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Implicit processing of contralesional stimuli and ipsilesional oculomotor capture in neglect

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„[…] der Raum [ist] nichts anderes, als die Form aller äußeren Erscheinungen, unter der uns allein Gegenstände der Sinne gegeben werden können. Die Sinnlichkeit, deren Form die Geometrie zum Grunde legt, ist das, worauf die Möglichkeit äußerer Erscheinungen beruht […]“

- Immanuel Kant, Prolegomena zu einer jeden künftigen Metaphysik die als Wissenschaft wird auftreten können

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AF	Arcuate fasciculus
BIT	Behavioral inattention test
CoC	Center of cancellation
CT	Computer tomography
EmC	Extreme capsule
IOF	Inferior occipitofrontal fasciculus
IPC	Inferior parietal cortex
IPL	Inferior parietal lobule
LH	Left hemisphere (of the brain)
MdLF	Middle longitudinal fasciculus
MRI	Magnetic resonance imaging
NIHSS	National Institutes of Health Stroke Scale
PnP	Pencil-and-paper (test)
RH	Right hemisphere (of the brain)
S2S	Search-to-sample
SOF	Superior occipitofrontal fasciculus
SLF	Superior longitudinal fasciculus
STG	Superior temporal gyrus
TPJ	Temporo-parietal junction
V1	Visual area 1

1. Introduction

1.1 Spatial neglect

Most of our interactions with the world have a spatial aspect. Disorders of spatial processing radically affect the ability to accomplish daily routines. The neglect syndrome is exemplary of such impairments. It describes the incapacity of a subject to attend and respond to stimuli in a certain part of space despite the full physiological functions of sensory systems (Vallar and Bolognini, 2014). Due to its association with lesions in the right hemisphere of the brain (Appelros et al., 2002; Weintraub and Mesulam, 1987; Becker and Karnath, 2007; Bowen et al., 1999) the most commonly neglected side of „the patient's world" is situated contralesionally, to their left (Stone et al., 1993). The examples and depictions in the current work will thus reflect spatial relations characteristic of left neglect.

The interaction with the affected individuals is memorable: their bodily position is unnatural, with their midline, including their heads and eyes, turned slightly to the right as their default perception of straight ahead (Karnath and Rorden, 2012). When addressed from the left, they tend to remain irresponsive or look for the interlocutor on the opposite side, a phenomenon known as allochiria/alloacusis (Bisiach and Vallar, 2000).

One could argue that individuals with neglect exist within a different ontology. They behave as if half of the world never existed in the past, doesn't exist now, and will never exist in the future (Becchio and Bertone, 2006). Simple activities like grooming oneself, having a meal, or taking a walk are complex undertakings for these patients: they miss half of the food on their plates, bump on corners or shave only half of their faces (Karnath, 2006). At the same time, many of those affected are unaware of the missing piece in their experience (Karnath and Rorden, 2012).

Some of the mentioned symptoms might call sensory impairments to mind. Nevertheless, neglect is not a disorder of sensory systems. Such dysfunctions can occur simultaneously but independently in those affected by brain lesions. A suitable example might be hemianopia, a close differential diagnosis for neglect. It consists of a loss of sight in half of the visual field, most usually caused by lesions along the visual pathway. The two disorders can be distinguished by a neurological finger perimetry test. In neglect, the visual system is mostly intact on an anatomical and functional level and, unlike in hemianopia, visual deficiencies can be compensated for a short time. This can be achieved by offering the patient salient stimuli (bottom-up) or verbal instructions (top-down) (Karnath, 2006). The two diagnoses are, in effect, distinguishable both on an anatomical and functional level. In practice, however, they might co-occur, leading to overlapping clinical manifestations.

1.2 Etiology and relevance

The cause of neglect is most frequently right hemispheric (RH) cerebral injury in form of a large middle artery stroke. Less typical are brain tumors or neurodegenerative diseases like Alzheimer's, corticobasal degeneration, posterior cortical atrophy, etc. (Vallar and Bolognini, 2014; Li and Malhotra, 2015). Stroke is one of the most common disabling health issues globally, reaching an incidence of 13.7 million/year, eighty million people worldwide live with its consequences (Lindsay et al., 2019). The same source estimates one in four people over the age of 25 will have a stroke in their lifetime. Globally, the ischemic type is twice as frequent as hemorrhagic stroke (Lindsay et al., 2019). More than 20% of acute stroke patients develop neglect symptoms (Appelros et al., 2002). Most of the affected individuals recover spontaneously, while a third of neglect patients never retrieve their full attentional faculties (Karnath et al., 2011b). Evidence suggests that suffering from dysfunctions of spatial attention can impair the rehabilitation process, serving as a negative predictor for the reacquisition of functional autonomy (Luvizutto et al., 2018). Patients with unilateral neglect experience longer hospitalization periods and slower recovery compared to equally impaired subjects with brain lesions but without neglect (Gillen et al., 2005).

In the next 30 years, an increase of 3% in stroke incidence is expected worldwide, leading to 27% more post-stroke patients than today (Wafa et al., 2020). During the recent pandemic, the infection with the novel COVID-19 virus has been linked to neurological symptoms and hypercoagulability (Beyrouti et al., 2020; Nannoni et al., 2021; Wool and Miller, 2021). While the exact neurological relevance of the novel virus remains to be quantified, research suggests it might increase the probability of vascular events. Some sources identify COVID-19 as an independent risk factor for stroke (Belani et al., 2020). Not only do cerebrovascular events and their consequences remain relevant, but a surge in brain-injury-related disability in the following decades is also to be expected. The neglect syndrome counts as one of the most debilitating consequences of brain injury, whose exact pathophysiology needs further elucidation.

1.3 Frames of reference

Neglect can manifest in one or a multitude of sensory (visual, tactile, auditory) and motor modalities, without being of a motor or sensory nature in itself. This explains the emergence of very heterogenous clinical pictures of the same underlying attentional deficit. In addition, different frames of reference for the manifestation of the symptoms exist. One of them is the subject's own body: here, the patients tend to disregard their somatic sensations and functions. Motor manifestations can mimic hemiparesis despite fully functional limbs. Some patients fail to recognize their extremities (somatoparaphrenia) and lack insight into their disability (anosognosia) (Li and Malhotra, 2015). In contrast to the personal manifestations, neglect can also exclusively affect the external space and the objects within it to various extents: from the near to the peri-personal, to the far space (Vallar and Bolognini, 2014).

Another important distinction described in the literature (Karnath, 2006; Vallar and Bolognini, 2014) is the ego- versus allocentric neglect. In the former case, the subject doesn't attend to stimuli in the left hemispace, including personal and extra-personal coordinates. The point of reference here is the sagittal midline of the individual. In the latter case, the left side of objects remains undetected regardless of their position relative to the patient, with the object itself serving here as a point of reference.

Simultaneous allo- and egocentric neglect has been reported in more than half of the neglect patients (Yue et al., 2012), with some studies reporting numbers higher than 90% (Rorden et al., 2012). Allocentric symptoms occur only in subjects with substantial egocentric ones, while the severities of both deficits correlate (Kleinman et al., 2007; Rorden et al., 2012). Consequently, it has been reasoned that the egocentric frame of reference might be more relevant to the core symptoms (Corbetta and Shulman, 2011). Overall, extra-personal egocentric neglect is a more frequent entity (Vallar and Bolognini, 2014).

1.4 Diagnostics

Various diagnostic tools for neglect are used for neglect worldwide (Menon and Korner-Bitensky, 2004) but, unfortunately, no gold standard exists (Bowen et al., 1999). Here, a selection of specifically designed tests and diagnostic measures are discussed. For instance, the Behavioral Inattention Test (BIT) or the Catherine Bergego Scale constitute sensitive diagnostic tools for neglect (Vallar and Bolognini, 2014).

The Catherine Bergego Scale relies on a checklist of everyday life situations, assessing the performance of a patient in grooming, navigating usual paths, adjusting clothing, and other similar activities. Consistent pathological ignoring of contralateral space is being rated on a score between 0–4, with 0 designating no neglect and 4 indicating severe impairments. In addition, it offers a questionnaire for assessing the self-awareness (anosognosia) of a subject. Patients' answers are put in relation to the detected behavioral abnormalities (Bergego C., 1995).

BIT (Wilson et al., 1987) includes both behavioral and paper-and-pencil (PnP) tests. The functional ability is evaluated by pictorial scanning, reading, time telling, map navigation, and other daily activities. The most effective and widely used assessment method includes PnP tasks like cancellation, line bisection, copying, and drawing tests. These generally require a fixed position of the paper sheet in relation to the midline of the patient, avoiding trunk movement.

In cancellation tasks, the patient is asked to find and mark a target (letter or symbol) between distractors. The targets are equally distributed over the two halves of the paper sheet. In effect, the severity of impairments is proportional to the number of missed targets on the left (Diller et al., 1974; Weintraub and Mesulam, 1985; Gauthier et al., 1989). Line bisection (Albert, 1973) implies finding and marking the middle of horizontal lines, without using any tools to approximate length. A correlation between the exact aberration of the patient's mark from the midline and the severity of neglect has been established (Schenkenberg et al., 1980). Finally, the subject can be asked to copy simple figures (e.g. a flower, a house, etc.) or draw a clock from memory. Here, the affected might miss let parts of the depicted objects or whole figures on the left. The performance of the patient across different tests is usually averaged and a diagnosis can be secured if the defective behavior was assessed in more than one test (Vallar and Bolognini, 2014). Generally, cancellation tasks have been found to constitute a more sensitive measure in quantifying neglect than line bisection (Ferber and Karnath, 2001; Azouvi et al., 2002).

