Asymmetries of visuospatial attention in peri- and extrapersonal virtual space

Von der Philosophischen Fakultät der Rheinisch-Westfälischen Technischen Hochschule Aachen zur Erlangung des akademischen Grades einer Doktorin der Philosophie genehmigte Dissertation

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Tag der mündlichen Prüfung: 14. Dezember 2010

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"Reality is merely an illusion, albeit a very persistent one."

Albert Einstein
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Summary

Kurzfassung der Dissertation

In dieser Dissertation wurde der Einfluss räumlicher Tiefe auf die Verteilung visuellräumlicher Aufmerksamkeit, sowie die Interaktion der allgemeinen Aktivierung mit der visuellräumlicher Aufmerksamkeit bei gesunden Probanden untersucht.


Das Netzwerk der visuell-räumlichen Aufmerksamkeitsausrichtung scheint jedoch nicht isoliert zu arbeiten. Klinische, experimentelle und bildgebende Studien zeigen auf, dass die visuell-räumliche Aufmerksamkeitsausrichtung mit dem Netzwerk der allgemeinen Aktivierung sowohl anatomisch, als auch funktionell überlappt (Bartolomeo, 2000; De Renzi,

Studie 1 dieser Dissertation untersucht daher den Zusammenhang von allgemeiner Aktivierung und visuell-räumlicher Aufmerksamkeit. Gesunde Probanden wurden unter 24 Stunden Schlafentzug gesetzt und deren Fähigkeit zur verdeckten visuell-räumlichen Aufmerksamkeitsausrichtung wurde zu vier Zeitpunkten (21:00 Uhr, 01:00 Uhr, 05:00 Uhr und 09:00 Uhr) gemessen. Dabei wurden die Stimuli sowohl im peri-, als auch im extrapersonalen, virtuellen Raum dargeboten. Zum Zeitpunkt maximaler Müdigkeit (im Sinne maximal reduzierter allgemeiner Aktivierung) zeigte sich eine signifikante Aufmerksamkeitsasymmetrie im Sinne einer verlangsamten Reorientierung der Aufmerksamkeit in das linke Gesichtsfeld im extrapersonalen Raum. Die reduzierte allgemeine Aktivierung führte somit zu einer dem Neglect ähnelnden Aufmerksamkeitsverteilung. Dieser Befund ist ein weiterer Hinweis auf die postulierte anatomische und funktionelle Überlappung der beiden Aufmerksamkeitsnetzwerke.


Die Ergebnisse dieser Studie unterstützen die Hypothese einer rechtshemisphärischen Dominanz für Aufmerksamkeitsfunktionen. Die unterschiedlichen Ausprägungen der Aufmerksamkeitsasymmetrien in Abhängigkeit von der Raumtiefe entsprechen der Annahme, dass visuell-räumliche Aufmerksamkeit im peripersonalen und im extrapersonalen Raum von
unterschiedlichen neuronalen Verarbeitungspfaden gesteuert wird. Darüber hinaus zeigt die Tatsache, dass die Ergebnisse der horizontalen und der vertikalen Orientierung nicht signifikant miteinander korrelieren, dass beide Prozesse im Gehirn unabhängig voneinander repräsentiert sind.
Summary

This thesis examined the influence of spatial depth on the distribution of visuospatial attention in three-dimensional virtual space, as well as the functional interaction of the networks of alertness and visuospatial attention in the healthy brain.

Although visuospatial attention in healthy people seems to be equally distributed across the left and right visual hemifield, the dominance of the right cerebral hemisphere in attentional functions leads to small, albeit statistically significant “overattention” towards the left visual hemispace. This phenomenon is called “pseudoneglect” (Bowers & Heilman, 1980; Nicholls et al., 1999). Contrary to that, right hemisphere lesions result in a pathological “neglect” of the left visual hemispace (Heilman, et al., 1979; Vallar et al., 2003), which is much more pronounced than pseudoneglect. Although neglect and pseudoneglect usually occur along the horizontal axis, both were also observed in vertical orienting.

Both, the phenomenon of neglect and the phenomenon of pseudoneglect might differ depending on the spatial depth attended to: Near space, also called “peripersonal” space or far space, called “extrapersonal” space. Processing of both areas of space is supposed to rely on two different cortical visual processing streams (Ungerleider & Mishkin, 1982; Goodale & Milner, 1992) and normal as well as pathological asymmetries of visuo-spatial attention might differ depending on the distance of stimulus presentation (Committeri et al., 2007; Halligan & Marshall, 1991; McCourt and Garlinghouse, 2000; Shelton, Bowers & Heilman, 1990; Varnava et al., 2002).

Clinical, experimental, and functional imaging studies suggest overlapping neuronal networks as well as functional interactions of alertness and visuospatial attention within the right hemisphere of the brain (Bartolomeo, 2000; De Renzi, et al., 1989; Fernandez-Duque & Posner, 1997; Gitelman et al., 2002; Karnath, et al., 1998; Robertson, et al., 1998; Vallar, 2001).

In Study 1, healthy participants underwent 24 hours of total sleep deprivation and were tested at four points during the night (9 p.m., 1 a.m., 5 a.m., and 9 a.m.) for their ability to...
covertly orient and reorient attention in virtual peri-and extrapersonal space. At the 9 a.m. experimental session, a highly significant slowing of reorientation towards the left visual hemifield was observed in extrapersonal space. Thus, the maximally reduced level of arousal led to a neglect-like visuo-spatial reorienting behavior in the participants and this provides further evidence for the proposed anatomical and functional overlap of the two attentional systems.

Study 2 investigated the influence of depth on pseudoneglect in healthy young participants by presenting a variation of the greyscales task and a landmark task in different depth locations (peripersonal, extrapersonal) and different orientations (horizontal, vertical) within three-dimensional virtual space. A horizontal leftward bias (pseudoneglect) for both tasks was found, which was stronger in peripersonal than in extrapersonal space. For the vertical condition, an upward bias was observed in the greyscales task, but not in the landmark task. These results support the hypotheses of right hemispheric dominance for visual spatial attention. Furthermore, the differences in attentional asymmetries with respect to depth suggest dissociable neural mechanisms for visual attentional processing in near and far space and the lack of significant correlations implies independence of horizontal and vertical stimulus processing.
Neglect and pseudoneglect are two phenomena of visuospatial attention which do not only portray attentional asymmetries of the injured and the healthy brain respectively, but reflect the cerebral asymmetry concerning the networks of attention in the human brain in general. To account for the three-dimensional space we live in and interact with, this thesis will examine the influence of spatial depth on attentional asymmetries as well as the functional interaction of the networks of alertness and visuospatial attention. The studies in this thesis utilize Virtual Reality (VR) techniques to bridge the gap between standardization and ecological validity in attentional research and the results are discussed in the light of recent research on visuospatial attention in the healthy and the injured brain.

1.1 A short introduction to attention

"Everyone knows what attention is. It is the taking possession by the mind, in clear and vivid form, of one out of what seem several simultaneously possible objects or trains of thought. Focalization, concentration of consciousness are of its essence. It implies withdrawal from some things in order to deal effectively with others, and is a condition which has a real opposite in the confused, dazed, scatter-brained state which in French is called distraction and Zerstreutheit in German." - William James (1890).

Numerous reviews, theses and articles about attention start with the famous quote by William James defining the term “attention”, and this thesis will not make an exception. Even though attention was rather regarded as a uniform concept, the quote already hints towards different aspects of attention, like attentional selection or general alertness, which are essential parts of current neuropsychological models of attention (see 1.2). The concept of “attention” has been mentioned throughout earlier centuries, but Gottfried Leibnitz was the first to examine the concept more closely in the 18th century (Van Zomeren & Brouwer, 1994). However, the first empirical examinations of attentional functions were made some 100 years later by Wilhelm Wundt (1874) und Franciscus Donders (1869). Donders already distinguished
between different modalities (visual, tactile, acoustic), which he used to examine simple responses as well as selective attention by recording reaction times.

In the years to follow, little effort was made to examine attention until the research of the concept experienced an upswing within the second half of the 20th century. Cherry (1953) developed the paradigm of dichotic listening and Broadbent (1958) presented his filter model of attention, which is supposed to be the first actual theoretical model of attentional selection. This theory is also called the “bottle-neck theory” of attention, since Broadbent postulates an early “bottle-neck” within the attentional process that selects which stimuli are filtered out and which stimuli are further processed for meaning. This model is based on a strictly serial processing system which forwards information according to an “all-or-nothing” principle.

Treisman (1964a,b) took up the idea of sensory filters, but emphasized the possibility of unattended information slipping through the filter and consecutively influencing the processing of information attended to. In contrast to Broadbent’s “all-or-nothing” principle, Treisman’s so-called “attenuation theory” relies on a “more-or-less” principle. A further elaboration of these models was then made by Deutsch & Deutsch (1963), who proposed that the selection of relevant stimuli happens later within the attentional process, prior to actual reaction.

However, attention research was mostly focused on the selection aspect of attention and still was merely regarded as a uniform concept. Starting in the 1960’s, the focus was moved towards understanding attention as a concept which includes multiple aspects and underlying discrete neuronal networks. Posner & Boies (1971) developed an approach of subdividing attention into subsystems and this approach was specified by Posner and colleagues in the following years. The examination and identification of these attentional networks as well as their interactions have become an important area of attentional research until today.
Since the main focus of this dissertation is concerned with aspects and networks of visuospatial attention, alertness and their interactions, the next chapter will present the most influential neuropsychological models of attention.

1.2 Neuropsychological models of attention

In contrast to general, as well as cognitive psychology models of attention, neuropsychological models refer to the neural areas and networks of the brain, by which attentional subsystems are subserved. Prior to the emergence of functional brain imaging techniques, brain scientists used to draw their conclusions and hypotheses from the examination of patients with brain lesions and the ensuing attentional deficits. An important phenomenon is the neglect syndrome, which frequently occurs after lesions of the right cerebral hemisphere (see also 1.4.4). Especially the works of Heilman et al. (1980 & 1993), Kinsbourne (1970, 1993) and Mesulam (1981, 1985, 1990 & 2002) evolved from the analyses of neglect symptoms after brain lesions within the right hemisphere. The theoretical approach of Posner and colleagues was first founded on lesion studies as well and was later enhanced by functional imaging studies. Even though the majority of models, classifications or frameworks based on these lesion studies were modified following more recent imaging results, it is remarkable that they were mostly confirmed and just specified respectively.

1.2.1 Mutual inhibition of cerebral hemispheres (Kinsbourne (1970; 1993))

In Kinsbourne's model, rightward shifts of attention are controlled by the left hemisphere and leftward shifts of attention by the right hemisphere, respectively. Accordingly, he assumed two processors which are reciprocally connected as well as mutually inhibiting. Thus the left hemisphere processor inhibits the right hemisphere processor and vice versa. Following brain damage, the right hemisphere loses (part of) its capacity to inhibit the left hemisphere processor and thus leaves the left hemisphere overactivated, resulting in hypoattention towards the contralesional field and hyperattention towards the ipsilesional field.
However a weak point of this model is that it can not explain the much greater incidence of hemispatial contralesional neglect following right hemisphere damage.

1.2.2 Dominance of the right hemisphere (Heilman, 1980 & 1993)

Heilman, Watson & Valenstein (1993) proposed that unilateral neglect is caused by disruptions of cortico-limbic-reticular loops, and that these disruptions lead to deficits in orienting reactions. Additionally, they were the first to draw a connection between visuospatial orienting and arousal. Lesions resulting in neglect symptoms are supposed to lead to asymmetric disturbances of arousal, by resulting in hypoarousal of the affected cerebral hemisphere, thus producing a decrease in preparation of responses towards stimuli in the contralateral visual hemifield.

The bigger incidence of neglect symptoms after lesions in the right hemisphere is explained by proposing that this hemisphere is more capable of coactivating the left hemisphere and that it is dominant in general for response preparation in both visual hemifields. Accordingly, the left hemisphere cannot adjust for a right hemisphere arousal deficit. Earlier, Heilman & Van Den Abell (1980) were able, by using EEG recordings of healthy participants, to demonstrate that the right parietal lobe is involved in directing visuospatial attention within the contralateral, as well as the ipsilateral visual field, while the left parietal lobe does not
have the ability to control attention within its ipsilateral visual field. Accordingly, lesions of the left hemisphere have far less consequences for visuospatial orienting than right hemisphere lesions, because the right hemisphere is capable of compensating some of the left hemisphere function while the left hemisphere is not.

1.2.3 Networks of Attention (Posner, 1971; 1984; 1990 & 1994)

Posner and colleagues have intensively studied attentional processes since the early 1970’s. Posner & Boies (1971) were the first to describe different subsystems of attention. Based on their findings, as well as other scientific evidence, Posner & Petersen (1990) postulated three networks of attention: The network of visuospatial orienting, the network of executive attention and the alertness network.

*The network of visuospatial orienting*

The network of visuospatial orienting controls overt and covert orienting of visual attention. Three specific processes, which are assigned to corresponding anatomical correlates, are supposed to be involved in visuospatial orienting:

First, attention needs to be *disengaged* from its current fixation point. This is supposed to be a function of the right posterior parietal lobe. Patients with lesions in this area are massively limited in their ability to disengage their attention in order to move it to another locus in space (Posner, Walker, Friedrich, & Rafal, 1984). Thus, visuospatial neglect is the most common consequence of right-hemisphere parietal lesions.

After disengaging the focus of attention from its current locus, it needs to be *moved* to its new target locus. Movement of attention is supposed to be a function of the superior colliculi (SC) in the midbrain and can either be performed overtly or covertly. In the first case, attention and eye movement are coupled, in the second case, attention is moved away from the current locus while the eyes remain fixed. Patients with degeneration in the SC e.g. show slowed shifting of attention and, and animal studies suggest that unilateral SC lesions result in neglect of the contralesional hemispace (Ogourtsova, Korner-Bitenskya, & Ptito, 2010).
Upon detection of the target, attention needs to be *engaged* to the new focus of attention. The anatomical correlate of the engage function is supposed to be the pulvinar in the midbrain which is involved in selecting relevant information for further processing. Lesions in the pulvinar result in deficits of engaging attention to a target in the contralesional field. Thus, the posterior parietal lobe, the SC and the pulvinar form an anatomical circuit or network for covert shifts of visual attention to spatial targets (Posner & Raichle, 1994). Lesions in either part of this network can result in deficits of visuospatial orienting, apparently with a greater incidence following parietal lesions.

![Figure 1.2: The network of visuospatial orienting (from Posner & Raichle, 1994).](image)

**The network of executive attention**

The function of the network of executive attention is to transfer objects into conscious processing (Posner & Raichle, 1994). After an object has been processed by the orienting network (see above), it needs to be identified and potential actions need to be prepared. Executive attention is a function of the frontal lobe, more precisely the cingulate gyrus. Especially bilateral lesions in these areas can prevent patients from executing intentional
The alerting network

The alerting network establishes and keeps up the alert state of the mind and increases responsiveness and action preparation. The alertness network appears to be strongly lateralized to the right hemisphere, more specifically to the right frontal lobe and it depends physiologically on the noradrenergic pathways arising from the brainstem (see 1.3.3). With reference to Heilman’s findings (see 1.2.2), Posner & Petersen (1990) propose this asymmetric processing of alertness in the right frontal cortex and point out how lesions in this area are often associated with alerting deficits.

Moreover, Posner and colleagues (1984, 1990, & 1994) emphasize that these three networks of attention cannot be considered to be isolated, but propose that they interact with each other. Especially the alerting network and the network of visuospatial attention are supposed to interact within the right cerebral hemisphere by joint modulation through noradrenergic afferences from the locus coeruleus (LC) (Morrison & Foote, 1986; Posner & Petersen, 1990). This interaction constitutes an important foundation of Study 1 in this thesis.
1.2.4 A cortical network for selective attention (Mesulam, 1981; 1985; 1990 & 2002)

Mesulam (1981) subdivides selective spatial attention into four subcomponents, which are associated with specific anatomical correlates in the brain that form a network of attention. The *reticular* component controls arousal (in terms of alertness) and vigilance. The *limbic* component, represented by the cingulate gyrus, regulates the spatial distribution of motivational valence. The *frontal* component, including the frontal eye fields (FEF), coordinates motor programs for exploration, grasping and fixation and last but not least the *posterior* parietal component provides an internal sensory map. Mesulam postulates that neglect symptoms can arise following lesions of any of the four components. Following Heilman and colleagues (see 1.2.2), he also stresses the dominance of the right hemisphere for attentional functions in the brain.
1.2.5 A theoretical framework of attention (Van Zomeren & Brouwer, 1994)

Van Zomeren & Brouwer (1994) divide the concept of attention into two main aspects which include specific attentional functions. However, they stress that their assumptions should be merely regarded as a theoretical framework rather than a model “carved in stone” and that the subcomponents are not independent but partially overlapping. They subdivide the concept of attention into the aspects of selectivity and intensity. In their model, the aspect of selectivity covers functions of focused attention and divided attention, while the intensity aspect includes alerting functions and sustained attention or vigilance. Additionally, Van Zomeren & Brouwer postulate a „supervisory attentional control“, which can either modulate the selectivity and the intensity aspect of attention. Sturm & Zimmermann (2000) enhance this framework by adding the aspects of spatial attention and “task switching” and differentiate the concepts of sustained attention (rapid sequence of relevant stimuli) and vigilance (low rate of relevant stimuli; high monotony).
Aspects of this theoretical framework found their way into computerized assessment systems like the “Test for Attentional Performance” (TAP; Zimmerman & Fimm, 2002) and the “WAF - Perception and Attention Functions” of the Vienna Test System (VTS) (Häusler & Sturm, 2009; Sturm, 2006).

