table 14b. Experiment 11b. Compatibility effects calculated as reaction times (RT's) and priming effects calculated as incompatible minus compatible trials in ms for fovea and periphery (left and right combined). P/F: ratio periphery divided by fovea.

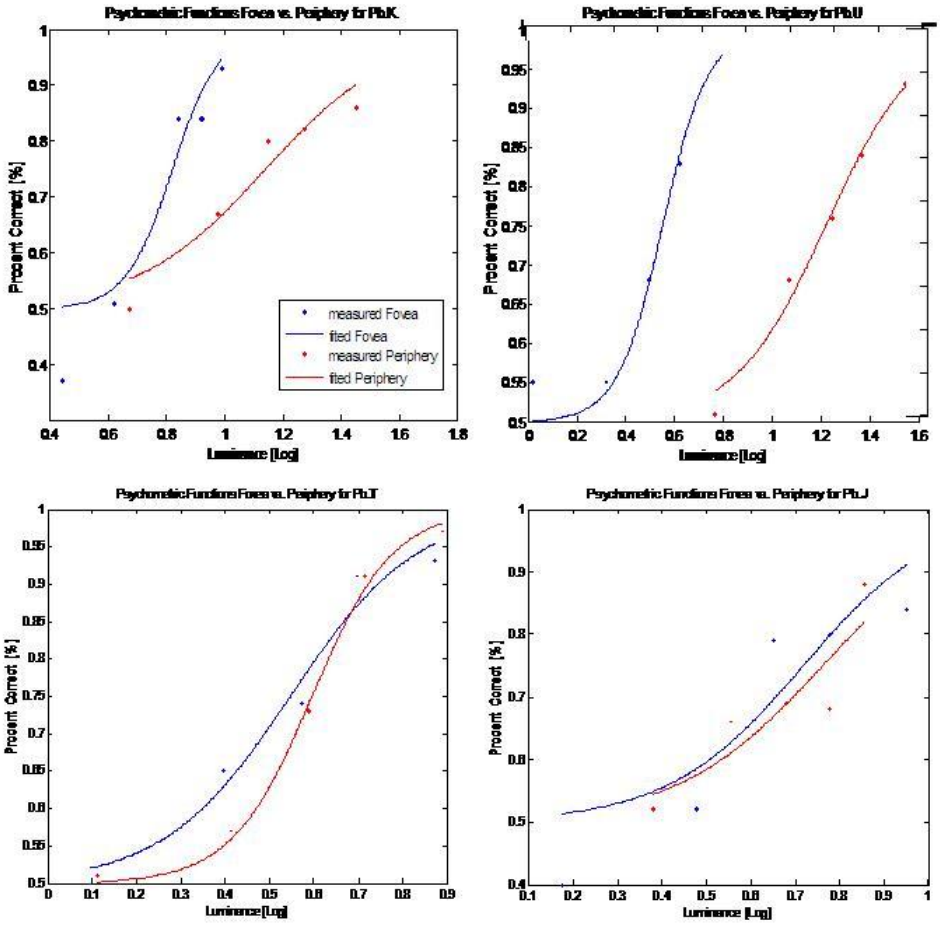
	Fovea		Periphery		Priming Effects	
Pb #	Compat	Incompat	Compat	Incompat	Fovea	Periphery
Pb1	467.4	461.2	463.0	472.9	-6.3	9.9
Pb2	466.1	451.0	459.5	470.1	-15.0	10.6
Pb3	449.7	446.4	457.2	470.0	-3.3	12.8
Pb4	436.1	434.7	457.7	469.6	-1.4	11.9
Pb5	430.6	457.0	462.3	473.6	26.4	11.2
Pb6	427.1	431.1	467.5	477.6	4.0	10.1
Pb7	472.6	480.2	475.2	484.5	7.6	9.3
Pb8	440.3	446.5	464.1	477.6	6.2	13.5
M	448.7	451.0	463.3	474.5	2.3	11.2
SEM	6.3	5.5	2.1	1.8	4.3	0.5

Table 15a. Experiment 12a. Priming effects obtained in fovea at different masked prime strengths calculated in %.

	Masked Prime Strength		
Pb#	0.55	0.65	0.75
1	3.8	1.5	2.7
2	-5.2	-11.8	-6.7
3	-11.1	-10.0	-10.1
4	12.4	-1.6	0.8
M	0.0	-5.5	-3.3
SEM	5.2	3.2	3.0

Table 15b. Experiment 12b. Priming effects obtained in periphery at different masked prime strengths calculated in %.

	Masked Prime Strength		
Pb #	0.55	0.65	0.75
1	5.6	-0.8	-10.4
2	-1.2	-8.4	1.6
3	-1.5	-18.5	-3.1
4	2.0	-1.8	8.9
M	1.2	-7.4	-0.7
SEM	1.7	4.1	4.0



Appendix Figure 3. (Experiment 12a). Individual Psychometric functions for orientation discrimination accuracy in % with increasing contrast of Gabors (luminance difference between black and white stripes) in fovea and in periphery. Psychometric functions described observer's performance on a physical aspect of a stimulus; here it is orientation discrimination performance as a function of luminance (luminance difference between black and white stripes in the Gabor). The higher the contrast in the Gabor the better the performance in orientation discrimination.