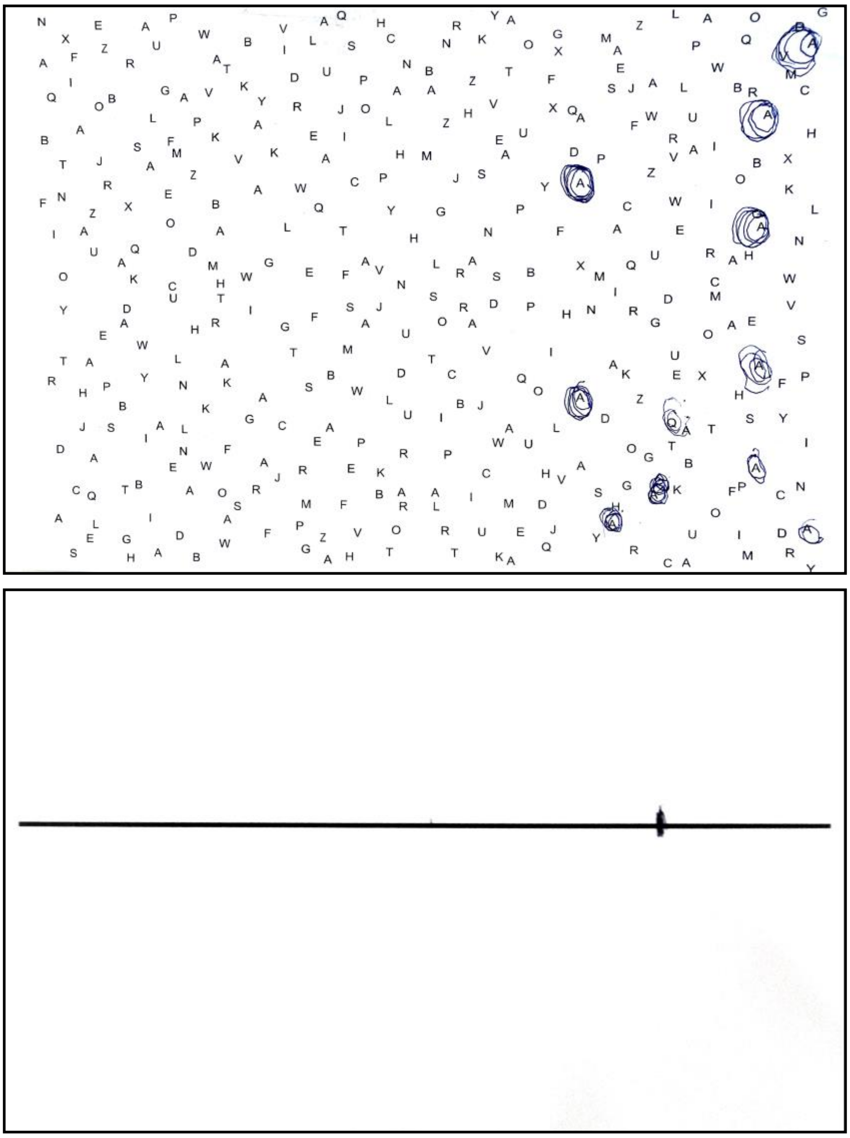

Figure 1: Examples of diagnostic tools for neglect.
Top: The letter cancellation task (Weintraub and Mesulam, 1985). Here, the subject is required to circle or cross out the letter „A“ among distractors on a paper sheet of DIN-4 size. Neglect patients typically start encircling the letters on the right side (here showing persevering behavior) and tend to ignore the contralesional one. Bottom: Line bisection (Albert, 1973). Here, the patient marked the midpoint of the line noticeably to the right. Sources of the images: own testing.

In addition to these diagnostic measures, more assessment tools can be included to determine precisely the type of impairments in a specific patient. For instance, the Ota task is suitable for distinguishing ego- from allocentric impairments (Ota et al., 2001).

Generally, it has been shown that a minimum of ten tests (behavioral and PnP) are needed to cover the various aspects of detection, dissociation, and severity of neglect (Lindell et al., 2007).

1.5 Theoretical models

Several pathophysiological mechanisms of the syndrome of neglect have been proposed. This section discusses some of the leading theories, which can be roughly divided into three types: attentional, representational, and transformational.

Attentional accounts

Kinsbourne postulates that each hemisphere is responsible for modulating the attention in the contralateral space. While doing so, each of the hemispheres inhibits the concurrent one. Since inhibition is disrupted by a given unilateral brain injury, a bias towards the „healthy“ side results. This particular theory is known under the name of the hemispheric imbalance model. (Kinsbourne, 1977; Kinsbourne, 1993) Though the idea of hemispheric cross-inhibition is partly supported by empirical data from transcranial stimulation studies (Vallar and Bolognini, 2014), Kinsbourne's theory cannot fully account for RH dominance in attentional processes and it leads to empirically contested predictions. For instance, it suggests that a neglect patient would consistently direct her attention to the right, eventually turning around her own axis, but this behavior does not typically occur (Karnath, 2006). Another argument against Kinsbourne's model is that, while it predicts the attentional imbalance to be symmetrical to the mid-sagittal plane of the trunk, such a clear-cut symmetry is not usually the case (Vallar and Bolognini, 2014).

Another attentional approach has been proposed by Posner (1987). Three main operations belong to the function of attention: disengagement from a focus, shifting of attention, and focusing on a new object. In this model, stimuli in both the hemispaces compete with one another. Neglect patients can only disengage their attention from the ipsilesional space when a much more salient stimulus on the contralesional side is presented. It has thus been postulated that not a lack of attention but the inability to disengage from a focus leads to its typical symptoms (Posner, 1987). One of the current theoretical frameworks builds on the "disengagement deficit", proposing that the semiology of neglect might be the result of a disturbed "priority map" of the environment, a neural representation of a default attentional orientation in space, influenced both by the salience of the stimuli and personal goals (Ptak, 2012).

Representational accounts

Bisiach and Luzatti (1978) have famously shown that neglect symptoms do not only affect immediate stimuli but the imaginary space as well (Bisiach and Luzzatti, 1978). In the experiment, neglect patients were asked to describe landmarks in the Piazza del Domo in Milan from memory. They have consistently omitted objects and buildings situated to the left of their perspective. When asked to describe the buildings from an adjusted position, in which now the omitted objects were included in their right space, the same subjects could recall them flawlessly. According to their interpretation neglect can thus be explained by a lack of mental representation.

Other hypotheses suggest the main cause of neglect is a distortion of the spatial representation, including both linear (Halligan and Marshall, 1991) and an-isometric compression of space (Bisiach et al., 1996). Accordingly, the ipsilesional space is represented in a compressed and the contralesional in a stretched manner. But contrary evidence has been provided, showing that the space does not appear to be distorted in neglect (Karnath and Ferber, 1999); instead, space exploration is distributed similarly to healthy subjects but around a novel center of symmetry, shifted to the right (Karnath et al., 1998). This finding has led to the articulation of another current theoretical model, described below.

The transformational account

The spatial representation might be organized around a center of attention modulated by proprioceptive, vestibular, and retinal information from the periphery. It has been proposed that neglect might result from an incorrect feeding of peripheral information into representational coordinates of space. The consequence is an abnormal adjustment of the bodily position relative to the external space, accompanied by the typical loss of awareness on the contralesional left side (Karnath and Dieterich, 2006).

Experimental results show that neglect symptoms can be diminished or even shortly abolished by the use of vibrational stimulation of neck muscles or caloric vestibular stimulation (Karnath et al., 1993; Schindler et al., 2002; Kamada et al., 2011). In this model, the shifted perception of the straight ahead of the patient constitutes one of the main characteristics of the disease, since it has been linked to defective information from the periphery.

As it will become apparent throughout this introductory chapter, there is evidence for multiple dissociable processes and corresponding cortical areas playing their part in neglect. Investigations into each of the components and their possible interplay are needed in order to achieve comprehension of the pathophysiology of the neglect syndrome (Vallar and Bolognini, 2014).

1.6 Anatomy

Numerous studies provide evidence for the higher incidence and severity of neglect succeeding RH lesions compared to LH ones. In the acute phase after cerebral injury, 85% of RH stroke patients exhibit neglect symptoms (Mesulam, 1981; Weintraub and Mesulam, 1987; Stone et al., 1993; Pedersen et al., 1997). Three main cortical areas, connected by white matter fiber tracts and building “a perisylvian network” (cf Fig. 2) (Karnath, 2009) within the RH have been identified as systematically correlating with spatial neglect: the temporoparietal junction and the inferior parietal lobule, the superior/middle temporal cortex and underlying insula, and the ventrolateral prefrontal cortex (Karnath and Rorden, 2012; Vallar and Bolognini, 2014; Karnath, 2009).

In addition, subcortical structures seem to play a substantial role in the etiology of neglect, in particular the putamen, the pulvinar, and the caudate nucleus. Approximately one-third of neglect patients show damage in the named subcortical areas (Karnath et al., 2002). While it has been reported that damage to the LH can similarly lead to spatial neglect, the adjacent symptoms tend to be milder and recover faster (Ten Brink et al., 2017). Homologous to the RH, a perisylvian network exists in the LH; lesions to these areas in the LH typically lead to aphasia, apraxia, and more rarely disruptions of spatial attention(Karnath, 2009).