1.3 Alertness

1.3.1 Definition

The concept of alertness constitutes the most basic aspect of attention and can be found in all influential attentional models. Only the labeling of the concept differs within the different frameworks: While Van Zomeren und Brouwer (1994) as well as Posner et al. (1987, 1990) use the term „alertness“, Heilman & Valenstein (1979) und Mesulam (1981) amongst others refer to it as “arousal”. However, there is consensus in attributing alertness to the intensity
aspect of attention (compare Van Zomeren & Brouwer, 1994).

Alerting or alertness designates the general preparedness for responding of an organism and forms the foundation for more complex attentional functions. It can be subdivided into three components, namely tonic, phasic and intrinsic alertness. Tonic alertness represents the state of being awake and its circadian fluctuations. Phasic alertness on the other hand denotes the ability to increase the alertness level following an external stimulus (e.g. a warning tone). Additionally, Sturm et al. (1999) propose the concept of intrinsic alertness, which describes a short-term, self-initiated preparedness in anticipation of an external stimulus (Sturm & Willmes, 2001), and they separate the concept from sustained attention or vigilance, which both require a more long-term allocation of attention. Intrinsic alertness thus represents a more top-down mechanism that differs from phasic alertness by the absence of external cues.

1.3.2 Operationalization

Measurements of tonic, phasic and intrinsic alertness are accomplished by simple reaction tasks. Patients or experimental participants are asked to respond following an acoustic or visual target stimulus, e.g. by pressing a button. The obtained reaction times represent a quantified measure of intrinsic alertness. If the patient or participant is provided with a warning tone or other alerting cue prior to target presentation, the resulting decrease of reaction time provides a quantified measure of intrinsic alertness. Finally, from repeated testing of alertness in the course of a day, conclusions regarding tonic alertness can be drawn. Common methods of measuring alertness functions include (amongst others) the Reaction Test (RT) of the Vienna Test System (VTS), the Test for Attentional Performance (TAP; Zimmermann & Fimm, 2002), and the “WAF - Perception and Attention Functions” of the VTS (Häusler & Sturm, 2009; Sturm, 2006) or the Attention Network Task (ANT) (Fan, McCandliss, Sommer, Raz, & Posner, 2002). A distinction of intrinsic and phasic alertness however, is only possible within the TAP and WAF batteries.
1.3.3 Functional neuroanatomy

The right cerebral hemisphere is supposed to be dominant for the alertness function (Heilman & Valenstein, 1979; Sturm et al., 1999; Sturm & Willmes, 2000). Lesion studies reveal how simple reaction times in patients with right hemisphere damage are significantly increased (Ladavas, 1987; Howes & Boller, 1975; Posner et al., 1987 & 1990). Posner & Petersen (1990) postulate that the noradrenergic system arising from the locus coeruleus (LC) plays a crucial role in the generation and maintenance of general alertness. The LC is a dense cluster of noradrenergic neurons within the dorso-rostral pons of the brainstem and forms the main source of efferent projections towards almost all cortical areas (Aston-Jones, 2005). Additionally, LC function is closely tied to the circadian sleep-wake rhythm (Aston-Jones, Chen, Zhu, & Oshinsky, 2001) via its indirect but pronounced connections with the suprachiasmatic nucleus (SCN), which is regarded as a “circadian pacemaker”. Morrison & Foote (1986) detected that noradrenergic innervation is much more pronounced within the right hemisphere and is especially connected with the posterior attention network (comprising the pulvinar, superior colliculus and posterior parietal lobe), which selects visual information for further processing (Posner & Raichle, 1994) (see also 1.2.3). Accordingly, Fernandez-Duque & Posner (1997) postulate that this conjunction of the noradrenergic system and the posterior attention network gives way to an interaction of the functions of alertness and visuospatial orienting (see 1.4.5).

Marrocco, Witte & Davidson (1994) point out as well that the noradrenergic system is bilaterally asymmetrically distributed and that cortical noradrenergic projections towards the right hemisphere are denser. New and salient stimuli activate the LC, and the noradrenergic LC neurons then increase the signal-noise ratio for cortical areas that process the relevant stimuli (Coull, Frith, Dolan, Frackowiak, & Grasby, 1997). Thus, Aston-Jones & Cohen (2005) postulate that the LC optimizes behavior and that phasic and tonic LC activity are closely tied (Aston-Jones, Rajkowski & Cohen, 1999), which means that in the state of low tonic LC activity, phasic LC activity can be inhibited which leads to a decrease in reaction performance. On the other hand, reaction performance can also be decreased by very high
LC activity, resulting in increased distractibility and thus decreased selective attention. This relationship is similar to the Yerkes-Dodson law which describes the interaction of arousal and performance in a parabolic way (Easterbrook, 1959). In general, phasic LC activity by salient stimuli points towards a crucial role of the noradrenergic LC system in the regulation of general arousal or alertness and wakefulness (Aston-Jones, 2005).

In a PET study, Sturm et al. (1999) examined which cortical and subcortical areas of the brain are involved in intrinsic alertness and postulated that the noradrenergic activation system may be influenced by top-down control, since animal lesion studies (e.g. Robinson & Coyle, 1980) show how lesions in the right frontal cortex lead to bilateral depletion of noradrenaline. To identify the subcortical and cortical areas involved in intrinsic alertness, Sturm and colleagues chose a simple reaction time paradigm in which participants were asked to respond as quickly as possible when a white dot appeared centrally on a black computer screen. Intrinsic alerting led to a significant increase of regional cerebral blood flow (rCBF) in the right anterior cingulate cortex (ACC; BA 32), right middle frontal gyrus (BA 9 and 10), in the brain stem reticular formation, the right inferior parietal lobe, the right thalamus as well as the right middle and superior temporal gyrus (BA 20 and 22) and the left inferior frontal gyrus (BA 44 and 45). Thus, apart from the BA 44 and 45 activations, all changes in rCBF were found within the right hemisphere and the activation pattern shows significant overlap with the alerting network proposed by Posner & Petersen (1990) (see 1.2.3). Based on their findings, Sturm et al. propose a right-hemispheric network established by frontal, parietal, thalamic and brain stem regions. They postulate that the ACC within the frontal lobe modulates the activity of noradrenergic neurons in the reticular formation and thus exerts top-down control of intrinsic alertness.

This top-down control by the ACC was also observed in a connectivity study by Mottaghy et al. (2006), who found right-hemispheric dominance of effective connections and identified the ACC as a coordinating center of the proposed right-hemispheric network of intrinsic alertness. A similar activation pattern was found in a study of auditory intrinsic alertness, albeit with some modality specific differences, e.g. additional activations within the right
precentral gyrus and inferior frontal activations instead of medial frontal gyrus activations in visual intrinsic alertness (Sturm et al. 2004). Sturm and Willmes (2000) postulate a supramodal right hemispheric network controlling intrinsic alertness. In their study, phasic alertness showed a more widespread activation pattern, which was nevertheless dominant within the right hemisphere and which showed additional cortical and subcortical activations, e.g. in the left superior and ventrolateral frontal gyri and the thalamus.

1.4 Visuospatial attention

1.4.1 Definition

Visuospatial attention enables the orientation towards relevant external stimuli. Posner (1980) discriminates between moving the spotlight of attention with (overt attention) and without (covert attention) eye movements. In general, the focus or ‘spotlight’ of attention moves towards a new relevant stimulus together with the eyes to enable foveal processing. This can either be achieved by smooth pursuit eye movements or saccadic eye movements of approximately 15 – 100 ms duration, which alternate with fixations of 15 – 2000 ms duration (Bierbaumer & Schmidt, 1996).

However, visuospatial attention or orienting can also be directed covertly without moving the eyes, in the sense that a person can focus attention to one part of space while the eyes are fixated to other parts of space. Posner et al. (1980) proved this by showing how reaction times following expected and unexpected stimuli in a paradigm containing predictive cues are faster for expected than for unexpected stimuli, reflecting the advantage of covert shifts of attention triggered by the spatial cues (see also 1.4.2). Posner and coworkers were the first to present experimental evidence for covert orienting of attention. Both covert and overt orienting of attention can either be a reflexive or deliberate response towards novel stimuli. As described within Posner’s model of visual attention (1.2.3), visuospatial orienting consists of three subcomponents: Disengaging from the current focus of attention, moving attention towards a new stimulus and engaging attention at the new focus.
1.4.2 Operationalization

Visuospatial orienting is mainly measured by reaction time paradigms, today mostly realized by computer software. Thus, the primary dependent variable is reaction time, but also accuracy, counting omissions and false reactions.

**Overt orienting**

Overt orienting can be measured in diverse ways. Examples for experimental operationalization of overt orienting are simple detection paradigms, visual search paradigms (e.g. the subtest “Visual Scanning” of the TAP (Zimmermann & Fimm, 2002), or so-called “gap-overlap” paradigms for examining eye movements. Visual search can be accomplished by using targets that differ sharply by one or more features from the surrounding distractors. The detection of those targets is achieved by a so-called “pop-out” effect, because the targets immediately catch the participant’s eye. Thus this kind of visual search is also called parallel or feature search and is rather regarded as a preattentive process without much involvement of visuospatial orienting. However, if the target is sharing one or more features with the distractors, the paradigm is a so-called conjunction or serial search paradigm. In this case, visuospatial orienting is heavily involved since the display needs to be actively and systematically searched for the target. Thus both orienting and focused attention are involved in completion of the task (Treisman & Gelade, 1980). Additionally, the stimulus display can either contain a target and the search is terminated by the participant’s reaction upon detection (self-terminating search), or the display does not contain a target and the participant terminates the task by signaling the absence of the target (exhaustive search), e.g. by a button press. Other paradigms for examining overt attention are e.g. the greyscales task, line bisection or landmark tasks (see 3.3 for details).

**Covert orienting**

Common tasks to examine covert orienting of visuospatial attention predominantly consist of cueing paradigms which originate from Posner (1980). Initially the participant is presented
with a fixation cross in the middle of the display and he or she is instructed to fixate it during the entire paradigm. The task is to respond with a fast button press upon detection of a target appearing to the left or to the right of the fixation cross. Before the target appears, the participant is provided with a spatial cue which indicates on which side the target is likely to appear. The cue can either be presented centrally or peripherally. A central cue usually consists of an arrow pointing in the direction of the anticipated target and a peripheral cue is usually a symbol which appears at the site of the potential target. Use of a central cue is generally considered as “endogenous” cueing, since the participant is required to actively orient attention in the direction of the arrow, while using a peripheral cue is called “exogenous” cueing, since the appearance usually results in automatic orienting towards the cue. After a cue-target interval of 100-300 ms or longer, the target appears to which the participant has to respond. In exogenous cueing paradigms however, intervals longer than 500 ms should be avoided since they can result in inhibition of return and thus in increased reaction times (Posner & Cohen, 1984).

![Spatial cueing paradigm](image-url)

**Figure 1.7:** Spatial cueing paradigm (from: Posner et al., 1982).

Usually, covert attention paradigms contain some invalid cues, which means that some of the cues indicate the wrong target location. If the ratio of valid to invalid cues is 50/50%, the
paradigm is considered to be non-predictive. Predictive paradigms usually consist of 60/40%, 70/30% or 80/20% ratios of valid and invalid cues. The difference between reaction times of valid and invalid trials represents the measure for covert attention. If a participant covertly orients his or her attention following a valid cue, detection of the target is faster than for invalid cues. In the latter case, the participant needs to reorient attention from the invalid cue location to the actual target location. The difference between invalidly and validly cued target reaction time is also called validity effect. A typical Posner cueing task is realized with the “Covert Attention” subtest of the TAP. Other paradigms, e.g. the Attention Network Test – ANT (Fan et al., 2002), additionally use neutral, non-predictive cues (e.g. bilateral cueing), trials without cues or vary the difficulty of the trials by using congruent and incongruent flanker stimuli. Therefore the ANT does not only examine orienting, but also phasic alerting and executive attention and thus all three subcomponents of Posner’s attentional network theory (see 1.2.3).

Another task to assess covert attention is the subtest “Neglect” of the TAP. Participants are asked to fixate a small square in the middle of the display and report changing letters inside this square. The rest of the display is filled with irregularly arranged numbers and the participant additionally needs to press a button upon detection of a small flickering stimulus amongst the numbers within the display. Since the eyes are continuously fixated on the center square, the flickering stimuli can only be detected by covert orienting.

1.4.3 Functional neuroanatomy
The neuroanatomy of visuospatial orienting has been intensively investigated. First, lesions studies tried to uncover the neuronal correlates of attentional processes by comparing lesion locations and the subsequent disorders of visuospatial attention. Later, at the beginning of the 1990’s, functional imaging allowed to observe the attentional networks in action and many of the theories that have been developed before have been partially confirmed as well as extended.
Introduction

Generally, the majority of studies agree that the right parietal lobe plays a crucial role in visuospatial attention (Corbetta, Miezin, Shulman, & Petersen, 1993; Heilman & Van den Abell, 1980; Posner et al., 1984 & 1987). Brain (1941) was one of the first persons to describe neglect symptoms following right-hemispheric parietal injuries. Today, the parietal lobe is merely considered as one important part of a widely distributed neuronal network consisting of a number of cortical as well as subcortical components.

Based on their clinical and experimental findings, Posner and colleagues (1971, 1990) proposed a network of visuospatial orienting, containing the posterior parietal lobe, the pulvinar of the thalamus and the superior colliculus, which regulate the attentional subcomponents of disengaging, moving and engaging attention (see 1.2.3), whereas Mesulam (1981) postulated four regions involved in a network of visuospatial attention, namely a posterior parietal, a limbic (ACC), a frontal, as well as a reticular component, which all possess a functional role within the network (see 1.2.4).

Clinical evidence shows that the network of visuospatial attention does actually consist of distinct and distant regions in the brain. Visuospatial neglect has been observed after unilateral lesions at very different sites in the cortex, including the posterior parietal lobe, its inferior part as well as the temporo-parietal junction (Vallar and Perani, 1986), the frontal lobe (Damasio, Damasio, & Chui, 1980; Heilman & Valenstein, 1972), or the superior temporal gyrus (Karnath, Ferber & Himmelbach, 2001).

One of the first elaborate imaging studies of the network of visuospatial attention was conducted by Corbetta, Miezin, Shulman, & Petersen (1993). Combining a peripheral covert orienting paradigm and positron emission tomography (PET), the study detected activations of the right superior parietal lobe (SPL) near the sulcus postcentralis (BA 7), associated with moving attention in the left visual hemifield. Moving attention in the right visual hemifield, however, was associated with bilateral activations of the superior parietal lobes, though activations in the contralateral areas were stronger. A central detection task on the other hand, yielded no significant activations in the parietal areas associated with the peripheral task. The directions of attentional movements within the respective hemifields resulted in
similar cortical activations. Thus, the authors conclude that the SPL is encoding the visual hemifield, but not so much the direction in which attention is moved. The findings from this study did confirm previous findings from lesion studies as well as resulting modeling approaches (e.g. Heilman & Van den Abell, 1980; Mesulam, 1981, Posner et al., 1971, 1990), which postulated an important role of the right parietal lobe in visuospatial orienting. This is in line with the prevalence of neglect symptoms after right hemisphere over left hemisphere lesions in parietal areas. In case of the latter, the right parietal lobe is supposed to be able to substitute attentional functions within the right visual hemifield, while the left parietal lobe is unable to do so. Corbetta et al. (1993) additionally detected superior frontal activations, which they attribute to motor aspects of attention. Interestingly though, the frontal and the parietal cortex are linked by parieto-prefrontal projections and both are connected by efferences with the ACC as well as subcortical areas (Goldman-Rakic, 1988) and lesions in these areas can result in neglect symptoms similar to those after parietal injuries (Janer & Pardo, 1991; Fimm et al., 2001). As mentioned above, even frontal lesions alone can be associated with the occurrence of neglect (Damasio et al., 1980, Heilman & Valenstein, 1972), a finding which underlines the notion of a widespread network controlling visuospatial attention.

Gitelman et al. (1999) examined this network of visual orienting based on the assumptions of Mesulam (1981). They postulate a network consisting of frontal parietal and cingulate cortices, each subcomponent of which makes a differential contribution to visuospatial orienting. Using a paradigm sensu Posner (1980) (see 1.4.2) that utilized endogenous arrow cues in combination with functional magnetic resonance imaging (fMRI), they found distinct parietal activations near the intraparietal sulcus (IPS) and the SPL in both hemispheres, however more pronounced within the right hemisphere. Additional activations were detected bilaterally in the premotor cortex, in the frontal eye fields (FEF), and the in the ACC. Subcortical activations were found in the right thalamus and bilaterally in the basal ganglia. Thus the findings support the network model of visuospatial orienting as well as the idea of right hemisphere dominance by detecting significantly stronger activations in the right parietal
lobe. The FEF activations are supposed to be of attentional but not oculomotor character, underlining their importance in covert orienting of attention.