Figure 2: Schematic overview of the two symmetrical networks, one for spatial attention in the RH and one for language and praxis in the LH.
According to this representation, the IPL, the ventrolateral frontal cortex, the superior/middle temporal cortex and insula are interconnected by white matter fiber tracts, building perisylvian networks: AF,SLF, SOF, MdLF, EmC and IOF, in both cerebral hemispheres in humans. Figure and explanation from Karnath (2009).

A possible explanation for the functional lateralization of the hemispheres might be that, in humans, the RH controls attention to both coordinates of space, while the LH is only responsible for the function of attention to the right, leading to an easier compensation of the symptoms (Corbetta and Shulman, 2011). It has been shown that in non-human primates space is symmetrically processed in both hemispheres; humans, in contrast, acquired additional functions like language, leading to the emergence of respective cortical representations in the LH. In effect, the shift of spatial processing to the right hemisphere can be regarded as a consequence of the phylogenetic transformation of the brain (Karnath, 2009).

The mentioned cortical areas, although all linked to neglect, can dissociate as to the specific function they fulfill. The heterogeneous loci of the lesions may correlate with the variety of clinical manifestations. A good example of such a fine distinction is, as mentioned above, extinction[1]. Since it can accompany neglect-like symptoms and might also occur independently, it suggests neighboring but separable anatomical correlates for each of the impairments. Extinction might be linked to an isolated unilateral (right-hemispheric) deficiency in the bottom-up system of attention, precisely affecting the TPJ (Karnath et al., 2003; de Haan et al., 2012).

An important idea in the wider context is that neglect, although largely perceived as unitary can be understood as a multi-layered phenomenon with dissociable components

[1] Deficient processing of contralesional stimuli occurring uniquely during bilateral stimulation.

(Vallar and Bolognini, 2014). By closely investigating the dissociable behavioral components in spatial inattention, a better grasp of the involved mechanisms can be achieved. One of the widely discussed distinctions includes the perceptual and motor-intentional aspects of the deficits, mirroring two potential mechanisms involved in neglect. Behavioral distinctions are often due to separate anatomical organization and it has been argued that deficiencies in each of the tasks are linked to damage in separate brain regions. As summarized by Vallar and Bolognini (2014), damage to the frontal cortex has been associated with impairments in motor-exploratory tasks. More posterior lesions to the inferior parietal lobule or parieto-occipital areas have been linked to impairments in perceptual tasks (Vallar and Bolognini, 2014). Functional and anatomical reasonings around the individual impairments found in neglect usually refer to the existence of two cortical networks shaping awareness: the dorsal and the ventral stream, discussed below.

1.6.1 The ventral and the dorsal stream

The processing of visual information can take different paths within the brain. Mishkin and Ungerleider (1982) have shown that the appreciation of an object's qualities and its spatial location build different functional entities. The shape, orientation, and size of an object, face and text recognition are processed in the inferior temporal, an object's position in space in the posterior parietal cortex (Mishkin and Ungerleider, 1982). Accordingly, Goodale and Milner proposed two main neural circuits for the processing of visual information in the brain: a ventral and a dorsal one (Goodale and Milner, 1992). The ventral neural stream represents the perceptual basis for the offline control of attention. The dorsal stream mediates the visual control of actions directed at those objects. Anatomically, the ventral system includes projections from the striate to the inferior temporal cortex while the dorsal one involves striate projections to the posterior parietal region, strongly linked to pre-motor regions of the frontal cortex involved in ocular control (Goodale and Milner, 1992).

Further on, Goodale (2011) mentions that the neurons in the inferior temporal cortex are sensitive to form, pattern and color, selectively responding to faces, hands, and the appearance of particular actions in others. It has been observed that monkeys with brain injuries confined to the inferior temporal cortex are defects in visual recognition of objects while their skill of catching flies, a visually demanding activity, remains intact. The same behavioral and anatomical pattern has been observed in humans: Cases of patients suffering from focal lesions along the ventral stream have been reported. While these patients displayed an inability to perceive the shape and orientation of an object, this fact didn't disrupt their ability to program and control grasping of the same object (Goodale, 2011). Possible dissociations within the two streams might represent underlying processes in visual neglect.

1.7 Aspects of visual processing: perception, exploration, and spatial attention

It has been reasoned that two distinct mechanisms can account for the impairments in the classical PnP tests used in neglect: the difficulty in generating an internal map of sensory representation of a percept (due to the inability to fully use sensory information on the left), or a failure to initiate or fully execute movements towards the neglected space (Coslett et al., 1990). These can be roughly summed up as perceptional and premotor deficits.[2] Premotor neglect (which is to be distinguished from motor neglect, mimicking left limb hemiparesis) can be apparent in the directional (leftward) slowness in the initiation of movements (Heilman et al., 1985) or an „exploratory" deficit of systematic search within extra personal space (Mesulam, 2000). [3] Oculomotor search, as a fundamental component of purposeful action (Pierrot-Deseilligny et al., 2002) can function as a measure of intentional deficits.

Some authors argue that cancellation tasks primarily involve active search and might be more suitable to detect motor-intentional deficits. Conversely, the line bisection task would be more suitable to detect perceptional deficits (Mesulam, 2000; Milner, 2002; Verdon et al., 2010). But since both tasks require a motor response to visual stimuli, pure perceptual and intentional aspects cannot be directly contrasted in a classical PnP setting. Thus, the two effects are typically confounded (Mesulam, 2000). Designs that reflect the

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[2] The same dichotomy can be conceptualized as representation and intention, perception and exploration, and representational and directional processes.

[3] Other variants of the dysfunctional planning and execution of action might include motor lack of persistence (inability to sustain movement) KERTESZ, A., NICHOLSON, I., CANCELLIERE, A., KASSA, K. & BLACK, S. E. 1985. Motor impersistence: a right-hemisphere syndrome. *Neurology,* 35**,** 662-6., motor akinesia (failure to initiate response), motor perseveration (incorrectly repeating a prior response) or hypometria (reduced amplitude of movements) HEILMAN, K. M. 2004. Intentional neglect. *Front Biosci,* 9**,** 694-705..

two processes separately but also in parallel are better suited to investigate the possible dissociation between the two processes of awareness. Evidence suggests a distinction between patients whose errors seem to reflect processing failure relating to the stimulus and others whose errors relate primarily to the spatial location or direction of the response (Harvey et al., 1995). For instance, in a study involving free viewing of a stimulus, neglect patients were able to distinguish whether a flower had petals on the left side or not. When asked to draw the flowers they consistently ignored the left side, leaving the depiction incomplete (Ishiai et al., 1996). This case illustrates the selective impairment in one of the processes of awareness: the exacerbation of the unilateral bias when goal-directed movement is required while exhibiting clear perception of visual features.

Another example of the same dichotomy is a study performed by Tegnér and Levander (1991). The authors performed an experiment designed to decouple the locus of visual attention from the direction of the arm movement. Subjects with neglect were asked to complete a version of the line-cancellation task in two conditions: one in the normal view of the paper sheet and another one, performed in a mirror and hidden original test paper. The mirror condition reverses the perception of the stimuli and the direction of the arm movement needed to bisect the stimuli. Thus, patients with perceptual neglect crossed the lines on the right in the normal condition and on the left in the mirrored condition. Patients with premotor neglect crossed the lines in both conditions on the right, the pattern resulting from their inability to plan and execute movements on the left regardless of the viewing condition. Although hypokinesia was not contrasted to exploration deficits and the eye movements have not been examined, the subsequent results point to the existence of two patterns of impairment: perception and action-related (Tegner and Levander, 1991).

To sum up, perception designates a representational process for shifting attention and orienting in space without overt eye- and head-movements (covertly). Roughly, it designates a global „map“ of the space from a fixed point of view. Motor-intentional processes, by contrast, imply visual or other types of motor search (Mesulam, 2000). In the following section an overview of the evidence concerning each of the two processes of awareness in neglect is provided.

1.8 Research rationale

Perception and (premotor) intention are two processes potentially shaping awareness. Their functional interaction in the brain is not fully elucidated. To examine perceptual and exploratory components of awareness, we designed a novel computer-based search task, in which perceptual and exploratory processes are investigated simultaneously but also in separate parts of the experiment. The task consisted in locating the identical geometrical figure for a sample, presented laterally at a point of fixation by singular use of eye movements. Since the experiment was designed with the possibility of testing non-human primates in mind, the current work lays the ground for future inter-species comparisons and exact anatomical studies within the networks contributing to perception and action, as well as oculomotor control. In the long run, a more profound and granular elucidation of the processes contributing to spatial attention/awareness and mechanisms leading to the syndrome of neglect are possible.

Impairments of perception should be apparent in the inability of the subject to extract information from the stimulus and thus in consistently lower success rates in the condition with the sample placed left (as the neglected stimulus is placed contralesionally). Intentional deficits should be reflected by the limited exploration and lower success rates in trials with the match placed left. In line with the subsequent research, we expect perception to be preserved and (pre)motor processes to be substantially disrupted in neglect.

2. Materials and Methods

2.1 Subjects

Individual neglect patients with a diagnosis of right-hemispheric stroke were the main target of the experiment. Three different groups served as controls: RH post-stroke patients without neglect, elderly and young subjects with no neurological/psychiatric impairment. All stroke patients were consecutively admitted to the Center of Neurology of Tübingen University. Brain lesions were confirmed by computer tomography (CT) or magnetic resonance imaging (MRI). In the healthy control groups, all participants were right-handed, had intact visual fields and oculomotor functions, and had a normal or corrected-to-normal vision. The study was conducted according to the 1964 Declaration of Helsinki and was approved by the Ethics Review Board of the Medical Faculty of Tüb ngen University under project number 131/2017BO2. All participants had both written and oral instructions in the task. After completing the experimental session, all subjects filled out a self-assessment questionnaire (in German) concerning subjective differences in the lateralized perception of the sample stimulus and subjective search difficulty in each of the hemispaces (see Supplementary).

2.2 Diagnostics

All RH patients were tested for spatial neglect. Neglect-specific tasks included letter cancellation (Weintraub and Mesulam, 1985), bells cancellation (Gauthier et al., 1989), and a copying test (Johannsen and Karnath, 2004). These tasks were presented on a DIN A4 sized 297 by 210 mm paper each. The maximum duration of each test was not fixed but depended on the patient being satisfied with his/her performance and confirming this twice. Neglect was diagnosed if at least two of the specific tests were rated above the cut-off values. In the cancellation tasks, the Center of cancellation (CoC) cut-off values were 0.081 for bells and 0.083 for letter cancellation (Rorden and Karnath, 2010).

Figure 3 shows the exact depiction used for the copying task, adapted exactly from (Fruhmann Berger et al., 2006). Here, patients had to reproduce line drawings of multiple objects placed across the horizontal sheet of paper, including a fuming house, an apple tree with the detail of left-sided stairs, a car, and a flower behind a fence. Missing contralateral details of any figure was graded with 1 point, and failing to depict any entire figure – with 2 points. Another point was added if contralesionally placed objects on the sample sheet were pictured ipsilesionally on the patient copy. A score higher than 1 (equivalent to > 12.5% omissions) hinted to neglect, while the maximum possible grade was 8 (Fruhmann Berger et al., 2006; Johannsen and Karnath, 2004). Subjects were tested for visual field defects and visual extinction using the usual neurological confrontation technique (Brott et al., 1989). Neglect was diagnosed if at least two of the tests above were rated above the cut-off values.

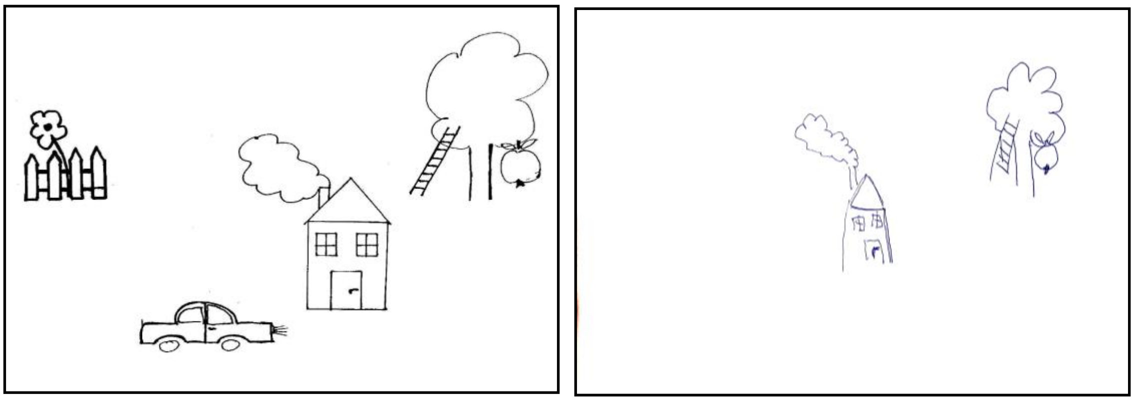


Figure 3: The copying task used in the test battery for neglect.
Left: sample of line drawings for the patient to copy and right: example of defective performance. Since the patient omitted entire figures on the left, the performance in this task should be rated with 4 points (2 for each of the missing objects). Source of the images: own testing.

2.3 Experimental setup

The subject was seated at an 80 cm distance from the stimulus presentation area (78x61 cm). Stimuli were back-projected on this presentation area by overhead Hitachi CP-S210 multimedia beamer. The screen resolution was set to 1024x768 pixels. Stimulus presentation and data acquisition were controlled over Matlab2016b, ran on an HP Elitebook Folio 1040 G2 Laptop operating Windows 10. The subject's head was fixed in place by a chin rest, the position of the eyes corresponding to the central fixation spot. The room was darkened during the experiment. The background of the stimulus presentation was set to dark grey to ensure better eye tracking. A QWERTZ keyboard was placed at a comfortable reaching distance from the subject for stimulus selection (space bar).

A Tobii X120 device, sampled at 60 Hz, was used for eye tracking. It was placed at 60 cm from the test person and 10 cm from the stimulus presentation area. It covered 14.5 cm of the inferior part of the projection, which was not used for stimulus presentation. To ensure accurate eye-tracking, the device was adjusted to the position of the subject's eyes. The fixation radiuses were set to 5° visual angle for all stimuli.

The sample-to-search (S2S) task

The computer-based visual search task aimed to disentangle perceptual and exploratory deficits in neglect. The task consisted of two conditions: a fixation period, where the participant attended covertly to a lateral stimulus, and an exploratory interval, where the participant actively inspected the screen, terminated by subject's target selection. Figure 4 displays the sequence of one trial. The trial started with the onset of a central red fixation dot. After fixation for 200 ms, a sample stimulus appeared for 500 ms pseudo-randomly on either the left or right side of the screen at 16° horizontal eccentricity (Fig. 4a). The subject was asked to maintain fixation throughout the whole 'fixation period' (Fig. 4a). If failed to do so, the trial was aborted and repeated later in the run. After sample presentation, the screen turned blank and three grey placeholders (small dots of 1° diameter in dark grey color; Fig. 4b) were visible. They marked the possible locations of the target stimulus and the two distractors in each trial. These locations were pseudo-randomly chosen from eight possible locations on the screen, situated 8° and 24° on the left and right side (cf. Fig. 4c). Pseudo-randomization controlled for a balanced presentation of the sample stimulus and the target stimulus on the left and right side of the screen: frequencies of trials with both sample and target on the right side, both sample and target on the left, sample right − target left, sample left − target right were kept constant. Positions of the 2 distractors per trial were fully randomized.

The subject's task was to find an identical target stimulus to the sample stimulus. In each trial, the sample stimulus was chosen from a set of four bilateral concave shapes (Fig. 4d). The two distractors were randomly chosen from the same set of 4 shapes. The height of all figures was kept constant at 4° visual angle. The 4 shapes were designed by bilaterally subtracting different half ellipses from identical rectangles. The total area of the figures was kept constant to ensure comparable salience. The differences between the targets resulted from varying degrees of curvature of the subtracted half ellipses. Curvatures were computed as the ratio of the semi-minor axis and the semi-major axis of each ellipse. The difference in curvature between the most similar targets was fixed at 0.2. Thus, the easiest distractor differed in curvature by 0.6 from the sample target. A few exceptions to this rule have been implemented for participants who reported great subjective difficulty in discriminating between the two most similar samples during training. In these cases, we increased the difference in curvatures of the most similar figures from 0.2 to 0.3, resulting in a difference of 0.9 between the sample and the easiest distractor. Sample presentation timing was set to 500 ms across all participants, except for TE, an 81 years old neglect patient. Because TE reported not seeing any stimulus under the 500 ms sample presentation condition, the onset time for him was gradually increased during the training and adjusted to 1000 ms for the experimental session.

At the end of the fixation period (cf. Fig. 4b), the subject started moving the eyes across the screen, searching for the target stimulus. Importantly, target or distractor stimuli showed up only if actively inspected by eye fixation. When the eyes moved away from the respective position, the stimulus (target or distractor) disappeared immediately again. The target and distractor stimuli were thus only examined serially. If the subject found the target stimulus, he/she fixated on it and simultaneously pressed the space bar on a keyboard. The total exploration time was set to 20 seconds. If no target was selected during this interval, the trial ended incomplete and was repeated later in the run. A pause of 1000 milliseconds separated the trials. No stimulus or placeholder was visible during this time. The entire experiment comprised 96 trials.

Each participant completed a training session before testing. It included a different set of shapes than those used for data acquisition in the main experiment. Training only lasted as long as the subject needed to get a grip on the task. Two-step calibrations in the eye-tracking software and Matlab task controller preceded each session. In the control groups, the experiment was performed in a single session lasting around one hour. It consisted of two identical runs of the S2S task, 48 trails each. Brain-damaged patients typically required extended training to get comfortable with the task. The testing sessions exceeded one hour by far.