Another study (Nobre et al., 1997) to assess Mesulam’s model of visuospatial attention (Mesulam, 1981) utilized PET and a covert attention paradigm with reflexive and non-reflexive cues. Reflexive cues were associated with right ACC, right posterior parietal, bilateral premotor and medial frontal activations as well as subcortical activations in the pulvinar of the thalamus. The contrast of both cueing conditions did not reveal any significant differences in the cortical activation pattern, except a slightly stronger left parietal activation in the non-reflexive condition that might be associated with disengaging of attention (Posner et al., 1984). Again, the study supports the network models of attention Mesulam (see 1.2.4) as well as Posner and colleagues (see 1.2.3), describing a right hemisphere dominance for visuospatial attention.

In an fMRI study, Beauchamp et al. (2001) examined the networks for both overt and covert orienting of visuospatial attention and found activations of the precentral sulcus, the intraparietal sulcus as well as the lateral occipital sulcus for both overt and covert orienting with stronger activations following overt orienting. While this study again supports the network models of attention, it also underlines the importance of oculomotor areas for both overt and covert attention. The overlap of the attentional network and the oculomotor network has been hinted at before in a meta-analysis by Corbetta (1998).

A somewhat different approach in studying the neural correlates of visuospatial attention is made by the team of Posner. Fan et al. (2005) studied the anatomy of attentional network by using the ANT (see 1.4.2), which probes orienting, alerting as well as executive control. They found right SPL activations for orienting as well as activations near the FEF. Similar results were found by Kelley, Serences, Giesbrecht, & Yantis (2008) for peripheral covert attention and Rosen et al. (1999) examined whether activations differ following exogenous versus endogenous cueing. They did not find any differences in the activations of the underlying attentional network, but registered additional activations in the dorso-lateral prefrontal cortex (BA 46) for endogenous cues, which indicate that processes of working memory might be
engaged in voluntary shifts of covert orienting.

Overt orienting is supposed to encompass a similar neuronal network. Gitelman, Parrish, Friston, & Mesulam (2002) examined neuronal activations patterns following visual search tasks and found involvement of the posterior parietal lobe and the FEF, with stronger activations in the right hemisphere, as well as subcortical activations of the colliculus superior. Corbetta (1998) already pointed out the interdependence of the systems for visuospatial attention and eye movements and thus that overt and covert attention rely on similar networks.

In summary, the described studies as well as other imaging studies (e.g. Kastner et al., 1999; Pessoa, Kastner, & Ungerleider, 2003) are indicating a widespread network of visuospatial orienting which contains frontal, parietal and subcortical components. Another recurrent theme of the studies is the identification of right hemispheric dominance within this network. This dominance is also expressed in healthy people by a phenomenon called ‘pseudoneglect’, which marks the tendency to ‘over-attend’ to stimuli within the left visual hemifield, in the sense of an attentional asymmetry (see 1.4.4).

1.4.4 Phenomenons of the distribution of visuospatial attention

Although the normal person might think that its visuospatial attention seems to be equally spatially distributed, the dominance of the right cerebral hemisphere leads to small, albeit statistically significant distortions of the way we perceive and react in space. Another, more striking evidence for right hemisphere dominance is the altered visuospatial attention following right hemisphere stroke or injuries. Both phenomena, called pseudoneglect and neglect, will be briefly outlined in the next two paragraphs to demonstrate how the right cerebral hemisphere plays a crucial part in directing attention in space.
Pseudoneglect

The term pseudoneglect refers to the asymmetric distribution of visuospatial attention in healthy persons. The term was originally coined by Bowers & Heilman (1980) and it is supposed to be the expression of the proposed right hemisphere dominance in attentional functions. Normal subjects tend to “overattend” to the left side of space, e.g. by making leftward errors in line bisection tasks, or in judging brightness and numerosity (Nicholls, Bradshaw, & Mattingley, 1999). Thus, pseudoneglect is opposite in direction to pathological neglect (see below) which might occur after right-sided brain damage.

Visuospatial neglect

Patients after right hemisphere damage show deficits in orienting towards stimuli in the left visual hemifield (Heilman, Watson, & Valenstein, 1979). Neglect of the right visual hemifield is rare, since attention in the right visual field is directed by both the left and the right cerebral hemispheres while the right hemisphere is the dominant one to direct attention within the left visual field (Corbetta et al., 1993).

Visuospatial neglect is expressed by severe inattention towards the left visual hemifield. Patients after right hemisphere lesions e.g. bisect lines right off the true center, copy only half of presented pictures or detect only right sided stimuli in visual search tasks. In severe cases, patients also might only shave or make up the right half of their faces. Furthermore, neglect can also occur multimodally and extend to e.g. the tactile or auditory senses (Kerkhoff, 1999; Pavani, Ládavas, & Driver, 2003).
Within the right hemisphere, the right parietal cortex is most important for visuospatial orienting and thus neglect is supposed to be most common after parietal injuries (Vallar, Bottini, & Paulesu, 2003, Vallar & Perani, 1986), although the role of the superior temporal gyrus in the development of visuospatial neglect has been discussed recently (Gharabaghi, Fruhmann, Berger, Tatagiba, & Karnath, 2006, Karnath et al., 2001). However, neglect symptoms may also occur after frontal lesions, in areas preoccupied with maintaining an alert state (Damasio et al., 1980, Fernandez-Duque & Posner, 1997) – a fact which indicates the proposed interaction of alertness and visuospatial attention (see 1.4.5).

Newer studies emphasize the importance of the integrity of fronto-parietal network by showing how disruption of white matter tracts, e.g. by intraoperative electrical stimulation (Thibeaut de Schotten, Urbinski, Duffeau et al., 2005) can elicit neglect-like symptoms. The structure critical in this context seems to be the right superior longitudinal fasciculus (SLF) (Bartolomeo, Thiebaut de Schotten, & Doricchi, 2007; Doricchi & Tomaiuolo, 2003; Shinoura et al, 2009) as lesions in this white matter region seem to lead to a disconnection of parietal and frontal structures which form part of the network of visuospatial attention (see 1.4.3).
1.4.5 Interactions of alertness and visuospatial orienting

Within their models of attention, Heilman & Valenstein (1978), Mesulam (1981) and Posner & Petersen (1990) already pointed out right hemisphere dominance of attentional functions, but also that the network for visuospatial attention might be modulated by the network of alertness (arousal). Clinical studies show how patients can develop neglect symptoms even after lesions of the network of alertness, e.g. following frontal lesions of the right hemisphere (Fernandez-Duque & Posner, 1997). Heilman & Valenstein (1978) postulated a connection of visuospatial orienting and alertness, in the sense of that the right hemisphere, which is dominant for arousal, might activate the left hemisphere, while the left hemisphere is unable to substitute for a right hemisphere arousal deficit following cortical lesions.

Posner & Petersen (1990) do stress the link between alertness and visuospatial orienting within their model of attention (see 1.2.3) by pointing out the dense innervation of the right hemisphere by noradrenergic efferences of the brain stem, particularly the LC (Morrison & Foote, 1986). Those noradrenergic efferences are notably pronounced at the posterior parietal lobe, the pulvinar and the colliculus superior – exactly those areas which Posner & Petersen link with the subcomponents of visuospatial orienting (see 1.2.3). While the posterior parietal lobe is widely innervated by noradrenergic neurons in general, the right temporoparietal junction (TPJ) is most densely innervated by ascending neurons of the LC (Beane and Marrocco, 2004; Marrocco et al., 1994; Morrison and Foote 1986).

Especially important in the context of study 1 (see 2) is the fact that the right TPJ plays a key role in the reorientation of visual attention towards previously unattended locations in the visual field. Lesions within the right TPJ are frequently associated with neglect symptoms (Friedrich, Egly, Rafal, & Beck, 2003; Thiebaut de Schotten et al., 2005; review in: Danckert & Ferber, 2006) and imaging studies also identified the link between TPJ and visuospatial reorienting (Corbetta, Kincade, Lewis, Snyder, & Sapir, 2005; Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000; Corbetta & Shulman 2002; Thiel, Zilles, & Fink, 2004). Corbetta and colleagues (2002) showed how the right TPJ was barely activated during cueing, but,
independent of the visual hemifield, displayed strong activations during reorientation of attention following invalid cues.

A multitude of studies show an anatomical overlap of the two attentional systems of orienting and alerting (Bartolomeo, 2000; De Renzi, Gentilini, Faglioni, & Barbieri, 1989; Gitelman et al., 2002; Karnath, Niemeyer, & Dichgans, 1998; Vallar, 2001), but clinical as well as experimental studies also point towards a functional overlap of these systems. In an influential study, Robertson, Mattingley, Rorden & Driver (1998) demonstrated this functional connection by manipulating neglect symptoms through phasic alerting. Since the reticular system, which modulates alertness (Aston-Jones, 2005; Mesulam, 1981; Posner & Petersen, 1990), is generally intact in neglect patients, they proposed that phasic alerting should result in improvement of visuospatial function in these patients. They probed this hypothesis by using a visuospatial orienting paradigm. In 25% of the trials, patients were given a central warning tone which they were instructed to ignore. While patients showed delayed reactions towards stimuli in their left visual hemifield in absence of the warning tone, this spatial bias was almost eliminated during parallel presentation of the warning tone. Accordingly, the authors postulate that phasic alerting by the warning tone lead to an acceleration of perception of left stimuli. To rule out that the central warning tone might have reoriented attention towards the left hemifield by its position, they examined whether right sided warning tones eliminated this effect by maintaining attention in the right hemifield. However, this condition lead to a significant improvement of leftward orienting either and the authors assume that the warning tone did indeed induce a phasic activation in the patients and resulted in an improvement of orienting towards the left hemifield. In their study, Robertson and colleagues did not only prove for the first time that non-spatial, phasic activation can improve visuospatial deficits, but conversely argue that these deficits can not solely be caused by the loss of neuronal function in the sensory areas of the brain since phasic alerting does not restore those. This modulation of orienting by phasic alerting suggests that decreased tonic alertness might play a role in the development of neglect symptoms following right hemispheric lesions.
Based on the findings of Robertson et al. (1998), Thimm, Fink, Kust, Karbe & Sturm (2006) examined whether long-term alertness training would improve visuospatial orienting in neglect patients. Intrinsic alertness in 7 patients was trained using the computer-based alertness training "AIXTENT" (Sturm et al., 1993; Sturm et al., 1994) over a period of three weeks. Before the training protocol, as well as one day (post 1) and 4 weeks (post 2) after completion of the training, the patients were tested with two covert attention paradigms (TAP subtests "neglect" and "visual field", see also 1.4.2) and an alertness paradigm (modification of the TAP "neglect" paradigm without the visuospatial orienting component) using fMRI.

At the “post 1” examination, they found significant reactivations of right-hemispheric areas associated with visuospatial orienting, namely the frontal cortex, the ACC, the precuneus and the angular gyrus. Especially the patients that showed an improvement in behavioral data, also showed increased perilesional activations in the right frontal cortex, which is interpreted by the authors as reactivation of parts of the alertness network. At the “post 2” examination, four weeks after completion of the training, activities in those areas that had been significantly reactivated at “post 1”, showed decreased activations. However the increased bilateral frontal, ACC and right angular gyrus activations sustained. Although this study shows that alertness training didn’t lead to a long-term reactivation of the network of visuospatial orienting, it stressed the important influence alertness can have on this network and underlines the hypothesis of a functional coupling of both attentional networks.

While Fernandez-Duque & Posner (1997) (based on experimental data) conclude that the mechanisms of orienting and alertness are independent, newer experimental studies with healthy participants also prove a functional link of both attentional functions. Bellgrove, Dockree, Aimola & Robertson (2004) showed how the individual intensity capacity of sustained attention modulated the magnitude of pseudoneglect. At the beginning of the study, the individual capacities of sustained attention, as well as potential attentional biases were examined. Spatial biases were measured using the greyscales task (Mattingley et al., 2004; Nicholls, Bradshaw, & Mattingley, 1999). The authors found a significant correlation
between errors in the sustained attention task and the asymmetry index of the greyscale task. While both the good and poor sustained attention groups revealed a significant leftward attentional bias, it was significantly ameliorated in the poor sustained attention group.

Callejas, Lupiáñez & Tudela (2004) examined interactions of the three attentional networks sensu Posner using the ANT (Fan et al., 2002) and found a significant effect of alerting stimuli on the validity effect during visuospatial cueing. In those cueing trials that were accompanied by an additional warning tone, the validity effect was significantly larger than in uncued trials. The authors interpret these findings as an acceleration of visuospatial orienting.

Sleep deprivation is another method to examine the interaction of alertness and visuospatial orienting. By decreasing alertness through sleep deprivation, Thomas et al. (2000) found a significant reduction of the cerebral metabolic rate of glucose (CMRglu) within the posterior parietal cortex, the thalamus and the prefrontal cortex – areas, which are concerned with directing visuospatial attention (see also 1.4.3). Behavioral studies of sleep deprivation and visuospatial attention support this interaction: Fimm, Willmes & Spijkers. (2006) examined healthy subjects by manipulating the level of tonic alertness by means of sleep deprivation. Covert attention was measured by an exogenous cueing paradigm sensu Posner (1980). Following 28 hours of sleep deprivation and significantly reduced arousal, they detected a significant slowing of reactions towards stimuli in the left visual hemifield as well as an acceleration of covert attention in the right visual hemifield. In line with these findings, Manly, Dobler, Dodds & George (2005) found a rightward shift of visuospatial attention in a landmark task in healthy participants after a period of relative sleep deprivation.

More evidence for the interaction of alertness and visuospatial orienting comes from pharmacological studies. Coull, Nobre & Frith (2001) support the interaction of both attentional networks by showing how the adrenergic antagonist clonidine modulated both reactions as well as neuronal correlates of the alerting and the orienting network of healthy participants by reducing the validity effect within the left but not the right visual hemifield. This
effect was also associated with reduced activation in the right superior parietal lobe. Clark, Geffen & Geffen (1989) also observed how clonidine and droperidol (a dopamine agonist) did not influence initial orienting following a valid cue but diminished the validity effect following invalid cues and conclude that noradrenaline and dopamine are playing an important role in disengaging attention.

1.5 Visual perception and attention in three-dimensional space

The majority of studies concerning visuospatial attention and its disorders use methods and paradigms presented in two-dimensional space, e.g. on computer screens, placed in near motor space of patients and participants. Near space, also called “peripersonal” space is defined as the space within arm’s reach and is closely linked with planning and executing manual movements and localization of objects. On the other hand “extrapersonal” space is defined as the space outside arm’s reach and taken to be involved in object identification (Goodale & Milner, 1992; Ladavas & Farne, 2004; Previc, 1998).

Different models of three-dimensional space have been put forward, which mainly differ with respect to parcellation of extrapersonal space. Three models will be described in more detail: Previc (1990) proposed two major space areas, a peripersonal one and a focal extrapersonal one. However, he additionally added the “extrapersonal ambient realm” which is supposed to be important in spatial orientation and postural control. The peripersonal space described in his model extends to about 30° lateral visual angle and is biased towards the lower visual field, representing reaching space. On the other hand, Previc describes the focal extrapersonal space as a football-shaped relatively small area (due to limited retinal capacities) which is processed by the ventral visual stream.
Another model has been put forward by Rizzolatti and colleagues (Rizzolatti & Camarda, 1987; Rizzolatti, Gentilucci, & Matelli, 1985), based on animal lesion studies. This model relies on three major spaces: personal space, peripersonal and extrapersonal space. Personal space is connected to oral and tactile processing at the body level, whereas peripersonal space is again based on reaching space and extrapersonal space, also called oculomotor space in this model, is based on the space beyond personal and peripersonal space. Each area is allegedly processed by different areas in the parietal and frontal cortices. The third model by Grüsser (1983) contains four major space realms: grasping space (including instrumental grasping space), near distant action space, far-distant action space and the visual background. Thus the model resembles Previc’s and Rizzolatti’s models except for a parcellation of action space into near-distant and far-distant.
Based on his 1990 model and some of the described models by other authors, Previc (1998) puts forward a modified model of his older version, containing four spatial realms: A peripersonal one, focal extrapersonal space, action extrapersonal space and ambient extrapersonal space.
Processing of both areas of space is supposed to rely on two different cortical visual processing streams (Goodale & Milner, 1992; Ungerleider & Mishkin, 1982). The dorsal stream is supposed to be specialized in spatial perception and has also been labeled as the “where” stream of the visual system. In this context, attention to peripersonal space is supposed to rely on dorsal visual stream processing and apparently biased towards the lower visual field. The ventral stream, also called “what” stream on the other hand, is specialized for perception and object identification and associated with attention to extrapersonal space, as well as allegedly biased towards central vision and the upper visual field (Previc, 1990 & 1998; Weiss et al., 2000).