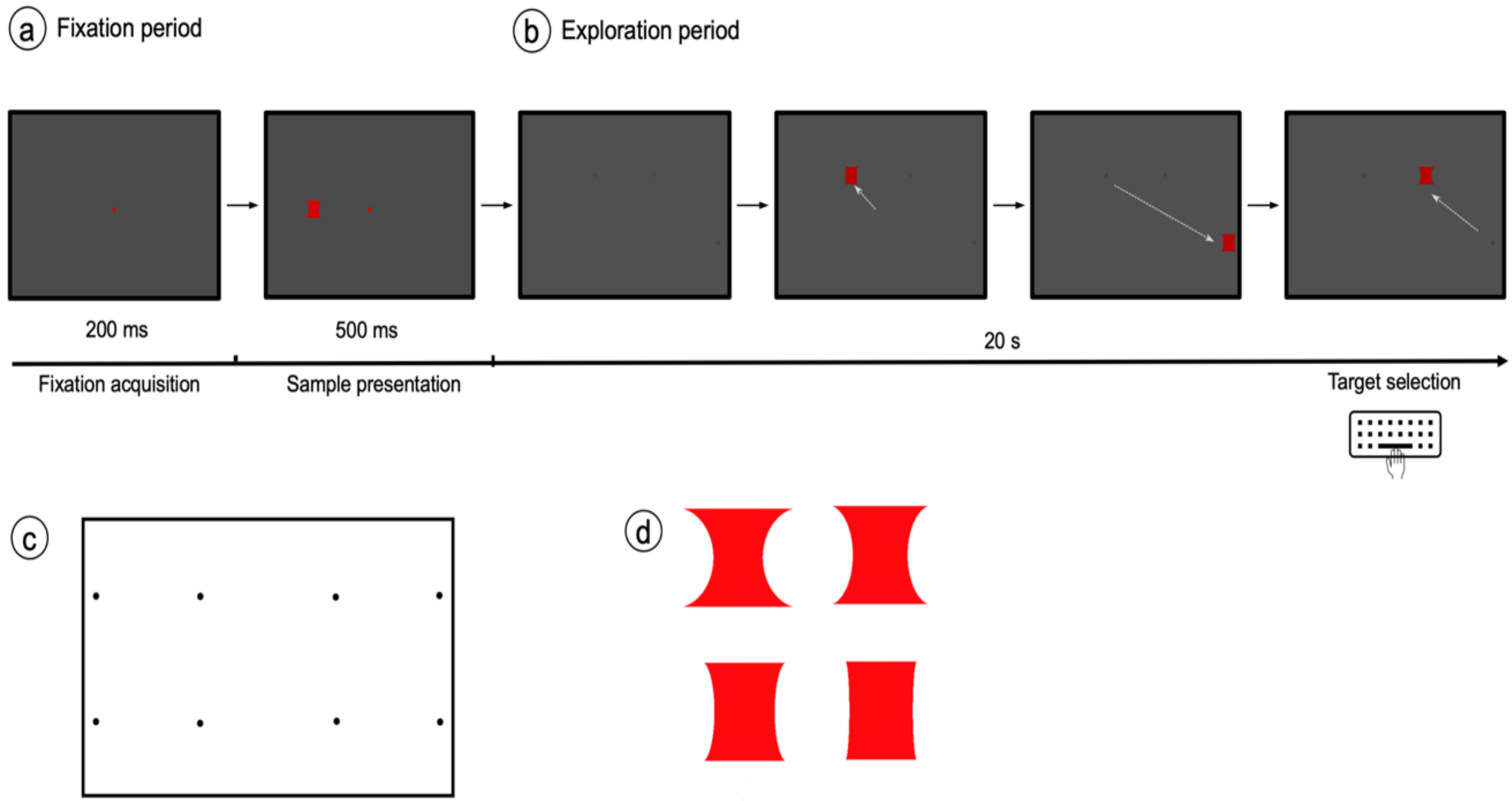


Figure 4: Task layout showing the sequence of one trial.
(a) Fixation period. (b) Exploration period. White arrows represent an exemplary exploration path by, e.g., three saccades. Here, the participant chose to inspect the closest target first. He/she performed a saccade to the left (8° eccentricity), detecting a distractor. Further on, the most distant object (24° eccentricity) was inspected, in this case: another distractor. Finally, a figure identical to the sample was inspected. The subject correctly recognized and selected it with a button press on the keyboard. (c) Eight possible positions (8° and 24° eccentricity on the left/right) of the 1 target and 2 distractor stimuli in the exploration period of a trial. (d) Stimulus shapes used for sample, target, and distractor stimuli in the experiment.

2.4 Task rationale

As neglect patients usually ignore the left side of space, the experimental design reflected the following rationale: performance in relation to the position of the samples was a measure of perceptual processes; performance in relation to the position of the matches reflected exploratory abilities. In the case of a predominant perceptual impairment (Fig. 5a), a lower success rate was expected in trials with the sample placed left, compared to those with the sample right. This result was anticipated independently of the position of the matches. In the case of a predominant exploratory impairment (Fig. 5b), a lower success rate in trials with the match left compared to trials with the match right was expected. This result was anticipated independently of the position of the sample. In case perception and exploration were equally affected (Fig. 5c), a higher success rate was expected only if both sample and match were placed on the right side, with poorer performance in any other configurations.

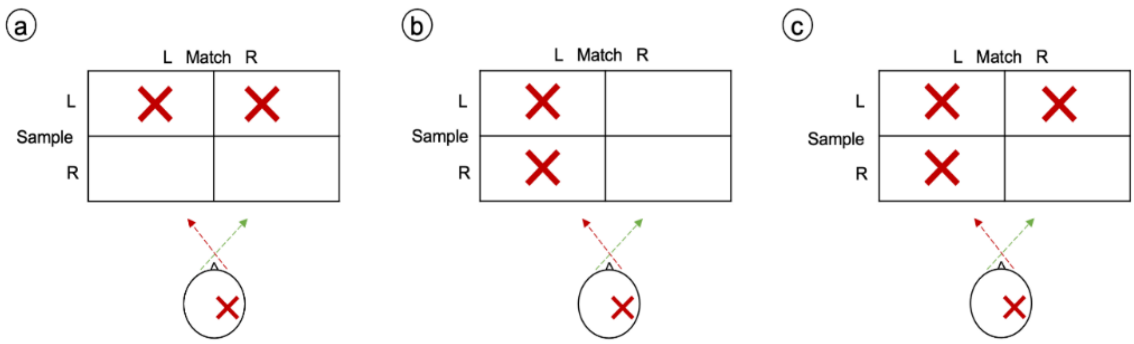


Figure 5: Rationale of possible results in the S2S task.
(a) Predominant perceptual impairment, (b) predominant exploratory impairment, and (c) combined perceptual and exploratory impairments.

2.5 Analysis

All data were analyzed in Matlab2012b. Statistical testing was performed using SPSS Version 27 as well as using executable files provided by Crawford and colleagues at https://homepages.abdn.ac.uk/j.crawford/pages/dept/psychom.htm. Statistical significance was reported at $p < 0.05$.

Exploration

Two different measures were used for the analysis of the exploratory behavior: scan paths during the trials (during purposeful search) and the spontaneous eye orientation across all inter-trial intervals (while no stimulus was presented and no task was given). The scan paths during the trials are graphic representations of the sum of eye positions across all trials, representing each location (a bin of 1x1 visual degrees) on the stimulus presentation area that has been crossed by the subject's eyes (as recorded by an eye tracker). Since all subjects without neglect exhibited symmetrical exploration patterns, we summarized them under a single plot representing the control group (n = 54). The exploration patterns of neglect patient cases were presented individually. The spontaneous eye orientation during inter-trial intervals was computed as the total time spent orienting the eyes towards each of the hemifields (left and right) independently, across all inter-trial intervals. Collected data were normally distributed, with a Shapiro Wilk test yielding the following results: left: $df = 54$, $p = 0.795$; right: $df = 54$, p = 0.814. For inter-group comparisons, independent samples t-tests were performed. For comparisons of the individual patients with the control groups, we applied a modified t-test (Crawford and Garthwaite, 2005). It computed and compared differences between an individual's scores on two conditions (e.g., left and right) to differences between scores under the same conditions observed in a control sample. This particular analysis was fit to detect possible differences in the performance of neglect patients, that result from lateralized deficiencies. It included a calculation of the probable percentage in the control population, that would exhibit a similar or higher difference between the same task results as in neglect. We reported the calculated results along with the significance testing, as they are helpful indicators of the abnormality of the specific lateralized (and thus dissociated) behavior in neglect.

Success rates

Success rates were defined as the fraction of trials where the correct match was selected divided by the total number of trials. The results were grouped based on the position of the sample (left vs. right) and the position of the matches (left vs. right). Consequently, four conditions with individual values were computed. Data were normally distributed. Shapiro Wilk test for the normal distribution of data yielded the following results: sample left: $df = 54$, $p = 0.375$, sample right: $df = 54$, $p = 0.293$, match left: $df = 54$, $p = 0.116$, match right: *df* = 54, $p = 0.416$. For comparisons of success rates between groups, ANOVA tests with the within-subject factors “sample position” and “match position” and the between-subject factors “group” were performed. To better understand the performance of neglect patients, we compared results of the individual patients with control groups in each of the task conditions individually, treating each of them as separate tasks and using single case statistics (Crawford et al., 2010) (that is, each of the results in the conditions sample left, sample right, match left, match right individually). For single case vs. controls comparisons, a modified t-test[4] (Crawford and Garthwaite, 2005) was applied. It compared differences between an individual’s scores on two conditions (e.g., sample placed left vs. sample placed right) to differences between scores under the same conditions observed in a control sample. This particular analysis was fit to detect possible contrasts in the performance of neglect patients, that result from lateralized deficiencies.

Interrupted fixations

Two related measures were used to analyze the eye fixation behavior: the total fraction of fixation interrupted and the frequency of involuntary saccades in each horizontal direction. Both data sets were not normally distributed, Shapiro Wilk tests for normal distribution of the data yielded significant results with *df* = 54 and $p < 0.0001$ in each of the data sets (total fraction of fixations interrupted and frequency of involuntary saccades in each of the horizontal directions).

The fraction of interrupted fixations was calculated as the total number of canceled trials due to sample-driven saccades divided by the total number of initiated trials (by the fixation spot onset). Comparisons between the groups were done using the Mann-Whitney U test. For comparisons of the single patient cases with the control groups we applied the bootstrapping method with 40000 resamples. While Crawford and Garthwaite’s test (Crawford et al., 2010) assumes a t-distribution, bootstrapping makes no prediction about the distribution of the data. The individual result of the neglect patient was compared with the 95-% confidence interval of the mean result computed in the control groups using 40000 resamples.

[4] Same as for the analysis of the spontaneous orientation.

For a more granular understanding of the fixation behavior, we computed the frequency of reflexive saccades in each horizontal (left and right) direction (the respective number of saccades in each condition divided by the total number of sample-driven saccades across all trials, alias the total number of fixations lost). Since the results were put in relation to the sample position, four conditions resulted from this computation (sample left: leftward and rightward saccades; sample right: leftward and rightward saccades). For differences in the percentage of fixation interruptions between each saccade direction (left vs. right), Wilcoxon signed ranked tests were computed in each group. For individual cases vs. group comparisons, the bootstrapping method with 40000 resamples was applied. In the control group, we computed confidence intervals for the differences in the frequency of involuntary saccades between two horizontal directions (f.i. left versus right). Results of neglect patients were put in relation to the 95% confidence interval of the mean difference in the control group (with 40000 resamples).

3. Results

3.1 Demographic and clinical data

A total of 69 subjects participated in the experiment. Four right-hemispheric stroke patients (of which one neglect patient) and one healthy elderly subject were unable to understand and/or perform the task and were thus excluded from the analysis. Their difficulties resulted either from cognitive impairments or lacking understanding of the technical setup. Another eight post-stroke patients were excluded, because they presented LH brain injuries, and were therefore not suitable as controls for our target subjects. Clinical and demographic data of all remaining subjects included in the current analysis are illustrated in Table 1 and the brain lesions of the included patients in Figure 6.

Table 1: Overview of the participants in the experiment.

	Controls				Neglect patients	
	Young healthy group	Elderly healthy group	RH stroke patients		HE	TE
			Acute	Chronic		
Total n=	25	21	4	4		
Age (years) mean (*SD*)	25.92 (3.214)	61.77 (6.53)	62.5 (6.13)	60.25 (7.5)	61	81
Sex (m/f)	7/18	10/11	4 m	3 m/ 1 f	f	m
Etiology (Ischemic/ Hemorrhagic)	-	-	I:4 /H:0	I:2 / H:2	Hemorrhagic	Ischemic
Time since stroke (days) mean (*SD*)	-	-	4 (2)	391.5 (18.7)	13	5
Visual field defect N present	-	-	0	0	no	no
Hemiparesis N present	-	-	3	3	yes	yes
Extinction N present	-	-	0	0	yes	no

Values are given in mean and *SD* values in the controls groups. I, Ischemic; H, Hemorrhagic; HE and TE represent pseudonyms of the two individual neglect patients.

Table 2: Detailed results of neglect testing in RH stroke patients.

Neglect PnP test	RH stroke controls	HE	TE
Letter cancellation task - CoC	0.016 (0.024)	0.031	0.33
Bells cancellation task - CoC	0.034 (0.029)	0.151	0.231
Line bisection deviation from center, %	0.259 (4.24)	28.19	5
Drawing task % omitted	4.69 (2.3)	37.5	37.5

Results of testing are given in mean and *SD* values for the control group of stroke patients. HE and TE represent pseudonyms of the two neglect patients.

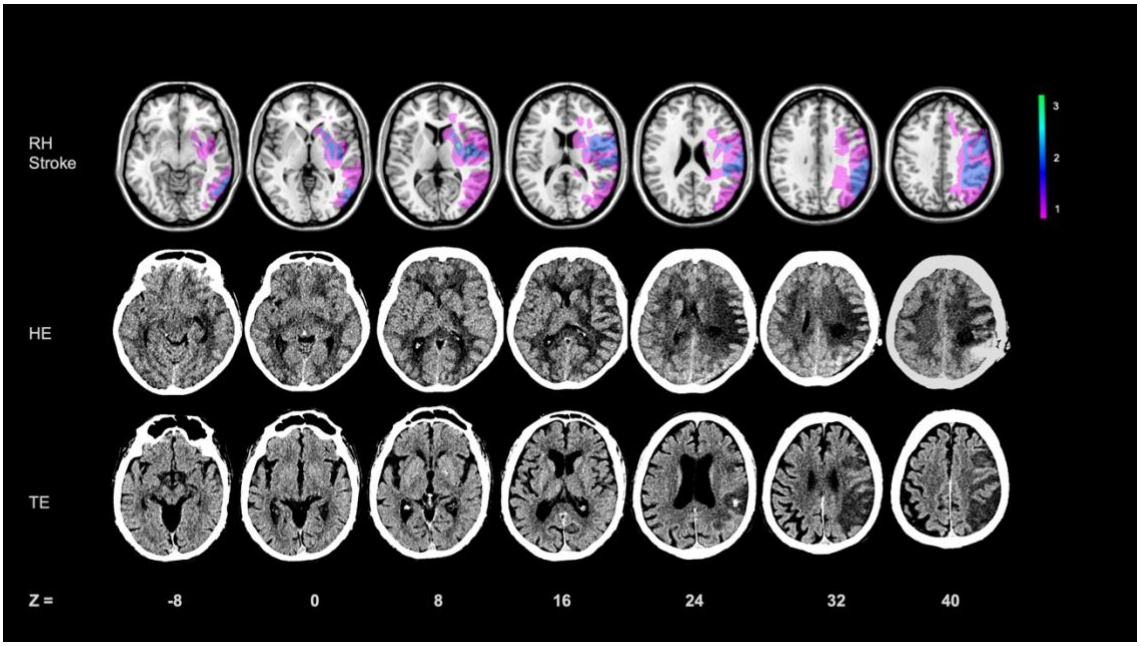


Figure 6: Simple lesion overlays of all RH stroke patients with and without spatial neglect.
RH Stroke: Simple overlay of the normalized lesions of the right-sided stroke patient group without neglect. Lesion boundaries were semi-automatically detected using the Clusterize algorithm on the SPM Clusterize toolbox (cf. (de Haan et al., 2015) on SPM 12 (www.fil.ion.ucl.ac.uk/spm). Normalization of CT or MR scans to MNI space with 1x1x1 mm resolution was performed by using the Clinical Toolbox (Rorden et al., 2012) under SPM12, and by using its age-specific MR or CT templates oriented in MNI space (Rorden et al., 2012). HE and TE: Original CT scans of the two right-sided stroke patients with spatial neglect. Numbers on the bottom indicate *Z*-coordinates in MNI space; the right in the presented images is the right hemisphere of the patients.

3.2 Preliminary observations

In the control groups, the total number of trials was 96. In the neglect single cases, the total number of trials varied due to the individual fitness level of the patients: HE accomplished a total of 87 trials in two runs; TE was able to complete only a single session of 38 trials. Results are given in percentages of the total. None of the neglect patients stated subjective differences in perception between the laterally (right or left) presented sample, nor in their search behavior on either of the (right or left) hemifields in the self-assessment questionnaire.

3.3 Exploration during trials

Figure 7 represents scan paths resulting from eye recordings, across all trials. In the control group exploration during the trial was roughly symmetrical, reaching 26° visual angle eccentricity to the most extreme horizontal points right and left of the screen. HE (Figure 7b) exhibited an overall restraint exploration behavior. Most importantly, the neglect patient inspected the two hemifields asymmetrically, frequently reaching 26° visual angle to the horizontal right of the screen, but rarely crossing the 18° mark to the left horizontal eccentricity. Nevertheless, the neglect patient HE was able to reach 24° to the left in three trials (out of 87).

The second neglect patient, TE, exposed the following exploration behavior during the trials: he systematically inspected up to 26° visual angle to the horizontal right while exhibiting a limited inspection of the left hemispace. On the left, he generally stayed within 14° visual angle from the center.