Brain (1941) provided the first indications that the two main areas of three-dimensional space outside the body are likely to be represented by differential cortical areas. He reported the first case of neglect that was restricted to peripersonal space and identified different deficits of visuospatial attention within peripersonal space and beyond, depending on inferior parietal
vs. superior parietal lesions. This dissociation of dorsal and ventral stream processing has been found in various clinical studies which describe patients showing dissociations of near and far neglect symptoms (e.g. Butler, Eskes, & Vandorpe, 2004; Committeri, Pitzalis, Galati et al., 2007; Cowey, Small, & Ellis, 1994 & 1999; Frassinetti, Rossi, & Ládavas, 2001; Halligan and Marshall, 1991; Mennemeier, Pierce, & Heilman, 1992; Shelton, Bowers, & Heilman, 1990; Vuilleumier, Valenza, Mayer, Reverdin, & Landis, 1998). Halligan & Marshall (1991) described a patient who, despite showing severe neglect in peripersonal space in a line bisection task, showed little or no neglect symptoms when asked to bisect lines in far space. In their study, Butler et al. (2004) asked patients to verbally report targets on scanning sheets placed in peri- and extrapersonal space and found relations between peripersonal neglect and dorsal stream lesions and extrapersonal neglect and ventral stream damage respectively.

But also animal studies (overview in Rizzolatti, Berti, & Gallese, 2000) as well as experimental and imaging studies in healthy subjects support the association of peripersonal space and dorsal attentional processing as well as extrapersonal space and ventral attentional processing (Committeri et al., 2007; Weiss et al., 2000). In a PET study, Weiss and colleagues examined neural activations in healthy participants during line bisection in near and far space. They found greater activations for task performance in near space within the dorsal visual stream (the left dorsal occipital cortex, left intraparietal cortex, left ventral premotor cortex and left thalamus) and ventral visual stream activations (bilateral ventral occipital cortex and right medial temporal cortex) upon performance in far space.

In an fMRI study, Committeri et al. (2007) examined 52 patients after right ischemic events and showed how extrapersonal space processing is dependent on the “integrity of a circuit of right frontal (ventral premotor cortex and middle frontal gyrus) and superior temporal regions, whereas awareness of personal space is rooted in right inferior parietal regions (supramarginal gyrus, post-central gyrus)”.
Another study by Bjoertomt, Cowey & Walsh (2002) used transcranial magnetic stimulation (TMS) to investigate visuospatial performance of healthy subjects. They stimulated the participants’ right posterior parietal cortex by TMS as well as the right ventral occipital during a landmark task (judgment of pre-bisected lines) in near (50cm) and far (150cm) space. In the non-stimulated baseline condition, subjects showed pseudoneglect tendencies that were more pronounced in peripersonal space. TMS of the dorsal visual stream resulted in a significant rightward shift of perceived midpoint in near space and TMS of the ventral visual stream resulted in a significant rightward shift of perceived midpoint in far space, respectively. These studies impressingly underline the near-dorsal and far-ventral segregation of visual processing.

1.5.1 Virtual Reality as a research method

Virtual Reality (VR) is a computer generated and interactive three-dimensional environment rendered in real-time. By generating stereoscopic three-dimensional surroundings, the impression of space, depth and immersion are evoked in the user and give him the opportunity of interaction\(^1\). The goal is to either recreate reality as closely as possible, e.g. in simulations, or to create new environments and realms.

In recent years, Virtual Reality found its way into the entertainment industry, research as well as industrial fields. Important areas of VR applications are education and training of pilots by flight simulations, industrial modeling and prototyping, architectural visualizations as well as medical simulations, treatment and training. While the main focus of VR applications is visualization, VR systems are capable of integrating acoustic and haptic impressions into virtual environments as well.

Lately, VR technology has also emerged in medical and psychological research and therapy.

\(^1\) The term and definition of Virtual Reality is used ambiguously. Some authors already define two-dimensional environments as VR. However, in the context of this thesis, the term VR is used in the more narrow sense and refers exclusively to three-dimensional stereoscopic presentation of computer generated environments.
Several therapeutic approaches greatly benefit from VR by e.g. allowing controlled exposure therapy in the treatment of phobias (Gorini & Riva, 2008) or post-traumatic stress disorder (PTSD) (Rizzo & Buckwalter, 2008; Rizzo et al., 2008), and neurological therapy makes use of VR techniques in motor rehabilitation following stroke (reviews in: Burdea, 2003; Henderson, Korner-Bitensky, & Levin, 2007).

But also neuropsychological research and therapy is taking on VR as an opportunity for “precise control of complex stimulus presentations in which human cognitive and functional performance can be accurately assessed and rehabilitated” (Rizzo & Buckwalter, 1998). While traditional neuropsychological methods often lack ecological validity, i.e. a lack of relevance to activities of daily life, VR assessment and therapy can provide the patient with more complex and relevant environments, whilst keeping exact control of stimuli and variables (see Figure 1.12). Thus, VR assessments can provide high ecological validity and high experimental control at the same time, as well as increased generalizability of the results (Gaggioli, 2003; Loomis, Blascovic, & Beall, 1999).

Figure 1.12: The tradeoff between experimental control and ecological validity (from: Loomis, Blascovich, & Beall, 1999)
Although standardized neuropsychological tests in virtual environments are still mostly under development, multiple efforts are made to bridge the gap between standardization and ecological validity in the assessment of various cognitive domains (Elkind, Rubin, Rosenthal, Skoff, & Prather, 2001; Matheis et al., 2007; Parsons & Rizzo, 2008; Tsirlin, Dupierrix, Chokron, Coquillart, & Ohlmann, 2009).

Thus, advantages of using VR in experimental neuropsychology are comparable to traditional computer-aided assessments concerning the exact repeatability and control of the experimental situation. At the same time, VR additionally allows for using three-dimensional stimuli in different realms of space. VR also gives the user the opportunity of interaction and immersion, thereby crucially enhancing ecological validity.

For the presentation of VR environments a number of special hardware and software requirements are essential; they will be outlined in the next two sections.

1.5.2 Hardware

Two separate pictures from different perspectives need to be presented to evoke a three-dimensional, stereoscopic impression in the user. From these two pictures, the eyes generate the plastic, three-dimensional “diorama”. There are different methods for visualization of Virtual Environments (VE). The most common devices for VR presentation are head-mounted displays (HMD), projection screens or so-called Cave Automatic Virtual Environments (CAVE) (Cruz-Neira, Sandin, DeFanti, & Hart, 1992). While a HMD generates separate pictures for each eye, a projection screen is provided with a stereo projector and special glasses help to generate the 3D-perception of the user: Shutter glasses contain liquid crystal and alternately display different perspectives for each eye by switching between darkness and transparency in synch with the refresh rate of the display system. Passive glasses create the impression of 3D by restricting the light that reaches each eye and interference glasses divide the visible color spectrum into narrow bands and thus slight color differences between the two eyes generate the stereoscopic impression. The CAVE merely
represents a room build out of several projection screens. It usually consists of four to six walls which are activated by several stereo projectors. Thus, the VE basically surrounds the user and the CAVE is currently considered to be the most immersive display system.

Interaction in VEs can be controlled by different interaction devices. While common computer keyboards and mice can be used, a range of special VR devices like the space mouse, flysticks or data gloves possess considerably more degrees of freedom. Some, like data gloves or the PHANTom® haptic device (SensAble Technologies), additionally allow the user to receive haptic feedback while touching and manipulating virtual objects. Last but not least, special electromagnetic or infrared tracking systems can be included in the VR setup, to track the users' position in space as well as updating the VE accordingly.

1.5.3 Software

VR presentations require special software, particularly since they have to generate complex stereoscopic VEs in real-time with a maximal frame rate. For modeling of three-dimensional objects, commercial vector graphic software like e.g. 3DStudio Max, AC3D and others are available. VRML (Virtual Reality Modeling Language) has become the standard graphic format for 3D modeling, which essentially is a text file format which describes the shape of the virtual object by means of coordinates, and which allows adding features like color, texture, transparency and lighting.

To present VR objects in stereoscopic simulations or experiments, an authoring system serving as the basic platform, e.g. WorldToolKit® (Sense8), as well as application software is necessary. While a wide variety of commercial and free software for reaction time measurement in experimental studies is available (e.g. E-Prime, Presentation®), as well as VR applications for therapeutic use in clinical psychology, like e.g. VR Worlds 2 by Psychology Software Tools, Inc. or NeuroVR 1.5 (Riva et al., 2009; Riva et al., 2007), time-critical VR experiments to date mostly rely on “custom-made” applications.
**ReactorMan VR application**

The Virtual Reality group at the Center for Computing and Communication of the RWTH Aachen University developed the NeuroMan framework and its ReactorMan application (Valvoda, Assenmacher, Dohle, Kuhlen, & Bischof, 2003) for the design and implementation of VR based neuropsychological experiments on their ViSTA platform (van Reimersdahl, Kuhlen, Gerndt, Henrichs, & Bischof, 2000). ReactorMan is the experimental application which allows the execution of neuroscientific experiments in virtual environments and enables script-based definition of experimental paradigms as well as logging of subjects’ reactions and reaction times to experimental stimuli (Valvoda, Assenmacher, Kuhlen, & Bischof, 2004).

The script language implemented in ReactorMan is based on LUA (http://www.lua.org/) and defines the sequences of stimuli and events within the experiments. The following paragraph briefly describes the setup of typical ReactorMan scripts, because they have been used for all experiments of this thesis.

The most basic element within the experimental setup is the definition of *scenes*, to which objects or text can be added. Additionally, interactions which define the optional response tools (like response buttons, keyboard keys, mouse etc.) for the setup are included. In a next step, the *trials* for the experiment are designed by defining the sequence of scenes and pauses, the parameters of position, orientation, display and pausing times as well as the interactions which end scenes and trials. The sequence of the trials is then defined within *blocks*. By “ORDER SHUFFLE” or “ORDER SEQUENCE” trials can either be run in the order defined by the order in the script or by randomized order. Additionally, the number of block repetitions can be determined. Finally, blocks are summarized in a *session* which forms the actual experimental definition.
1.5.4 Virtual Reality in the research of visuospatial attention

Some researchers have begun using VR techniques for the diagnosis and training of neglect patients. For example, Ansuini, Pierno, Lusher & Castiello (2006), Castiello, Lusher, Burton, Glover & Disler (2004) as well as Glover & Castiello (2006) used VR paradigms to improve neglect symptoms and found similar effects like e.g. those of prism adaptation and concluded that VR paradigms are capable of recreating links between affected and non-affected space in neglect patients. Buxbaum et al. (2008) utilized navigation in VR to detect lateralized impairments in stroke patients and Riva and colleagues (2009, 2007) developed the open-source VR platform NeuroVR, which can be adapted for clinical and experimental use for various cognitive domains, including attention (Carelli et al., 2009). Up to now, most of the studies are not making use of stereoscopic depth and/or utilize peri- and extrapersonal space for assessing the underlying attentional systems. Therefore research concerning visuospatial attention of healthy subjects and its potential biases in virtual environments is still sparse. So far, there are only a few studies using stereoscopic and depth enhanced VR to assess the distribution of visuospatial attention in peri- and extrapersonal space.

Maringelli, McCarthy, Steed, Slater & Umiltá (2001) examined visuospatial attention in a VR-setup using a head-mounted display; they showed how a virtual representation of one’s own body affected the distribution of attention by provoking a bias of visuospatial attention towards near body-centered space in presence and an attentional bias towards far space in absence of the virtual body. Losier and Klein (2004) also used a VR-setup to investigate
covert attention in peripersonal and extrapersonal space. They report an advantage for lower field targets in peripersonal space consistent with the proposed bias by Previc (1998). However, both VR studies did not report any horizontal attentional biases.

By using a rear-projected large-scale VR, Cocchini, Watling, Della Sala & Jansari (2007) examined how egocentric space in the back and front of persons is represented. They found an asymmetry in backspace representation in favor of left backspace. The right backspace was represented significantly smaller than the left one and thus the study shows the first evidence of pseudoneglect in backspace, similar to the widely investigated pseudoneglect in the frontal visual field.

1.6 Objectives

Based on previous studies presented in the introduction (1.4.5), Study 1 of this thesis will focus on the interaction of the alertness network and the network of visuospatial orienting dependent on (virtual) spatial depth. Study 2 will further examine whether biases of visuospatial orienting (i.e. pseudoneglect) in healthy participants (1.4.4.1) will differ subject to presentation in virtual peri- and extrapersonal space and whether attentional biases will not only occur along the horizontal, but also along the vertical axis.
2 Study 1: Low arousal modulates visuospatial attention in peripersonal and extrapersonal virtual space

2.1 Abstract
Clinical, experimental, and functional imaging studies suggest overlapping neuronal networks and functional interactions of alertness and visuospatial attention within the right hemisphere of the brain. To examine the interaction of arousal and visuospatial attention in peripersonal and extrapersonal virtual space, 20 healthy male adults were tested during 24 hr of sleep deprivation at four points during the night (9 p.m., 1 a.m., 5 a.m., and 9 a.m.). The main finding concerning covert orienting in a virtual environment is a highly significant slowing of reorientation toward the left visual hemifield in extrapersonal space due to decreased arousal. The results provide additional evidence for the proposed anatomical and functional overlap of the two attentional systems and indicate a modulation of visuospatial attention by the level of arousal in extrapersonal space.

2.2 Introduction
Clinical studies indicate that symptoms of neglect can be associated with lesions of the attentional alertness network. This is supposed to be caused by its substantial overlap with the posterior orienting network within the right cerebral hemisphere (Bartolomeo, 2000; De Renzi et al., 1989; Gitelman et al., 2002; Karnath et al., 1998; Vallar, 2001). While PET and fMRI studies suggest a right-hemisphere frontal and inferior parietal network subserving alertness (Fernandez-Duque and Posner, 2001; Sturm et al., 1999; Sturm and Willmes, 2001), the orienting network is associated with right frontal and superior, as well as inferior

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parietal cortical areas (Gitelman et al., 1999; Posner et al., 1984; Vallar, 2003). Additionally, it is subserved by subcortical structures such as the superior colliculus of the midbrain and the pulvinar and reticular nucleus of the thalamus (Posner and Petersen, 1990).

Indications of a functional coupling of the alerting and the orientation network arise from clinical findings as well as from experimental and rehabilitation studies. Robertson et al. (1998) were able to show a positive influence of alertness training on neglect symptoms. They proved that unilateralized warning tones, used to phasically increase alertness in neglect patients, improved their symptoms by diminishing their rightward bias of visuospatial attention. Thimm et al. (2005) demonstrated how computerized alertness training can improve visuospatial performance of neglect patients and that this is linked to reactivation in right hemisphere brain areas (frontal cortex, anterior cingulate cortex, precuneus and angular gyrus) associated with alerting and visuospatial attention. Bellgrove et al. (2004) demonstrated how individual differences in alertness capacity can modulate pseudoneglect (the small leftward attentional bias in healthy subjects), whereas Callejas et al. (2004) identified an accelerating influence of alerting on orienting. In a recent study (Fimm et al., 2006), attentional asymmetries in healthy subjects were provoked by short term sleep deprivation (28 hours) leading to a substantial reduction of arousal associated with a significant slowing of responses to stimuli presented to the left visual hemifield as well as a facilitation of covert reorienting of attention towards the right visual hemifield.

While a functional link of alertness and visuospatial attention has been demonstrated for patients and healthy subjects, all of the cited studies only investigated spatial attention in near (peripersonal) space. Traditionally, peripersonal space is defined as the space within arm’s reach and is closely linked with planning and execution of manual movements and localization of objects (Goodale and Milner, 1992; Ladavas and Farne, 2004), whereas far (extrapersonal) space is defined as the space outside arm’s reach and preoccupied with object identification, although these assignments can be partially modified (Berti et al., 2001; Longo and Lourenco, 2006). The dorsal visual stream primarily contributes to visual perception and attention to peripersonal space as well as to manual action in space whereas
the ventral visual stream is associated with attention to events in far extrapersonal space (Previc, 1998; Weiss et al., 2000). Some neglect patients show dissociations of impairment between peripersonal and extrapersonal visual space, with selective impairment within one and normal performance within the other spatial domain. These findings reflect the different contributions of the dorsal and ventral streams of visual processing to visuospatial attention. Brain (1941) was the first to report a case of neglect restricted to peripersonal space. Other studies assessing radial line bisection reported patients with ‘far’ (Shelton et al., 1990; Vuilleumier et al., 1998) or ‘near’ (Halligan and Marshall, 1991; Mennemeier et al., 1992) neglect symptoms, depending on lesion site and linking far-upper attentional neglect to lesions of the inferior temporal cortex and near-lower neglect symptoms to posterior parietal lesions. Butler et al. (2004) detected lateral gradients of increasing target detection from left to right in both peripersonal and extrapersonal space and identified relations between peripersonal neglect and dorsal stream lesions and extrapersonal neglect and ventral stream damage respectively. In a combined line bisection and PET study, Weiss et al. (2000), identified neural activations in the left dorsal occipital cortex, left intraparietal cortex, left ventral premotor cortex and left thalamus upon performance in near space and bilateral ventral occipital cortex and right medial temporal cortex activations upon performance in far space. Transcranial magnetic stimulation (TMS) of the right posterior parietal cortex and the right ventral occipital lobe provoked significant rightward shifts of the perceived midpoint in a line bisection task in near and far space respectively (Bjoertomt et al., 2002), thus underlining the near-dorsal and far-ventral segregation of visual processing. Maringelli et al. (2001) examined the distribution of visuospatial attention in a Virtual Reality (VR) setup using a head-mounted display and showed how a virtual representation of one’s own body affected the distribution of attention by provoking a bias of visuospatial attention towards near body-centered space in presence and an attentional bias towards far space in absence of the virtual body. Losier and Klein (2004) also used a VR setup to investigate covert attention in peripersonal and extrapersonal space. They report an advantage for lower field targets in peripersonal space consistent with the proposed bias by Previc (1998). Both VR studies did
not report any horizontal attentional biases.