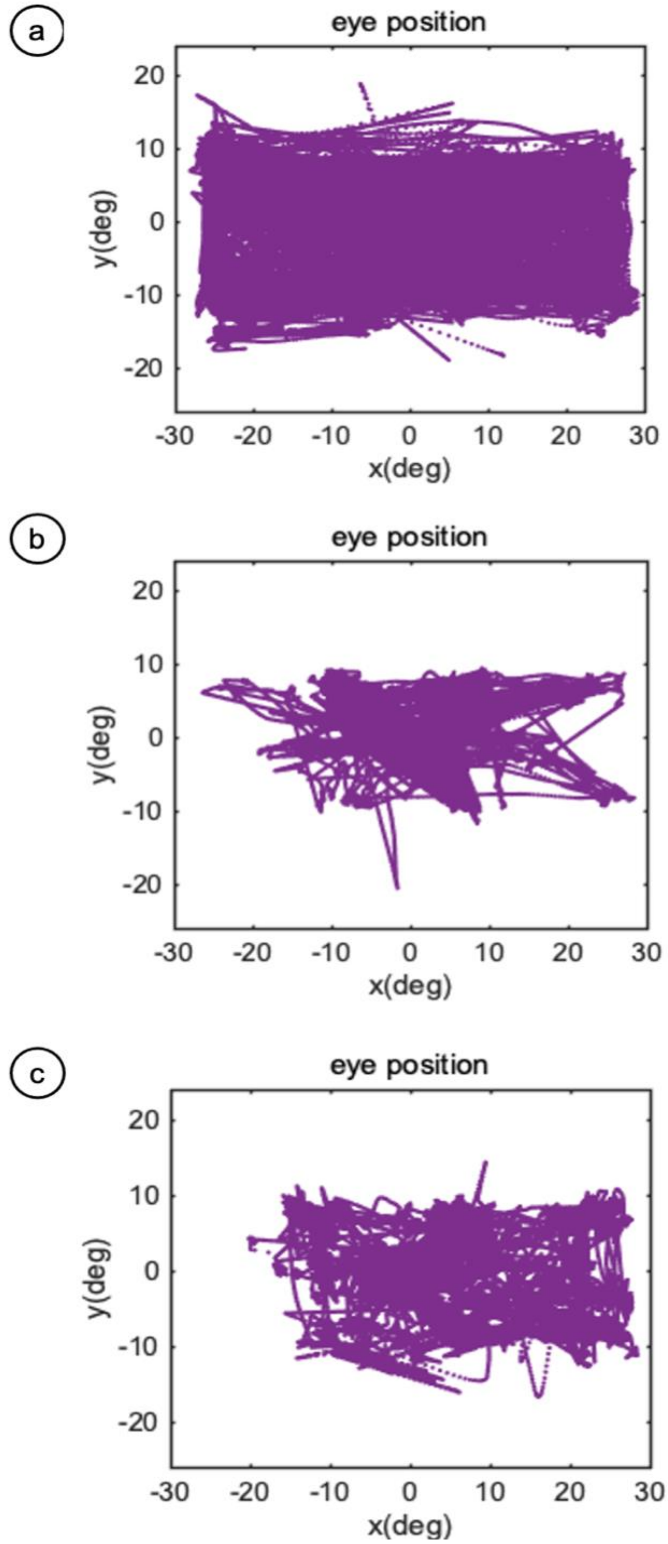


Figure 7: Scan paths across trials.

a) Controls b) Neglect patient HE c) Neglect patient TE.
Dotted lines represent eye movement traces across the presentation screen, each dot corresponding to an eye position recorded at the location for a bin of 1x1 visual degrees independently. Exploration patterns shown were computed across all completed trials.

3.4 Spontaneous orientation during inter-trial intervals

Young and elderly healthy controls

Both groups of healthy participants (young and elderly) explored the stimulus presentation area roughly symmetrically, mean results are specified in Table 3. No significant differences in the fractions of time spent exploring either of the hemifields were found between the two respective groups (left hemispace: $t = 0.708$, $p = 0.133$; right hemispace: $t = -0.705$, $p = 0.127$). Consequently, the groups of healthy young and elderly subjects were merged for further comparisons (n = 46).

RH stroke patients: acute and chronic

No significant differences in the fraction of time spent exploring either of the hemifields were found between the two groups of post-stroke patients without neglect, acute and chronic (left: $t = -0.549$, $p = 0.603$; right: $t = 0.549$, $p = 0.603$). The two groups were merged for further analysis.

Healthy participants vs. RH stroke patients

Mean results for the exploration of the stimulus presentation area in the merged RH stroke group are listed in Table 3. No significant differences in the fraction of time spent exploring either of the hemifields were found between the groups of healthy participants (young and elderly merged) and RH stroke participants (acute and chronic merged) (left hemispace: $t = -1.140$, $p = 0.343$; right hemispace: $t = 1.132$, $p = 0.345$). Since no difference in performance was found, the two groups (healthy and RH stroke participants) were summed into a big control group for further comparisons (n = 54).

Spontaneous gaze in neglect

Figure 8 exhibits the fraction of total time spent gazing towards each of the two hemifields in controls and the two neglect patients. The control group of 54 subjects exposed, on average, the following behavior: they inspected the stimulus presentation area roughly symmetrically, spending on average half of the time in each hemispace, exact values are given in Table 3.

HE, one of the neglect patients exhibited significant divergence between the amounts of time spent gazing towards each of the hemispaces, preferring the right hemispace to the left. This temporal difference was significant when compared to the same value in the control group ($t = 21.437$, df = 53, p(one-tailed) < 0.000).

TE, likewise, had a strong preference for the right hemifield in his spontaneous gaze orientation. The resulting difference in his gaze distribution between the two hemifields was significant when compared to the control group ($t = 38.911$, $df = 53$, p(one-tailed) < 0.0001).

The estimated percentage of the control population exhibiting a difference more extreme than the individual neglect patients HE and TE was equal to 0.

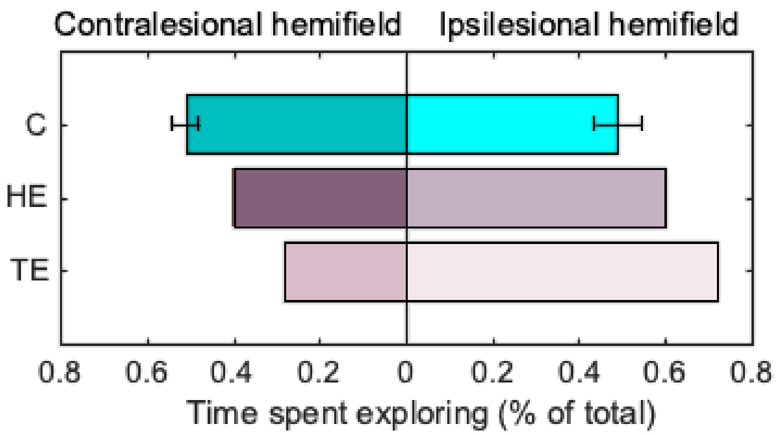


Figure 8: Fraction of total time spent exploring the hemifields of the stimulus presentation area across all inter-trial intervals.
In the control group, horizontal bars represent mean values, error bars represent *SD* values. C, merged control group of healthy participants and stroke patients without neglect. HE and TE, individual neglect patients.

Table 3: Means and SD values of the total exploration time.

	Left Hemifield		Right Hemifield	
Group	Mean	SD	Mean	SD
Y	0.5127	0.07675	0.4871	0.07681
E	0.4983	0.01249	0.5014	0.05717
H	0.5061	0.06820	0.4937	0.06819
RH stroke	0.5350	0.05043	0.4650	0.05043
C	0.5115	0.06660	0.4883	0.06658
HE	0.40		0.6	
TE	0.28		0.72	

The values given were computed across all inter-trial intervals for each of the groups of participants in the experiment and grouped by hemifields. Y, young healthy subjects; E, elderly healthy subjects; H, merged group of healthy young and elderly participants (n = 46); RH stroke, merged group of acute and chronic stroke patients (n = 8); C, all controls (n = 54), HE and TE, the individual neglect patients.

3.5 Success rates

Young and elderly healthy controls

The two groups of healthy participants, young and elderly, achieved similar average success rates regardless of the sample or match position. The respective means of their results are presented in Table 4.

The main effect of sample position on the average success rates was not significant ($F(1,44) = 0.075$, $p = 0.785$, *partial* $\eta^2 = 0.002$). No significant interaction effect between group and sample position was found ($F(1,44) = 0.387$, $p = 0.537$, *partial* $\eta^2 = 0.009$). The main effect of group (young/elderly) on the average success rate (coupled to sample position) was not significant ($F(1,44) = 0.005$, $p = 0.942$, *partial* $\eta^2 = 0$).

The main effect of match position on the success rate was not significant ($F(1,44) = 0.215$, $p = 0.645$, *partial* $\eta^2 = 0.005$). No significant interaction effect between group and match position was found ($F(1,44) = 0.007$, $p = 0.933$, *partial* $\eta^2 = 0$). The between-subjects effect was not significant ($F(1,44) = 0.024$, $p = 0.879$, *partial* $\eta^2 = 0.001$). For further comparisons, the two groups of healthy individuals, young and elderly, were merged into a single control group.

RH stroke patients: acute and chronic

Statistical tests were performed to assess existent differences in performance between patients with acute brain damage and those with longer-lasting injuries to the right cerebral hemisphere. Results are presented as follows:

The main effect of sample position on the average success rate was not significant ($F(1,6) = 2.189$, p = 0.189, *partial* $\eta^2 = 0.267$). No significant interaction effect between group and sample position was found ($F(1,6) = 2.189$, $p = 0.189$, *partial* $\eta^2 = 0.267$). The main effect of group (acute or chronic brain injury) on the average success rate was not statistically significant ($F(1,6) = 2.430$, $p = 0.170$, *partial* $\eta^2 = 0.288$).

The main effect of match position on the average success rate was not significant ($F(1,6) = 0.486$, $p = 0.512$, *partial* $\eta^2 = 0.075$). No significant interaction effect between group and match position was found ($F(1,6) = 0.018$, $p = 0.897$, *partial* $\eta^2 = 0.003$). The main effect of group (acute or chronic brain injury) on the average success rate was not

statistically significant ($F(1,6) = 2.407$, $p = 0.172$, *partial* $\eta^2 = 0.286$).
The two groups of subjects with acute and chronic brain damage were merged into a single group of right-hemispheric stroke patients for further comparisons.