Despite extensive research in the field of visuospatial attention, attentional visual field asymmetries in the two different spatial zones have never been examined in relation to arousal, although findings might be highly interesting in regard to the underlying spatial systems, their role in neglect and their relevancy for therapeutic approaches of different neglect characteristics. In this study, the level of arousal was systematically manipulated by sleep deprivation and its effect on visuospatial attention in virtual space in healthy subjects was investigated.

Given that the networks of alertness and attention share common anatomical structures within the inferior parietal cortex and considering previous experimental findings (Fimm et al., 2006), as well as the alertness training studies of Robertson et al. (1998) and Thimm et al. (2006), an influence of decreasing alertness on visuospatial attention in both peri- and extrapersonal space is expected to occur, albeit to a different extend. The reported clinical and experimental dissociations of neglect symptoms suggest that the intensity of potential attentional asymmetries between the left and the right visual field might vary subject to the depth of stimuli presentation. Additionally, there is strong evidence that the posterior parietal cortex is more densely innervated by activating afferences of the locus coeruleus (LC) than the temporal lobe (Morrison and Foote, 1986) and sleep deprivation is assumed to lead to widespread decreases in global and regional cerebral metabolic rate of glucose (CMRglu) in the posterior parietal lobe (Thomas et al., 2000). These significant CMRglu reductions in sleep deprived subjects were specifically found in areas involved in alertness, attention and other cognitive functions, namely in the thalamus, the prefrontal and the posterior parietal cortices. Accordingly, it is expected that the dorsal pathway might be more affected by low arousal than the ventral pathway and thus resulting in a more pronounced attentional asymmetry effect within the applied covert attention paradigm in peripersonal space. Since the posterior parietal cortex is crucial in redirecting attention to previously unattended locations (Petersen et al., 1989; Posner et al., 1984; Thiel et al., 2004), a stronger asymmetry effect for invalidly cued targets is expected.
2.3 Method

2.3.1 Subjects

20 male participants with an age range of 21 to 31 years (mean=26.2 years) took part in the study. All subjects were non-smokers, right-handed (according to a German version of the Edinburgh Handedness Inventory (Oldfield, 1971)), without any former history of neurological or psychiatric disease and all reported normal depth perception and normal or corrected-to-normal visual acuity. All persons gave their informed consent to the participation in the study, which was approved by the local research ethics committee.

2.3.2 Procedure

Participants were instructed to sleep a minimum of 6 and a maximum of 8 hours in the night prior to the study, to get up no later than 9 a.m. as well as to avoid any stimulating substances and medication on the day of the study.

The participants arrived at the lab at 4:30 p.m.. At the beginning of the study protocol, subjects were tested for their ability to distinguish between different levels of virtual depth and peripersonal vs. extrapersonal space with a short VR paradigm (Armbrüster et al., 2005), which required distance estimations of ten spheres of equal retinal sizes in distances between 30 cm and 330 cm. All participants succeeded in sequencing the stimuli according to their distance and judging the spatial realms. Additionally, at 5 p.m. as well as at 7 p.m., they were tested for their ability to covertly orient attention with the subtest “Covert shift of attention” of the Test for Attentional Performance (TAP; Zimmerman and Fimm, 2002). Only subjects with good abilities in depth perception, eye fixation (which was visually controlled by the experimenter) and displaying a sufficient validity effect (>20 ms) in the covert orienting task were included in the study and completed the virtual reality paradigms repeatedly throughout the night. Two subjects were excluded because of deficits in covert orienting and the investigation was aborted after the 5 p.m. session.

The main experimental sessions were carried out at 9 p.m., 1 a.m., 5 a.m. and 9 a.m.. During
the breaks, participants were allowed to drink, eat, read, surf the internet and listen to music. They were not allowed to take any naps or consume any stimulating beverages or medications and were constantly monitored by the investigator.

2.3.3 Apparatus and Software

The virtual setup was displayed on a BARCO Baron™ rear projection desk. An active stereo system was used in order to enable immersive stereoscopic visualization. The participants wore shutter glasses, which enable 3D-perception of projected stimuli. The subject’s head was fixated by a chin rest to reduce head movements and changes of perspective. Additionally, head movements were tracked with an electro-magnetic head-tracker (Flock of Birds™) to monitor the subjects, but also to enhance the subject’s depth perception by minimal motion parallax.

Since timing precision in common computer operating systems can be critical for psychological reaction time experiments (Myors, 1999), a special reaction-time hardware was developed (Valvoda et al., 2004; Wolter et al., 2007). This system provides data with potential sampling and delay errors below 0.01 ms, and thus enables the realization of real-time reaction-time experiments in platform-independent virtual environments.

To generate the Virtual Reality paradigm, the ReactorMan software - a part of the NeuroMan system (Valvoda et al., 2003) - was used. ReactorMan enables the definition of setups for VR-based experiments, provides information about the runtime behavior of the software and the participants’ reactions to events and interaction devices and together with the reaction-time hardware features the possibility to log the overall chronological behavior with specific timing characteristics (Valvoda et al., 2004).

2.3.4 Task

The task consisted of a covert attention paradigm following the covert attention tasks of Posner (Posner, 1980; Posner et al., 1984) in a 3D Virtual Reality environment. Four white-
shaded balls were presented in a unichrome blue virtual space at two different planes of depth: two in peripersonal (50 cm) and two in extrapersonal space (240 cm), one per plane of depth in left and one in right visual hemispace respectively (23° and 17° visual angle from the fixation point in extrapersonal and peripersonal space). A small green star in the middle of the resulting rectangle served as a fixation point (see Fig. 1).

While the participants were instructed to keep their eyes fixed on the green star, one of the four balls changed its color to yellow and slightly decreased in its size for 150 ms to induce a covert shift of attention towards the cued location. After a pseudo-randomized cue-target interval of 250, 300, 350 or 400 ms, one of the balls changed to red, indicating the target stimulus. Subjects were instructed to press a button with their right index finger as quickly as possible upon detecting the target. To ensure predictability of the target location it appeared at the cued location with a probability of 70% and accordingly at one of the uncued locations with a probability of 30%. Thus, invalidly cued targets required a covert shift of attention either horizontally (e.g. peripersonal right to peripersonal left), diagonally (e.g. peripersonal right to extrapersonal left) or radially (e.g. extrapersonal left to peripersonal left) across the 3D visual space. With three pseudo-randomized inter-trial intervals (1500, 2000, 2500 ms), the whole session consisted of 144 invalid trials (12 per condition) and 336 valid trials, which summed up to 480 trials and lasted for approximately 25 minutes.
The task was presented every four hours during the night (9 p.m., 1 a.m., 5 a.m. and 9 a.m.), resulting in a total duration of sleep deprivation of about 24 hours.

Additionally, participants’ body temperature was measured at the beginning of each session with a digital in-ear thermometer (Braun IRT 3520 ThermoScan, Type 6012) as an indicator of physiological arousal (Van Someren, 2000). They were also asked to rate their mood status on a standardized questionnaire, the Befindlichkeitsskala BfS (von Zerssen, 1976), as well as their fatigue (as a measure of subjective arousal) on a combined 5/50 rating scale (Heller, 1985), which asked the subjects to first rate their fatigue on a verbal scale and then to refine the intensity of the fatigue within the category (wide awake = 0-10, awake = 10-20, neither awake nor tired = 20-30, tired = 30-40, extremely tired = 40-50).
2.3.5 Statistical analysis

To compare the participants’ performance in the sessions with the highest and the lowest levels of arousal depending on the amount of sleep deprivation, the data were analyzed with the SPSS-package (version 14.0) computing Pearson correlations and a repeated measures analyses of variance for the reaction times with the factors validity (validly cued targets vs. horizontally, radially and diagonally invalidly cued targets), side (target position in the left vs. right visual hemifield), depth (peripersonal vs. extrapersonal space) and time (of experimental session; 9 p.m., 1 a.m., 5 a.m., 9 a.m.). Significance levels were adjusted with the Greenhouse-Geisser correction when appropriate. Stimulus-onset asynchrony (SOA) was not included as a factor due to undersized amounts of data within the resulting cells. However, preliminary separate analyses did not detect any interactions with one of the other factors. Over all, reaction times faster than 100 ms (anticipative reactions) and slower than 1000 ms (distinct delayed reactions) were excluded from the analysis, representing 9.5 % of all trials. Median reaction times were log-transformed in order to correct for skewness of distribution before including them in the repeated measures analysis of variance.

2.4 Results

2.4.1 Descriptive measures of body temperature, fatigue and mood

The repeated measures analyses of variance for body temperature (F_{1,19}=24.447; p<.001), fatigue (F_{1,19}=46.859; p<.001) and mood (F_{1,19}=26.559; p<.001) all reveal highly significant main effects of time. Mean average body temperature was maximal at the 9 pm. session (36.65 °C), reached the minimum at 5:00 a.m. (36.05 °C) and slightly increased again at 9 a.m. (36.18 °C) (9 p.m. vs. 1 a.m.: F_{1,19}= 30.425; p<.001; 1 a.m. vs. 5 a.m.: F_{1,19}= 42.506; p<.001; 5 a.m. vs. 9 a.m.: F_{1,19}= 4.957; p<.05; reverse Helmert contrasts). The mean average of fatigue was lowest at 9 p.m. and highest during the last session at 9 a.m. The amount of fatigue increased highly significantly from one session to the next one, except for the last session (9 p.m. vs. 1 a.m.: F_{1,19}= 100.881; p<.001; 1 a.m. vs. 5 a.m.: F_{1,19}= 64.266;
Study 1: Low arousal and visuo-spatial attention

p<.001; 5 a.m. vs. 9 a.m.: F_{1,19} = 29.679; p<.001; reverse Helmert contrasts). A similar profile could be observed for the mood values resulting in lowest ratings (good mood) at 9 p.m. and highest ratings (bad mood) at 9 a.m., respectively (9 p.m. vs. 1 a.m.: F_{1,19} = 23.688; p<.001; 1 a.m. vs. 5 a.m.: F_{1,19} = 34.170; p<.001; 5 a.m. vs. 9 a.m.: F_{1,19} = 21.904; p<.001; reverse Helmert contrasts). Self-reports of fatigue and mood correlate (Pearson product-moment correlation) significantly at 1 a.m. (r=.488; p<.05 two-sided), 5 a.m. (r=.451; p<.05 two-sided), and 9 a.m. (r=.624; p<.01 two-sided), indicating that sleep deprivation is associated with the emotional state of the participants. Both increases of subjective measures also correspond well with the decrease of body temperature, except for its slight increase at 9 a.m. (see Fig. 2), though it was still significantly (F_{1,19}=78.235; p<.001) below the baseline at this point.

Figure 2.2: Measures of temperature, self-reported mood, and fatigue.

2.4.2 Behavioral measures of covert attention

A 4 x 2 x 2 x 4 (factors: validity, side, depth and time) repeated measures analysis of variance of reaction times resulted in highly significant effects of VALIDITY (F_{3,57}=76.809; p<.001), DEPTH (F_{1,19}=16.548; p<.001) and TIME (F_{3,57}=10.431; p<.001). Highly significant simple contrasts of VALIDITY can be found for all three types of invalid cues, showing a most pronounced validity effect for diagonal reorientation (F_{1,19}=211.427; p<.001) followed by horizontal reorientation (F_{1,19}=158.416; p<.001) and radial reorientation (F_{1,19}=62.791; p<.001) (see Fig. 3). The effect indicates that the VR-paradigm was highly capable of initiating covert shifts of attention in virtual space.
Figure 2.3: Median reaction times (RT) of valid, radially, horizontally and diagonally invalidly cued trials.

The subsequent statistical analyses are based on the 9 p.m. and 9 a.m. sessions which are the sessions with the shortest and longest amount of sleep deprivation, highest and lowest self-reported levels of arousal, body temperature significantly below baseline and slowest overall reaction times (see Fig. 3), revealed by a simple repeated measures analysis of variance of reaction times with the factor time, resulting in a highly significant effect of sleep deprivation on overall reaction times ($F_{3,57}=11.119; p<.001$), as well as significant increases of reaction time from one session to the other (9 p.m. vs. 1 a.m.: $F_{1,19}= 4.812; p<.05$; 1 a.m. vs. 5 a.m.: $F_{1,19}= 18.799; p<.001$; 5 a.m. vs. 9 a.m.: $F_{1,19}= 8.895; p<.01$; reverse Helmert contrasts).

2.4.3 Comparison of high (9 p.m.) and low (9 a.m.) levels of arousal

The 4 x 2 x 2 x 2 (factors: validity, side, depth and time) repeated measures ANOVA of reaction times reveals significant effects of VALIDITY ($F_{3,57}=51.203; p<.001$), DEPTH ($F_{1,19}=7.535; p<.01$) and TIME ($F_{1,19}=15.073; p<.001$). The highly significant main effect of VALIDITY indicates that covert shifts of attention were initiated by the paradigm and the main effect of TIME demonstrates a general increase of reaction times over the course of the night.
(see Fig. 3).

Additionally, two-way VALIDITY-by-SIDE ($F_{3,57} = 4.745; p < .01$), VALIDITY-by-DEPTH ($F_{3,57} = 3.497; p < .05$) and SIDE-by-TIME ($F_{1,19} = 4.661; p < .05$), as well as three-way interactions of VALIDITY-by-DEPTH-by-TIME ($F_{3,57} = 3.099; p < .05$) and VALIDITY-by-SIDE-by-TIME ($F_{3,57} = 4.318; p < .01$) were significant. Last but not least, the four-way interaction of VALIDITY-by-SIDE-by-DEPTH-by-TIME ($F_{3,57} = 3.364; p < .05$) is significant as well and the subsequent analysis and interpretations will concentrate on it.

In order to further explore this significant four-way interaction of VALIDITY-by-SIDE-by-DEPTH-by-TIME ($F_{3,57} = 3.364; p < .05$) separate analyses for peripersonal and extrapersonal targets were computed. Thus, the analysis was first split into two MANOVAs with three main factors (see Kirk, 1994). In case of a significant Validity-by-Side-by-Time interaction the analysis was then further split into 2 MANOVAs based on 9 p.m. and 9 a.m. respectively with two main factors (Validity, Side) each.

Whereas the VALIDITY-by-SIDE-by-TIME interaction in peripersonal space was not significant, the respective interaction in extrapersonal space proved to be significant ($F_{3,57} = 4.858; p < .05$). Subsequent separate analysis for extrapersonal targets at 9 p.m. and 9 a.m. yielded a significant VALIDITY-by-SIDE interaction at 9 a.m. ($F_{3,57} = 6.765; p < .01$).

According to simple a priori contrasts, this was based on horizontal conditions (horizontal vs. valid: $F_{1,19} = 9.953; p < .01$) whereas radial and diagonal conditions did not contribute significantly to this effect. Thus, the VALIDITY-by-SIDE-by-DEPTH-by-TIME interaction is mainly caused by a strong reaction time asymmetry to the disadvantage of left-sided targets at 9 a.m. when attention has to be shifted horizontally from right extrapersonal to left extrapersonal space (see Fig. 4 & Table 1).
2.5 Discussion

In this study, the maximally reduced level of arousal, induced by 24 hours of sleep deprivation, resulted in slowed reorientation of attention towards horizontal invalidly cued targets within the left extrapersonal visual hemifield. The results provide further evidence for the postulated influential role of the alertness network on the network of visuospatial attention (Bellgrove et al., 2004; Fimm et al., 2006; Manly et al., 2005; Robertson et al., 1998) in a 3D virtual reality setting. Thus, this study was able to replicate previous findings of a link
between low arousal and attentional asymmetries (Fimm et al., 2006). Furthermore, the data suggest an exclusive influence of arousal on reorientation of attention (invalid trials), which includes the mechanisms of disengaging, moving and engaging attention at the new location (Posner et al., 1984; Posner and Petersen, 1990). Though RT’s of the initial orientation to validly cued targets were significantly increased at 9 a.m., there wasn’t any significant asymmetry between left and right-sided correctly cued targets and attentional orienting was not affected by different levels of arousal, which is consistent with the preceding hypothesis. This is also in line with event-related fMRI-studies (Corbetta et al., 2000; Thiel et al., 2004) which identified different neuronal networks subserving attentional aspects of alerting, orienting and reorienting and especially showed a clear dissociation of orienting and reorienting of visuospatial attention. Additionally, the right temporo-parietal cortical junction (TPJ) was repeatedly identified as a key structure for reorientation of attention to previously unattended locations in clinical studies, demonstrating that lesions in this brain area are often associated with neglect symptoms (Friedrich et al., 2003; Thiebaut de Schotten et al., 2005; and in imaging studies: Corbetta et al., 2002; Corbetta et al., 2005; overview in: Danckert and Ferber, 2006). The right TPJ seems to play a crucial role in the observations made by this study. While the posterior parietal lobe generally receives strong noradrenergic (NA) projections, especially the right TPJ is densely innervated by ascending NA neurons of the locus coeruleus (LC), which is the main source of NA innervation of the cortex (Beane and Marrocco, 2004; Marrocco et al., 1994; Morrison and Foote 1986). Furthermore, the fronto-parietal alertness network in the right hemisphere receives strong and widespread NA projections from the LC (Posner and Petersen, 1990), emphasizing the role of NA projections in both orienting and alertness functions. Aston-Jones and Cohen (2005) suggest that one role of the LC system is to substantially contribute to the optimization of behavioral performance with phasic LC activity being closely tied to tonic LC activity (Aston-Jones et al., 1999). Coull et al. (2001) provided further evidence for the predominant role of the right hemisphere in arousal and attentional orienting using a covert orienting task. They showed how the adrenergic agonist clonidine modulated behavioral as well as neuroanatomical
correlates of human attentional orienting and alerting by attenuating the cost of invalidly cued targets in the left but not in the right visual field. This was associated with a decrease of right superior parietal activation during spatial orienting. Subsumed, the data of this study as well as other experimental evidence suggests that the LC and the TPJ might provide the anatomical link for the mediating influence of the alertness network on the network of visuospatial attention.

The original hypothesis of this study was a differential influence of low arousal on orienting of attention within the two spatial domains with a stronger asymmetry effect in peripersonal space. Contrary to that, it turned out to be the extrapersonal space being significantly affected by low arousal with respect to reorientation to horizontal invalidly cued targets. This observation together with present clinical evidence (Halligan and Marshall, 1991; Mennemeier et al., 1992; Shelton et al., 1990; Vuilleumier et al., 1998) points to a need for further, more detailed research. For instance it would be highly interesting to distinguish between multiple (more than two as in this study) layers of depth, as well as different heights in the visual field representing different aspects of visuospatial perception and action. Previc (1998) gives an overview on different models of parcelling 3-D space, and proposes four major zones of action: peripersonal, focal extrapersonal, action extrapersonal and ambient extrapersonal space. According to this model, the extrapersonal distance of 2.40 meters in this study corresponds with ‘action extrapersonal’ space. Though no direct manual action can be carried out in this space, objects in this distance can quickly be accessed by moving towards them. Therefore, ‘action extrapersonal’ space might be somewhat differently processed in the brain from ‘ambient extrapersonal’ space, and visuospatial attention within this domain could be differentially modulated by low arousal, respectively. Another issue might also complicate the interpretation of the obtained results (Quinlan and Cunlam, 2007). Though this study found main effects and interactions of depth (peripersonal vs. extrapersonal), the fixation point was located 145 cm from the subjects, beyond peripersonal in extrapersonal space. This might have confounded respective dorsal and ventral stream
activations and prevented a significant effect on reorientation in peripersonal space. Subsequent studies of visuospatial attention in virtual space (Heber et al., 2007) will have to account for this and keep fixation within the same depth plane of cues and targets.

In conclusion, results provide a further step in understanding the relationship between orienting and alerting and emphasize the assumption of right hemisphere dominance and the anatomical and functional overlap of the two attentional networks of alerting and orienting. This study was able to replicate previous findings of the direct influence of a low arousal level induced by sleep deprivation on visuospatial attention (Fimm et al., 2006) and to show that the smaller but neglect-resembling effect appears in extrapersonal space. These findings are relevant for the rehabilitation of neglect or attentional asymmetries in three-dimensional space (Butler et al., 2004; Halligan and Marshall, 1991; Mennemeier et al., 1992; Robertson et al., 1998; Shelton et al., 1990; Thimm et al., 2006; Vuilleumier et al., 1998). Furthermore, the functional interdependence of the two attentional networks might be relevant to Attention Deficit Disorders (ADD) as well, since various studies (Dobler et al. 2003; Dobler et al., 2005; Manly et al., 2005; Nigg et al., 1997; Sheppard et al., 1999; Voeller and Heilman, 1988) describe neglect symptoms or visual space biases in children with ADHD; potential therapeutic approaches might account for the functional overlap of alertness and visuospatial attention.
3 Study 2: Horizontal and vertical attentional biases in three-dimensional virtual space

3.1 Abstract

The present study investigates the influence of depth on pseudoneglect in healthy young participants (n = 18) within three-dimensional virtual space, by presenting a variation of the greyscales task and a landmark task, which were specifically matched for stimulus–response compatibility, as well as perceptual factors within and across the tasks. Tasks were presented in different depth locations (peripersonal, extrapersonal) and different orientations (horizontal, vertical) within three-dimensional virtual space, using virtual reality technique. A horizontal leftward bias (pseudoneglect) for both tasks was found, which was stronger in peripersonal than in extrapersonal space. For the vertical condition, an upward bias was observed in the greyscales task, but not in the landmark task. These results support the hypotheses of right hemispheric dominance for visual spatial attention and this study is the first to examine horizontal and vertical orienting biases with the greyscales task in peripersonal and extrapersonal space. Furthermore, the differences in attentional asymmetries with respect to depth suggest dissociable neural mechanisms for visual attentional processing in near and far space and the lack of significant correlations implies independence of horizontal and vertical stimulus processing.

3.2 Introduction

The right cerebral hemisphere plays a dominant role in directing visuospatial attention, particularly illustrated by hemispatial neglect symptoms occurring almost exclusively after right hemisphere lesions (Mesulam, 1999; Smania et al., 1998). However, asymmetries of

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visuospatial attention are not restricted to neurological patients: in neurologically healthy subjects, a phenomenon called ‘pseudoneglect’ can be observed. The term was coined by Bowers and Heilman (1980) and refers to the asymmetrical perception of (or response to) objects in space, which is found in the absence of neural pathology and which is usually opposite in direction to the asymmetry found in neglect patients: while normal subjects generally bias judgments of relative magnitude towards the information contained on the left side of a stimulus, patients after right hemisphere damage show deficits in orienting towards stimuli in the left visual hemispace (Heilman, Watson, & Valenstein, 1979).

Pseudoneglect is a highly reliable, statistically significant phenomenon (Jewell & McCourt, 2000; McCourt, 2001) and widely accepted measures to examine pseudoneglect include line bisection tasks, or the greyscales task (Mattingley et al., 2004). While both methods are used to detect attentional asymmetries, they do not measure exactly the same: in line bisection tasks, participants are either asked to actively bisect presented lines or to passively judge pre-bisected lines (also called “landmark task”) (Jewell & McCourt, 2000). The greyscales task by Mattingley and colleagues (2004) requires luminance judgments of bars which are continuously shaded from black to white. Nicholls, Bradshaw, and Mattingley (1999) examined whether pseudoneglect differs between judging brightness, numerosity or size and found clear leftward biases for all three kinds of tasks and thus showed how pseudoneglect can be assessed by multiple attentional paradigms. The right hemisphere dominance for visuospatial attention apparently results in ‘overattendance’ towards the left visual hemispace in healthy subjects (Heilman & Van Den Abell, 1980; McCourt & Jewell, 1999; Mesulam, 1999; Nicholls, Mattingley, Berberovic, Smith, & Bradshaw, 2004) thus causing overestimation of length, magnitude, quantity or luminance of stimuli in the left visual hemispace. Mattingley and colleagues (2004) compared attentional biases in the greyscales task in different participant samples. The results showed a leftward bias for healthy control subjects, an extreme rightward bias in right hemisphere lesion patients and a leftward bias in left hemisphere lesion patients.
Pseudoneglect and attentional asymmetries in general, are associated with the assumption of right hemisphere dominance for visuospatial attention. While the left hemisphere predominantly controls attentional processes within the contralateral hemispace, the right hemisphere is involved in the distribution of attention within both hemispaces (Heilman & Van Den Abell, 1980; Mesulam, 1999). As a consequence, healthy people ‘overattend’ to the left hemispace, which results in a leftward bias of visuospatial attention (pseudoneglect). Thus, clinical neglect and pseudoneglect each reflect the cortical asymmetry with respect to spatial attention and while both neglect and pseudoneglect share several features, it remains uncertain, whether similar neural mechanisms are involved in the general development of symptoms. Furthermore, clinical evidence suggests dissociable neural processes underlying perception and attention within near and far space (Goodale & Milner, 1992; Previc, 1998).

Near (peripersonal) space is defined as the space within arm’s reach and is closely linked to planning and execution of manual movements and localization of objects, whereas far (extrapersonal) space is defined as the space outside arm’s reach and preoccupied with visual search and object identification. Accordingly, peripersonal space is associated with the dorsal cortical pathway and extrapersonal space with the ventral cortical pathway in the brain (Goodale & Milner, 1992; Ladavas & Farne, 2004; Previc, 1998; Weiss et al., 2000). Interestingly, in some neglect patients, the incidence and intensity of neglect symptoms does depend on viewing distance (Cowey, Small, & Ellis, 1999; Halligan & Marshall, 1991; Mennemeier, Wertman, & Heilman, 1992; Shelton, Bowers, & Heilman, 1990; Varnava, McCarthy, Beaumont, 2002). Similar dissociations have been observed in healthy subjects, predominantly in line bisection studies: Varnava et al. (2002) found a leftward bias in peripersonal space and a rightward bias in extrapersonal space. Likewise, McCourt and Garlinghouse (2000) found that pseudoneglect was stronger in peri- than in extrapersonal space. In a Positron Emission Tomography (PET) study, Weiss et al. (2000) examined line bisection performance in healthy subjects and found distinct neural activities depending on acting in near vs. acting in far space. These results are in line with the suggestion that the ventral visual stream is primarily involved in attending to far space, whereas the dorsal visual
stream is involved in attending to near space (Goodale & Milner, 1992; Previc, 1998). Other studies suggest that neglect and pseudoneglect are not just observed in the horizontal but also in the vertical plane (Fink, Marshall, Weiss, & Zilles, 2001; Jewell & McCourt, 2000; McCourt & Olafson, 1997; Mesulam, 1999; Nicholls et al., 2004; Shelton et al., 1990), but it remains controversial whether attention along the horizontal and vertical meridians does rely on identical, overlapping or distinct neural mechanisms. While neglect of the upper visual field is associated with temporo-occipital damage (Mennemeier et al., 1992; Shelton et al., 1990), neglect of the lower visual field most commonly occurs after uni- or bilateral parietal lesions (Rapcsak, Cimino, & Heilman, 1988), reflecting ventral and dorsal stream processing respectively, as well as underlining the proposed functional biases of upper visual field and extrapersonal space, and lower visual field and peripersonal space (Previc, 1990, 1998). However, studies examining healthy participants show inconsistent results. While some studies suggest different neural mechanisms involved in vertical and horizontal orienting (Mao, Zhou, Zhou, & Han, 2007; McCourt & Olafson, 1997; Post, O’Malley, Yeh, & Bethel, 2006), others failed to find any differential attention related neural activation dependent on vertical or horizontal orientation (Fink et al., 2001; Macaluso & Patria, 2007) and thus propose multidirectional networks for orienting or at least partially overlapping mechanisms (Drain & Reuter-Lorenz, 1996). Nicholls et al. (2004) found an upward response bias for vertical greyscales and a leftward response bias for horizontal greyscales. By employing additional 45° oblique conditions as well as examining both healthy participants and neglect patients, they conclude that both spatial biases might stem from relatively independent neural processes.

In summary, clinical and experimental evidence suggests that different neural mechanisms are involved in visuospatial attention in peripersonal and extrapersonal space and that they might differ depending on stimulus orientation.

In this study, a landmark task and a variation of the greyscales task were presented in different locations and orientations within three-dimensional space using a Virtual Reality (VR) paradigm. VR techniques are used in psychological research to increase experimental
realism and experimental control, without decreasing ecological validity (Loomis, Blascovich, & Beall, 1999) and enable standardized, replicable examinations. In the context of dissociating peri- and extrapersonal space, three-dimensional VR presentation of stimuli also enhances the impression of “reachable” vs. “non-reachable” stimuli. This study seeks to answer the following questions: Can attentional asymmetries observed in healthy people in the past be replicated? If so, how are these potential asymmetries influenced by different characteristics of the task (luminance vs. distance judgments), stimulus orientation (horizontal vs. vertical) and location (peripersonal vs. extrapersonal) in three-dimensional space? Based on previous findings described above, a leftward bias of visuospatial attention in all locations in the horizontal conditions is expected to be observed as well as a downward bias in peripersonal and an upward bias in extrapersonal space in both the greyscales and the landmark task.

3.3 Method

3.3.1 Participants

Eighteen volunteers (14 female, four male), aged 19–33 years (mean = 23.05; SD = 23.23) took part in this study. All participants were strongly right-handed (according to a German version of the Edinburgh Handedness Inventory (Oldfield, 1971)), had normal or corrected-to-normal visual acuity and no history of neurological or psychiatric disease. All persons gave their informed consent to the participation in the study, which was approved by the local research ethics committee.

3.3.2 Procedure

At the beginning of the study protocol, participants rated their fatigue on a 5/50 rating scale (Heller, 1985) and completed the alertness task of the Test for Attentional Performance (TAP; Zimmermann & Fimm, 2002). Since several studies report a relationship between the degree of alertness and observed attentional asymmetries (Bellgrove, Dockree, Aimola, &
Robertson, 2004; Fimm, Willmes, & Spijkers, 2006; Heber, Valvoda, Kuhlen, & Fimm, 2008; Manly, Dobler, Dodds, & George, 2005), even in healthy participants, the level of the participants’ alertness in this study was controlled. Additionally, participants were tested for visual and stereo acuity (Titmus Test) as well as the ability to distinguish virtual peri- and extrapersonal space and only those with normal visual and stereo acuity, normal alertness levels and correct identification of virtual depth were included in the study.

Each participant was asked to complete four experimental blocks (horizontal, vertical – each in peripersonal and extrapersonal space). The greyscales and the landmark tasks were carried out in one block each and the order of the blocks within each task, as well as which task the participant started the session with, was balanced.

### 3.3.3 Apparatus and Software

The virtual setup was displayed on a rear projection screen (2.40 x 1.80 m). A stereo projector (resolution 1024 x 768 pixels) was used to allow immersive 3D visualization. The participants wore passive Infitec filter glasses, which enable stereoscopic perception of the projected stimuli. The subject’s head was fixated by a comfortable chin rest. Head movements were tracked by an infrared tracking system (Qualysis Pro Reflex MCU240) to monitor the participants’ behavior and to enhance depth perception by minimal motion parallax. To generate the VR paradigms, the ReactorMan software (Valvoda, Assenmacher, Kuhlen & Bischof, 2004; Wolter, Armbruester, Valvoda & Kuhlen, 2007) was used.

### 3.3.4 Tasks

#### 3.3.4.1 Greyscales task

The greyscales stimuli consisted of two bars (10 mm high) presented in parallel on the projection screen in a unichrome blue virtual space without any additional depth information. The greyscales were shaded from white on one side to black on the other side and were arranged in parallel, with mirror-reversed gradients (see Fig. 1).
Figure 3.1: The two horizontal configurations of the greyscales task.

The greyscales were presented in three lengths (short, medium and long), two orientations (horizontal, vertical) and at two planes of depth (peripersonal, extrapersonal). The original size of the stimuli (on the projection screen) was 120 mm, 190 mm, 260 mm. For the peripersonal condition, stimuli were presented at a distance of 30 cm and for the extrapersonal condition at a distance of 270 cm from the eyes of the participant, while the participants’ distance to the projection screen was 70 cm. Despite the two different positions in depth, all stimuli were designed to be of equal retinal size, resulting in equal visual angles (short 22.62°, medium 31.64°, long 46.68°). The different lengths of the greyscales were presented randomly within the four experimental blocks (horizontal-peripersonal, horizontal-extrapersonal, vertical-peripersonal, vertical-extrapersonal).

Participants’ (forced-choice) responses were recorded by two buttons which were placed next to each other for the horizontal, and on top of each other for the vertical condition. The participants were asked to judge which half (horizontal condition: left vs. right; vertical condition: upper vs. lower) of the pair of stimuli appeared darker and to press the respective
response key (left or lower button: left hand; right or upper button: right hand). Participants were not told that there wasn’t actually any difference in luminance for the greyscales. Each stimulus pair was presented for 3 seconds and was followed by an inter-trial interval of 1.5 seconds. Each of the four experimental conditions consisted of 108 trials, resulting in a total amount of 432 trials. Participants did not receive any feedback on accuracy during testing.

Different from the experiments of Mattingley et al. (2004), a decision was made to change the arrangement of the buttons (side by side, not one above the other for the horizontal condition). Thus, the stimulus-response compatibility was maintained and enabled a direct comparison with the landmark task. Instructions were also slightly different as the participants in this study were asked to decide which half of the pair of greyscales appears darker. Mattingley and colleagues asked for a decision about which one of the two greyscales appeared overall darker. However, this response instruction likely yields an incongruity between decision, response and observed bias: While the task aims to assess a horizontal bias, the subject is instructed to select the upper or lower stimulus and press the upper or lower response button accordingly. By modifying the instruction, this incongruity of match decision, response and bias direction is minimized. Thus this paradigm utilizes a more space-based approach compared to the object-based approach of Mattingley and colleagues.

3.3.4.2 Landmark task

Stimuli for the landmark task consisted of high-contrast lines (100% Michelson contrast) (see fig. 3) of 10 mm height, modeled roughly similar to landmark stimuli used in other studies (e.g. McCourt & Garlinghouse, (2000); McCourt & Olafson, 1997). Analogous to the greyscales task, the lines were presented in three lengths (short medium and long), two orientations (horizontal, vertical) and at two planes of depth (peripersonal, extrapersonal) (see Fig. 3.2). Visual angles of the stimuli were equal in peri- and extrapersonal space and
were identical to the greyscales task.

![Figure 3.2: The two horizontal patterns of the landmark task.](image)

The lines were presented for 3 seconds, followed by an inter-trial interval of 1.5 seconds. All lines were pre-transected at one of 20 transector locations on the line (10 to the left and 10 to the right of veridical center) and the range of transections was between -0.5 cm and +0.5 cm from the actual veridical center. Participants were asked to make forced-choice decisions regarding the transector location relative to the veridical center, by pressing one of the two response buttons. Alike to the greyscales task, response buttons were either arranged side by side (horizontal condition) or on top of each other (vertical condition). The participants were required to judge whether the bisection was made to the left or right (horizontal condition), or above or below veridical center (vertical condition) and to press the corresponding button (left or lower button: left hand; right or upper button: right hand).

Each condition of the landmark task consisted of 120 trials (6 decisions for each transector location within each of the two patterns a and b being displayed in fig. 3), resulting in a total number of 480 trials. Line lengths and transector locations were randomized within the different experimental blocks (horizontal-peripersonal, horizontal-extrapersonal, vertical-peripersonal, vertical-extrapersonal).
3.3.5 Statistical analysis

Asymmetry scores were computed for all participants and all conditions. For the greyscales task, the number of right responses was subtracted from the number of left responses for the horizontal conditions or the upper visual field responses from the lower visual field responses for the vertical conditions, respectively. The results were divided by the total number of responses and were multiplied by -1. Thus, a negative asymmetry score represents a leftward or lower visual field bias whereas a positive score refers to a rightward bias or upper visual field bias of attention.

In contrast to the greyscales task, the landmark task contained correct responses and false responses. Thus, false left responses were subtracted from false right responses or false lower responses from false upper responses. Again, the result was divided by the total number of responses, multiplied by -1 and parallel to the greyscales task, a negative asymmetry score represents a leftward or lower visual field bias and a positive score indicates a rightward bias or upper visual field bias of attention.

The data were analyzed by repeated measures analyses of variance using the SPSS package (Version 18.0). Each condition of the greyscales and the landmark tasks was analyzed separately. The factors for both tasks’ analyses were LENGTH (120 mm, 190 mm, 260 mm) and DEPTH (peripersonal, extrapersonal) and the dependent variables in both tasks were the obtained asymmetry scores. Significant interactions were further explored by post-hoc paired t-tests or one-sample t-tests (both Bonferroni-corrected). Additionally, pearson correlations of both tasks, as well as across tasks were computed to explore whether performances across stimulus orientations or tasks were significantly related. Effect sizes were calculated using the tool G*Power (Faul, Erdfelder, Lang, & Buchner, 2007).
Study 2: Horizontal and vertical attentional biases

3.4 Results

3.4.1 Greyscales task

3.4.1.1 Horizontal greyscales

A repeated measures ANOVA revealed highly significant main effects of LENGTH ($F_{2,34} = 11.372; p < .001$; Greenhouse-Geisser corrected) and DEPTH ($F_{1,17} = 13.253; p < .001$) and the two factors do not significantly interact with each other. Longer lines resulted in a stronger leftward bias and the bias was more pronounced in peripersonal space. Post-hoc t-tests show significant differences between short and medium ($t_{17} = 4.716; p < .001$, Bonferroni corrected; effect size = 1.112) and short and long ($t_{17} = 3.761; p < .01$, Bonferroni corrected; effect size = 0.887) lines whereas medium and long lines did not differ significantly. Additionally, the leftward bias only differs significantly from zero for medium ($t_{17} = -4.138; p < .01$, Bonferroni corrected; effect size = 0.976) and long greyscales ($t_{17} = -3.843; p < .01$, Bonferroni corrected; effect size = 0.906) in peripersonal space.

![Figure 3.3: Effects of LENGTH and DEPTH in the horizontal condition of the greyscales task.](image)

3.4.1.2 Vertical greyscales

For the vertical condition, highly significant main effects of DEPTH ($F_{1,17} = 28.786; p < .001$),
Study 2: Horizontal and vertical attentional biases

and LENGTH ($F_{2,34} = 21.750; p<.001$; Greenhouse-Geisser corrected) were found. Again, the two factors do not significantly interact.

Upward biases are observed in both peripersonal and extrapersonal space, but are significantly more pronounced in peripersonal space. Furthermore, the upward bias increases with longer greyscales (see fig. 4), with all pairwise length differences being significant after Bonferroni correction: short vs. medium ($t_{17} = 3.852; p<.01$; effect size = 0.908), short vs. long ($t_{17} = 5.49; p<.001$; effect size = 1.294) and medium vs. long ($t_{17} = 3.595; p<.01$; effect size = 0.847).

Asymmetry scores significantly differ from zero for medium peripersonal ($t_{17} = 7.197; p<.001$; Bonferroni corrected; effect size = 1.696) and medium extrapersonal ($t_{17} = 4.140; p<.01$; Bonferroni corrected; effect size = 0.976), as well as long peripersonal ($t_{17} = 10.717; p<.001$; Bonferroni corrected, effect size = 2.526) and long extrapersonal ($t_{17} = 7.937; p<.001$; Bonferroni corrected, effect size = 1.871) stimuli.

Figure 3.4: Effects of LENGTH and DEPTH for the vertical condition of the greyscales task.

The average asymmetry scores of peri- and extrapersonal space were significantly correlated
within both the horizontal ($r=.818; \ p<.001$) and vertical task ($r=.697; \ p<.01$). However, no significant correlations were found between the horizontal and vertical conditions (peripersonal: $r=-.181, \ p=.473$; extrapersonal: $r=-.015, \ p=.954$).

### 3.4.2 Landmark task

#### 3.4.2.1 Horizontal landmark task

Participants misjudged the deviation of the transector location from the actual line center in 48.3% of the trials. The results of the repeated measures ANOVA of the false response biases revealed highly significant main effects of DEPTH ($F_{1,17}=18.679; \ p<.001$) and LENGTH ($F_{2,34}=18.722; \ p<.001$). Long lines resulted in strong leftward biases in peripersonal, but not in extrapersonal space (see fig. 5 and table 1).

The judgments shift into a leftward bias with increasing stimulus lengths, with all pairwise length differences being significant after Bonferroni correction: short vs. medium ($t_{17}=3.732; \ p<.01; \ \text{effect size} = 0.880$), short vs. long ($t_{17}=5.688; \ p<.001; \ \text{effect size} = 1.341$) and medium vs. long ($t_{17}=3.040; \ p<.05; \ \text{effect size} = 0.716$).

In this context, the long lines in peripersonal space are the only lines showing a significant leftward asymmetry from the actual midline ($t_{17}=-3.567; \ p<.05$; Bonferroni corrected, effect size = 0.841), while the apparent rightward asymmetry of the short lines in extrapersonal space just misses significance.
3.4.2.2 Vertical landmark task

The analysis of the vertical condition revealed no significant effects. Participants misjudged the direction of the transector deviation from the actual line center in 52.7% of the trials and the responses show a tendency towards a lower field bias (32.0%) in both peri- and extrapersonal space. For all lengths and depths, the distribution of false responses was similar, and account for ~30% in false bottom responses and ~20% of false top reactions. Asymmetry scores significantly differ from zero only for medium peripersonal ($t_{17} = 3.093; p<.05; \text{Bonferroni corrected}; \text{effect size} = 1.696$) and medium extrapersonal ($t_{17} = 3.835; p<.01; \text{Bonferroni corrected}; \text{effect size} = 0.976$) stimuli.

Again, comparable to the greyscales task, performances of peri- and extrapersonal space were significantly correlated within both the horizontal ($r = .925; p<.001$) and vertical task ($r = .877; p<.001$). Once more, no significant correlations were found between the horizontal and vertical conditions (peripersonal: $r = .230, p = .358$; extrapersonal: $r = .308, p = .241$).

3.4.3 Comparison of greyscales and landmark task performance

To explore whether biases in the greyscales and landmark task are based on common or
separate mechanisms, Pearson correlations of both tasks’ horizontal as well as vertical conditions were computed. Across both depths and orientations, no significant correlations were revealed (peripersonal: $r=-.098$, $p=.698$; extrapersonal: $r=-.030$, $p=.907$), which suggests that different mechanisms are engaged in the execution of both tasks.

Table 3.1: Means and standard deviations (SD) of asymmetry scores of the different conditions in the greyscales and landmark tasks.

<table>
<thead>
<tr>
<th></th>
<th>Peripersonal</th>
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<th>Extrapersonal</th>
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<td>SD</td>
<td>Mean</td>
<td>SD</td>
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<tr>
<td>Greyscales task</td>
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<td>Horizontal</td>
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<tr>
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<td>0.391</td>
<td>$0.083$</td>
<td>0.346</td>
</tr>
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<td>0.370</td>
<td>$-0.147$</td>
<td>0.369</td>
</tr>
<tr>
<td>Long</td>
<td>$-0.342^a$</td>
<td>0.377</td>
<td>$-0.198$</td>
<td>0.368</td>
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<tr>
<td>Vertical</td>
<td></td>
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<tr>
<td>Short</td>
<td>$0.201$</td>
<td>0.301</td>
<td>$0.003$</td>
<td>0.340</td>
</tr>
<tr>
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<td>0.268</td>
<td>$0.232^a$</td>
<td>0.238</td>
</tr>
<tr>
<td>Long</td>
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<td>0.237</td>
<td>$0.373^a$</td>
<td>0.199</td>
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<tr>
<td>Landmark task</td>
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<td>Horizontal</td>
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<tr>
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<tr>
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<td>$-0.058$</td>
<td>0.166</td>
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<tr>
<td>Vertical</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short</td>
<td>$-0.108$</td>
<td>0.167</td>
<td>$-0.093$</td>
<td>0.188</td>
</tr>
<tr>
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<td>$-0.148^a$</td>
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*a Indicate biases that are significantly different from zero.

3.5 Discussion

The present study sought to investigate attentional asymmetries in healthy people by using a variation of the greyscales task and a landmark task, in a VR environment. The goal was to test whether presenting the two tasks in different spatial locations (peripersonal, extrapersonal) and different orientations (horizontal, vertical) within three-dimensional virtual space had any influence on magnitudes and directions of potential attentional asymmetries.
3.5.1 Greyscales task

Similar to earlier studies, this study showed a leftward bias (pseudoneglect) in healthy participants in the horizontal condition of the greyscales task (Mattingley et al., 2004; Nicholls et al., 1999; Nicholls & Roberts, 2002; Nicholls et al., 2004). The effect was mostly based on medium and long stimuli in peripersonal space. In addition to the horizontal greyscales tasks used in most studies, a vertical condition was added and an upper visual field bias was detected for medium and long stimuli in both peripersonal and extrapersonal space which was significantly more pronounced in peripersonal space.

This finding is in contrast to the assumption of Previc (1990; 1998), who proposes that the upper visual field is more engaged in distance vision while the lower visual field is biased towards action within praxis space. Following this suggestion, it would be expected to find an upward bias in extrapersonal space and not in peripersonal space. However, an earlier study by Nicholls et al. (2004; 2006) found similar results for vertical greyscales in peripersonal space (on a computer screen). Thus the proposed association of dorsal processing and downward space as well as ventral processing and upward space put forward by Previc (1990; 1998) and Drain & Reuter-Lorenz (1996) does not seem to apply for attentional biases measured by the greyscales task. The different stimuli characteristics compared to e.g. line bisection tasks might have resulted in different neural processing and thus different bias qualities. Also, for both the horizontal and vertical conditions, longer stimuli resulted in a higher magnitude of attentional asymmetries. Earlier studies report similar effects of increasing leftward bisection errors in proportion to length in line bisection tasks in normal participants (Jewell & McCourt, 2000; McCourt & Jewell, 1999).

Although this study used a variation of the greyscales task (with modified instructions), it was still able to reveal significant attentional asymmetries. This further supports the utility and reliability of the greyscales task. Nicholls et al. (2005) investigated the effect of different strategies (global and comparison strategies) on pseudoneglect for luminance judgments and
found pseudoneglect for both strategies, although the effect was stronger for the global strategy (Nicholls et al., 2005).

Finally, the lack of significant correlations between horizontal and vertical greyscales performance, similar to Nicholls et al. (2004), emphasizes the suggestion of different cortical mechanisms employed by the two directional biases.

3.5.2 Landmark task

The results of the landmark task replicate findings of earlier studies that observe a leftward bias (pseudoneglect) in healthy participants in the line bisection task (McCourt & Jewell, 1999; McCourt & Olafson, 1997; Varnava et al., 2002). While a significant leftward bias was observed in peripersonal space only and exclusively for the long lines, Varnava et al. (2002) found a progressive left-to-right shift of the biases from peri- to extrapersonal space that was independent from line length, by using a line bisection task on a computer screen placed at different viewing distances. In another study, Gamberini, Seraglia & Priftis (2008) detected an abrupt shift of the perceived midpoint from left of the true midpoint in peripersonal space to the right of the true midpoint in extrapersonal space using a virtual line bisection task. Additionally, they were able to expand virtual peripersonal space by virtual stick use, similar to previous clinical observations (Berti & Frassinetti, 2000).

Whether the differences in bias shifts are caused by the different setups used (rear projection, computer screen and head mounted display) or the different distances utilized to present extrapersonal space (270 cm, 120 cm and 90 cm) is difficult to assess. While the extrapersonal distance (270 cm) in this study was the farthest and resulted in no detectable bias, the shortest extrapersonal distance (90 cm) used by Gamberini et al. (2008) resulted in an abrupt shift of spatial biases between peri- and extrapersonal space. If there was a clear association of peripersonal space and leftward bias as well as extrapersonal space and rightward bias, one would expect an opposite pattern, with greater extrapersonal distances
resulting in larger rightward shifts and shorter extrapersonal distances resulting in smaller shifts of spatial bias direction, thus presenting an increasing rightward bias with increasing distance.

In contrast to the greyscales task, the analysis of the vertical landmark task revealed neither significant effects nor interactions of depth and stimulus length. However, there seems to be a slight bias towards the lower visual field with medium stimulus length. This contradicts previous findings of vertical line bisection biases that found vertical biases towards the upper visual field (e.g. Drain & Reuter-Lorenz, 1996; Jewell & McCourt, 2000; McCourt & Olafson, 1997).

While the landmark task displays a clear transection of the stimuli into two parts, the greyscales have no distinctive transection but display a continuous transition from white to black. Thus the general strategy for making a decision for the transector location can either employ a comparison of the lengths of the two stimulus parts or, in the vertical condition, a judgment about transector deviation from one’s own optical horizon. Since the participants’ heads were fixated by a chin rest, their own optical horizon was more or less fixed. As a consequence, participants might have employed a deviation strategy and thus judgments might have been facilitated and were predominantly correct. However, Drain & Reuter-Lorenz (1996) were able to show upward attentional biases for both strategies in another landmark task, so this might not be a sufficient explanation for the absence of any directional bias in the presented task.

3.5.3 General discussion

As expected in the hypotheses, a leftward bias (pseudoneglect) in healthy participants in both the greyscales and the landmark task was observed. However, for the vertical conditions, the data showed a marked difference in the results of the two tasks: While an upward bias occurred in the greyscales task, a similar effect in the landmark task could not be detected. Moreover, the differences in greyscales and landmark task performance are also underlined by the absence of any significant correlations between both tasks. While a direct comparison
is slightly complicated by the fact, that a greyscales item actually contains two stimuli vs. one stimulus in a landmark item, both tasks were otherwise constructed for maximum comparability by matching lengths, depth of presentation and motor responses.

The dissociation of greyscales and landmark task performance might be related to the different nature of the tasks. While the greyscales task requires luminance judgments, the landmark task calls for judgments on the basis of relative length of the line halves. However, other studies did find vertical asymmetries with line bisection or landmark tasks (review by Jewell & McCourt, 2000; Drain & Reuter-Lorenz, 1996; McCourt & Olafson, 1997) and thus it is unlikely that the discrepancy between the results is caused by different task characteristics alone. Then again, Nicholls, Smith Mattingley, & Bradshaw (2006) suggest that the vertical perceptional bias is reliant on environmental coordinates. Using the greyscales task, they showed how changes in body reference and environmental reference frames did eliminate the usual upward bias in vertical luminance judgments. Again, this cannot account for the missing bias within this study since the participants remained within the same body reference frames throughout the whole experiment. In the presented experiment, the stimuli were presented on a large projection screen which basically covered the entire visual field. This setup might have eliminated any environmental reference frame and thus a potential vertical bias in the landmark task, but it does not explain the significant upward bias found in the vertical greyscales task.

Studies suggest that magnitudes of attentional asymmetries vary with the length of stimuli (Jewell & McCourt, 2000; McCourt and Garlinghouse, 2000; McCourt & Jewell, 1999) and this was also the case in both tasks of this study. While there didn’t occur a significant rightward bias in shorter lines, observe a tendency of a cross over effect (see Fig. 5) was observed. This indicates a potential tendency of the leftward error of healthy participants ‘crossing over’ and becoming a rightward bias with decreasing line length – an effect that has been observed in neglect patients and healthy subjects before (Jewell & McCourt, 2000; McCourt & Jewell, 1999; Mennemeier et al., 2005). Possible explanations for the effect of line
length and the cross-over effect include the activation-orienting hypothesis (Kinsbourne; 1993; Reuter-Lorenz, Kinsbourne, & Moscovitch; 1990) which proposes two competing attentional gradients in the left and right cerebral hemispheres. As a consequence of task-driven stronger activation of the right cerebral hemisphere, attention towards the left visual hemispace is being increased, especially towards the periphery and thus with longer lines. Another possible explanation is the orientation/estimation hypothesis put forward by Mennemeier et al. (1992, 2005), which regards attentional asymmetries and the cross-over effect in line bisection as a consequence of both attentional biases and systematic errors in magnitude estimation. Both theories might be able to explain the effects found in this study.

Unlike previous studies, this study used a VR paradigm in order to explore a potential influence of depth on the attentional biases. Although all stimuli had the same retinal size, an effect of depth occurred, revealing attentional asymmetries emphasized in peripersonal space, in both the greyscales and the landmark task. This finding is in line with earlier studies using line bisection tasks in peripersonal and extrapersonal space (McCourt & Garlinghouse, 2000; Varnava et al., 2002). Bjoertomt, Cowey & Walsh (2002) investigated performance in a line bisection task in healthy participants and found a leftward bias of visuospatial attention in a line bisection task which was stronger in near than in far space. However, application of transcranial magnetic stimulation (TMS) to the right posterior parietal cortex or the right ventral occipital lobe, lead to a significant rightward shift of visual spatial attention in near and far space, respectively. These dissociations of near and far space are in line with the results of this study and suggest that different neural mechanisms are responsible for the dissociation of attentional biases. Acting in near space is thus considered to be associated with processing in the dorsal visual stream, while acting in far space is related to the ventral visual stream (Goodale & Milner, 1992; Previc, 1998; Weiss et al., 2000).

The absence of significant correlations between both tasks, as well as between stimulus orientations within the tasks, suggest relative independence of horizontal and vertical orienting as well as greyscales and landmark task performance. This finding is in line with the
results of Nicholls et al. (2004), who conclude that horizontal biases may reflect asymmetries in activation between the hemispheres, whereas vertical biases may reflect dorsal and ventral stream activation asymmetries.

In conclusion, this study shows evidence for a leftward bias (pseudoneglect) in healthy individuals by presenting a variation of the greyscales task and a landmark task in three-dimensional virtual space. Apparently, this is the first study to employ a direct comparison of landmark and greyscales performance, which was matched for perceptual features as well as motor responses. As expected, the observed leftward biases were almost exclusively present within peripersonal space, which supports the suggestion of different neural mechanisms for visual attention with respect to viewing distance and respective dorsal and ventral stream processing. Furthermore, this study was able to show that attentional asymmetries are also observable in the vertical plane when investigated by the greyscales task, but the lack of significant correlations between the two stimuli orientations in both tasks suggest rather independent processes of horizontal and vertical orienting.

Finally, this study is the first one to assess spatial biases with the greyscales task in a VR environment. Its differential effects within peri- and extrapersonal space show that VR is an appropriate research tool to assess depth related visual cognition and its comparison to real space, which might also prove itself beneficial for more systematic clinical assessments for neglect patients in the future.
4 General discussion

The studies presented in this thesis examine the influence of virtual depth on visuospatial attention. Additionally, Study 1 shows how the spatial distribution of attention can be modulated by the level of alertness of the participants. In this study, decreased alertness levels led to a significant rightward bias of visuospatial attention in extrapersonal space. In Study 2, horizontal and vertical spatial biases in participants with normal alertness levels were observed with different stimulus materials and these biases were mostly restricted to peripersonal space. Furthermore the data support the view that horizontal and vertical orienting do indeed rely on different cortical mechanisms.

Due to the different nature of the tasks (overt vs. covert attention) and methodological reasons, the two studies are not directly comparable. Nevertheless, both studies show how the healthy human brain is prone to spatial biases and both studies reflect the dominance of the right cerebral hemisphere in visuospatial attention. Additionally, the distinct influence of spatial depth on biases of visuospatial attention reflects the dorsal and ventral stream processing of peripersonal and extrapersonal space respectively.

Study 1 stresses the important impact of alertness on visuospatial orienting and is in line with previous findings in healthy people and neglect patients (see 1.4.5). In this study, only reorientation in extrapersonal space showed a rightward bias after 24 hours of sleep deprivation, while other studies (Fimm et al., 2006; Manly et al., 2005) carried out on PC monitors (i.e. in peripersonal space) also found enhanced rightward biases after sleep deprivation. Furthermore, it was discussed how the findings might be related to the nature of the experimental setup and the results might also be limited by the nature of perception in VR in general (see below). Future studies need to account for these issues, to elaborate on whether the alertness network and the network of visuospatial attention do indeed interact during shifts of attention in both peripersonal and extrapersonal space. On the other hand, the modulation of visuospatial reorienting in extrapersonal space might be selective to the location of the functional overlap of visuospatial attention and alerting. As already discussed
General discussion

(see 2.5), the TPJ might be the crucial site for this anatomical overlap. And moreover, Corbetta, Kincade & Shulman (2003) suggest that the TPJ is part of a more ventral fronto-parietal network that is concerned with alerting and thus the effect of low arousal may have become exacerbated within the ventral visual stream and thus lead to selective spatial bias in extrapersonal space in this study. Recent studies further suggest, that not the TPJ per se, but also the underlying subcortical white matter tracts, especially the superior longitudinal fasciculus (SFL), are involved in the network of visuospatial attention. Accordingly, disconnection within the SFL might lead to severe persisting neglect symptoms (overview in: Doricchi, Thibeaut de Schotten, Tomaiuolo, & Bartolomeo, 2008). In the context of this study, this raises the question whether reduced LC activity might functionally influence SFL connectivity. Interestingly enough, higher white matter diffusion (including the SFL) seems to be associated with decreased cognitive vulnerability to total sleep deprivation (Rocklage, Williams, Pacheco, & Schnyer, 2009) and this indicates that connectivity in the brain is functionally influenced by arousal to some degree. If and how this applies to visuospatial attention and decreased arousal on a functional and/or anatomical level remains to be examined.

In Study 2, the level of alertness was controlled for (see 3.3.2) to exclude any influence of decreased alertness on visuospatial attention as detected in Study 1. In this study, the focus was on “normal” attentional biases in virtual space (i.e. pseudoneglect) and horizontal and vertical biases depending on viewing distance were detected, which were mostly in line with studies performed in real space, with the exception of the vertical landmark task (see 3.5.2). Nevertheless, the data indicate differential processing of both peri-and extrapersonal space, as well as horizontal and vertical orienting in the brain.

To further validate and explore the brain networks and interactions engaged in the mechanisms examined in both of the studies in this thesis, fMRI can be a helpful tool. The specific modulation of reorientation in this study is in line with neglect studies that emphasize the role of disengagement deficits in the development of hemispatial neglect (Posner et al.,
1984; Losier & Klein, 2001) and this provides functional evidence for the anatomical link of disengage processes and arousal functions in the brain. Corbetta et al. (2005) found selective TPJ activation during reorienting of attention and in this context, it would be of great interest to explore whether TPJ activation would be selectively influenced by low levels of alertness during peri- vs. extrapersonal orienting tasks.

In general, fMRI studies might shed light on the open question whether attention in peri- and extrapersonal virtual space is processed in a comparable way within the dorsal and ventral visual streams respectively, as studies in real space indicate (see 1.5). However, it is still largely unknown whether real and virtual depth perceptions are entirely comparable: In natural scene perception, both the primary depth cues of stereopsis (convergence of the eyes) and accommodation (of the lenses) cooperate to give rise to the impression of spatial depth. In VR presentation however, the eyes have to rely on stereopsis only to calculate spatial distances as the accommodation of the lenses is always tied to the projection plane (Wann, Rushton, & Mon-Williams, 1995). Due to the mismatch of stereopsis and accommodation, it is not entirely clear how and if the brain processes virtual depth information in the same manner or similar as natural depth. Behavioural studies (e.g. Armbrüster et al., 2005; Armbrüster, Wolter, Kuhlen, Spijkers, & Fimm, 2008) show that distance estimation in virtual space tends to result in slight underestimation of peripersonal distance and slight overestimation of extrapersonal distance. This finding indicates that the different nature of perception in real vs. virtual space might indeed be based on different processing of virtual depth.

While VR technology and functional brain imaging have been combined in recent years, (e.g. Adamovic, August, Merians, & Tunik, 2009; Hoffmann, Girshick, Akeley, & Banks, 2008), so far only one study appears to have investigated how the brain actually processes stereoscopic presentation of virtual depth. Beck et al. (2009) performed an fMRI study on processing of virtual objects in near end far virtual space. Interestingly, the activation pattern of near and far spatial processing were somewhat reverse to what has been identified for real
space perception in the past (Weiss, Marshall, Zilles, & Fink, 2003; Weiss et al., 2000): near-space conditions resulted in more pronounced activations along the ventral stream and far-space conditions showed more pronounced activations along the dorsal visual stream. However, the study was carried out with a head mounted display (HMD) with a rather small field of view (30°) and the only depth cues were eye convergence and perceived size. The fact that the objects in near and far space were not matched for retinal size, may have additionally contributed to the unexpected activation patterns.

Thus to date, research on virtual depth processing in the brain is mostly limited by hardware issues. Apart from limited fields of view in fMRI-compatible HMDs and the lack of motion parallax due to the fixed head position in the scanner, the convergence – accommodation mismatch is still not solved and not all HMDs do allow control of inter-pupillary distance (IPD) which is critical, especially for near space viewing.

In the presented studies, most of the factors mentioned above were controlled for by utilizing minimal motion parallax, by matching retinal sizes of the peri- and extrapersonal stimuli, by calibrating the VR system according to participants’ individual IPDs and by using large scale projection screens with an extensive field of view. Only the convergence – accommodation issue could not be avoided. The presentation of the stimuli was matched as closely as possible to mimic real space and especially the results of Study 2 are in line with other studies examining spatial biases in real space (see 3.5.3). Thus this should have resulted in sufficient ecological validity to draw conclusions upon spatial distribution of healthy as well as sleep-deprived participants. Another recent study conducted with the same hard- and software setup (Heber, Hauke, Rausch, Kuhlen, Fimm, & Müsseler, 2010) showed how the perception of moving stimuli in extrapersonal space was more accurate for foveopetal (towards the fovea) than with foveofugal (towards the periphery) movements. This dissociation was not observed in peripersonal space and apparently the results reflect the specialization of the ventral visual pathway for identifying objects appearing near the fovea.
Thus, these findings present some additional validity for assessing attentional functions in virtual depth.

Yet, future research needs to elaborate on the neural processes involved in VR perception and its comparability to real space perception. While, as mentioned above, fMRI - HMDs will probably keep on showing substantially limited ecological validity, other techniques might be helpful to shed some more light on the near-dorsal and far-ventral segregation of visual depth processing in VR. EEG measures have been used to examine spatial presence (Baumgartner, Vako, Esslen, & Jäncke, 2006) and Bjoertomt et al. (2002) used TMS to examine dorsal and ventral processing in a “real space” paradigm, which might be replicated in VR environments in the future. Both TMS and EEG have the advantage that they can be combined with large scale projections while VR and fMRI can only be combined by using a HMD.

Few behavioral approaches however have already tried to validate VR depth presentation with the help of matched VR and real space presentation in healthy participants (Gamberini et al., 2008), but similar studies comparing the performance of neglect patients in virtual vs. real peri- and extrapersonal space have not been reported yet. But whether virtual depth processing in the brain is comparable to real depth processing is crucial for the development of VR applications for the diagnosis and therapy of visuospatial disorders like neglect, since especially these disorders might substantially benefit from VR technology. Neglect symptoms can differ subject to presentation of depth (see 1.4), but common tests of visuospatial attention (see also 1.4.2) only concentrate on assessing spatial biases on a computer screen or by classic paper-pencil tasks (clock-drawing, line cancellation, copying, etc.), and thus might easily overlook extrapersonal neglect symptoms. Therapy tasks are again presented on a computer screen and/or on paper and do not account for extrapersonal neglect. Considering that reconstitution of visuo-cognitive function relies on brain plasticity and therefore requires specific training of the damaged and adjacent neuronal areas, VR
diagnostics and therapy might positively enhance neuropsychological rehabilitation, e.g. of extrapersonal neglect.

But not only visuospatial functions do benefit from VR therapy. An important therapeutic field, in which VR is already utilized frequently, is the area of motor rehabilitation, especially of the upper extremities (review in: Sveistrup, 2004). In this context, especially peripersonal spatial biases need to be accounted for as they yield the potential to be a confounding performance factor. Other areas of VR applications like large scale architectural presentations, prototyping or entertainment (3D- cinema) might be less prone to be influenced by spatial biases even though designers might benefit from taking perceptual and attentional issues into account. More time-critical applications like flight simulations or even computer games, which utilize stereoscopic presentation, might be influenced more strongly by visuospatial biases. Whether this is indeed critical for performance in the respective tasks requires to be validated individually according to the actual perceptual demands.

In summary, the results of both studies presented in this thesis do stress the impact of both, the level of alertness as well as spatial depth on visuospatial orienting. While further validation of VR technology in assessment and therapy of brain functions is crucial, the results encourage the view of differential processing of peri- and extrapersonal space, even if the tasks are presented in a VR environment. Furthermore, they indicate how VR has become a promising tool, which might reveal its high potential for tailor-made assessment and therapy tasks, depending on individual peri- and/or extrapersonal neglect symptoms. Beyond that, the incidence of visuospatial asymmetries being dependent on depth of presentation, yields further implications for the design and application of stereoscopic VR environments in therapy, education, training and entertainment, especially if time-critical responses of the users are crucial.

Functional overlap of the networks of alertness and visuospatial attention is still an unresolved question from an anatomical point of view, at least within the healthy brain. If and where exactly the two networks overlap needs to be investigated more closely, by e.g. taking
advantage of modern imaging methods (e.g. Diffusion Tensor Imaging (DTI), high resolution fMRI) or physiological methods (EEG, TMS) and their correlation with behavioral data.
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References


ReactorMan VR software application:


(last visited on July, 19th, 2010)


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<td>temporo-parietal junction</td>
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Danksagung

Bruno Fimm: Herzlichen Dank für konstruktive und lebhafte Diskussionen, Deine uneingeschränkte Unterstützung und für alles, was ich in den letzten Jahren von Dir lernen durfte!

Prof. Klaus Willmes-von Hinckeldey und Prof. Jochen Müsseler: Herzlichen Dank für die Betreuung dieser Arbeit und die damit verbundenen Unterstützungen und Anregungen!

Prof. Will Spijkers: Vielen Dank für die Weitergabe meiner Telefonnummer an Bruno Fimm und die Nutzung des Equipments und des Labors in der Rochusstraße!

Jakob Valvoda, Marc Wolter und Torsten Kuhlen: Vielen Dank für die technische Unterstützung meiner Projekte!

Sarah Siebertz: Vielen Dank für die Unterstützung in Studie 2 dieser Arbeit!

Alle Versuchspersonen: Vielen Dank für das Durchleiden ganzer Nächte oder einiger Stunden im Dienste der Wissenschaft!

Kollegen und Freunde und die vielen, die im Laufe der Jahre zu beidem geworden sind: Herzlichen Dank für inhaltliche und moralische Unterstützung, und dass Ihr den Arbeitsalltag im Klinikum so angenehm macht!

Meine Eltern, Renate und Wolfgang Heber: Für Eure Liebe und Unterstützung, und dass Ihr mir alle Wege und Türen im Leben offen gehalten habt ohne mich jemals zu drängen, kann ich Euch niemals genug danken!
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