RH stroke patients vs. healthy controls

Patients with right-hemispheric injuries consistently achieved lower success rates than controls regardless of the sample or match presentation condition. Mean results are presented in Table 4. This observation was confirmed by the following statistical analysis:

The main effect of sample position on the average success rate was not significant ($F(1,52) = 1.398$, $p = 0.242$, *partial* $\eta^2 = 0.26$). No significant interaction effect between group and sample position was found ($F(1,52) = 1.833$, $p = 0.182$, *partial* $\eta^2 = 0.034$). The main effect of group (healthy or stroke) on the average success rate (related to sample position) was statistically significant ($F(1,52) = 10.018$, $p = 0.003$, *partial* $\eta^2 = 0.162$).

The main effect of match position on the success rate was not significant ($F(1,52) = 0.363$, $p = 0.549$, *partial* $\eta^2 = 0.007$). No significant group*match position interaction effect was found ($F(1,52) = 0.908$, $p = 0.345$, *partial* $\eta^2 = 0.017$). The main effect of group on the average success rate (coupled to match position) was statistically significant ($F(1,52) = 10.203$, $p = 0.002$, *partial* $\eta^2 = 0.164$).

Neglect single cases

Since RH control patients exhibited significantly lower success rates than the group of healthy (young and elderly) subjects, each of the two control groups was separately compared to the single cases, HE and TE. Results are presented below (cf Figure 9).

Neglect vs. healthy controls

Comparisons of results of the neglect patient and healthy controls in each sample and match presentation condition

Regardless of sample or match position, each of the neglect patients achieved significantly lower success rates than controls (Sample right: HE vs healthy participants: $t = -4.674$, $p = 0.00001$, TE vs healthy participants: $t = -4.130$, $p = 0.00008$; Sample left: HE vs healthy participants: $t = -3.801$, $p = 0.00022$, TE vs healthy participants: $t = -$

4.280, $p = 0.00005$; Match right, HE vs. healthy participants: $t = 3.058$, $p = 0.00187$, TE vs healthy participants: $t = -1.959$, $p = 0.02814$; Match left, HE vs healthy participants: $t = -5.319$, $p < 0.00001$, TE vs healthy participants: $t = -5.517$, $p < 0.00001$).

Divergence of success rates related to sample position

HE's performance in the S2S task was not influenced by the sample position. No significant difference in success rates related to sample position was found when compared to the control group of healthy subjects ($t = 0.836$, $df = 45$, p(two-tailed) = 0.4077). Statistically, the percentage of the control population exhibiting a difference more extreme than the individual was estimated to be 20%.

TE, the other neglect patient, exhibited similar results. No significant divergence was found between the two scores when compared to the same difference in the group of healthy controls ($t = 0.143$, $df = 45$, p(two-tailed) = 0.887). The estimated percentage of healthy controls expected to exhibit a difference more extreme than the individual was 44.35%.

Divergence of success rates related to match position

The difference between the two scores (match right vs. match left) of HE was significant when compared to the same difference in the healthy control group ($t = 2.382$, $df = 45$, p(one-tailed) = 0.01074). Only 1% of the general (healthy) population was expected to acquire a difference in performance between the two conditions more extreme than HE.

Neglect patient TE achieved a significantly higher hit rate in the trials with the match on the right, compared to trials with the match on the left, the divergence between the two scores was significantly higher than the same difference in the healthy control group ($t = 3.782$, $df = 45$, p(one-tailed) = 0.00023). Only 0.02% of the general population was expected to achieve a more extreme difference in performance in the S2S task related to match position.

Neglect vs. RH stroke patients without neglect

Comparisons of success rates between individual neglect patients and patients with right-hemispherical injuries without neglect in each sample and match presentation condition

Compared to right-hemispheric stroke patients (n = 8), neglect patient HE achieved significantly lower success rates in all sample and match presentation conditions (Sample right: $t = -3.116$, $p = 0.00847$; Sample left: $t = -3.488$, $p = 0.00508$; Match right: $t = -2.375$, $p = 0.02464$; Match left: $t = -3.850$, $p = 0.00315$).

Comparisons of success rates of TE yielded significantly lower success rates in both sample presentation conditions (Sample right: $t = -2.559$, $p = 0.01880$; Sample left: $t = -4.031$, $p = 0.00249$). The same patient had a significantly lower success rate when compared to RH stroke patients without neglect when the match was to be found left ($t = -4.032$, $p = 0.00249$) but exhibited similar results to the control group of right-hemispheric stroke patients without neglect when the match was presented on the right ($t = -1.112$, $p = 0.15138$).

Divergence of success rates in relation to sample position

HE exhibited no significant dissociation in success rates related to sample position when compared to the group of RH stroke patients without neglect ($t = 0.301$, $df = 7$, $p = 0.77118$). Out of the right-hemispheric stroke population, 38.6% of individuals are expected to exhibit a difference more extreme than this particular neglect patient.

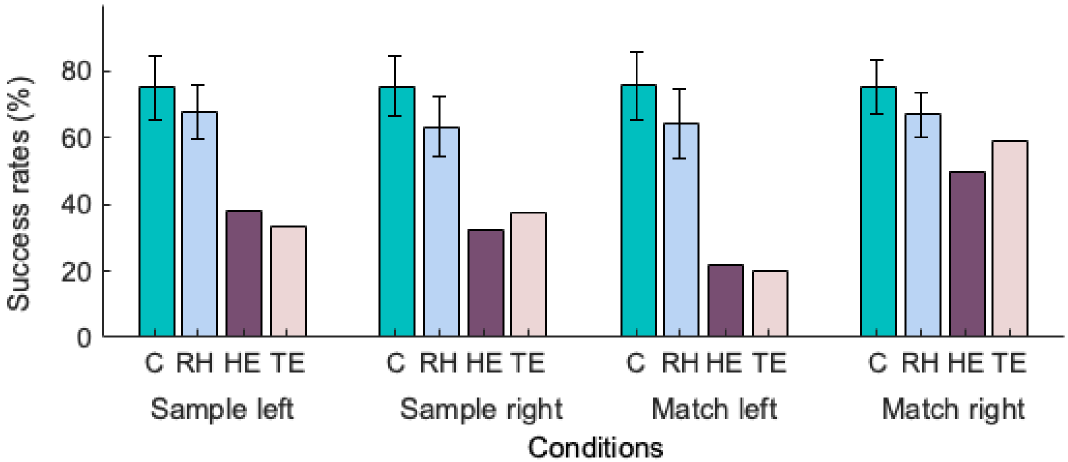
When compared to right-hemispheric stroke patients, TE did not exhibit a significant dissociation in success rates related to sample position ($t = 1.148$, $df = 7$, $p = 0.29$). The percentage of right-hemispheric stroke patients exhibiting a difference more extreme than this particular subject was estimated to 14.41%.

Divergence of success rates in relation to match position

Compared to the difference in success rates related to the match position in RH stroke controls, the dissociation observed in HE's result was not significant ($t = 1.219$, df = 7, p(one-tailed) = 0.13). Thirteen percent of right-hemispheric stroke patients were expected to achieve an even higher difference in performance related to the match position than this particular neglect patient.

TE's performance in the S2S test was significantly influenced by the match position, a difference that was not observed in the control group of subjects with right-hemispheric injuries but without neglect (t = 2.376, df = 7, p(one-tailed) = 0.025). Only 2.45% of the right-hemispheric post-stroke patients are expected to show a difference in performance related to match position more extreme than this particular patient.

Figure 9: Success rates, grouped by left and right sample and match positions.
Bar charts represent computed mean values in the control groups of healthy participants (C) and RH stroke patients (RH), error bars represent *SD* values. C, control group of healthy young and elderly individuals;



RH, patients with right-hemispheric strokes but without neglect; HE and TE, individual neglect patients.

Table 4: Mean and *SD* of the success rates of all participants.

group	sample	Mean	*SD*	match	Mean	*SD*
E	R	0.7599	0.07586	R	0.7520	0.06720
	L	0.7470	0.08922	L	0.7589	0.10386
Y	R	0.7492	0.10303	R	0.7493	0.09245
	L	0.7509	0.09653	L	0.7542	0.09827
H	R	0.7541	0.09082	R	0.7505	0.08104
	L	0.7509	0.09653	L	0.7563	0.09975
RH stroke	R	0.6328	0.09313	R	0.6693	0.06722
	L	0.6797	0.08102	L	0.6434	0.10368
HE	R	0.325	-	R	0.5	-
	L	0.38	-	L	0.22	-
TE	R	0.3750	-	R	0.59	-
	L	0.3333	-	L	0.2	-

The computed values are given for each, right (R) and left (L) presentation condition. E, control group of elderly healthy subjects; Y, control group of young healthy subjects; H, merged group of healthy young and elderly participants; RH stroke, control group of patients with right hemispheric stroke but without neglect; HE and TE, individual neglect participants.

3.6 Interrupted fixations

Percentage of lost fixations across all trials

The fraction of lost fixations was computed by dividing the number of interrupted trials by the total number of initiated trials. Table 5 shows the percentage of lost fixations in each of the tested groups, with the respective median, minimum, maximum, and standard deviation values (non-parametric data).

Table 5: Percentage of interrupted fixations out of the total initiated trials.

	Values in %	Median	SD	Min.	Max.
Y	-	6.7961	5.26080	0	20.66
E	-	9.90	12.18184	1.03	44.83
RH	-	21.2639	18.50696	7.69	67.79
HE	0.785				
TE	0.857				

Data (non-parametric) is given in median, minimum, maximum, and *SD* values in control groups; individual values are given for the two single neglect patients. Y, control group of young healthy subjects; E, control group of elderly healthy subjects; RH, control group of patients with right hemispheric stroke but without neglect; HE and TE, individual neglect participants.

Young vs. elderly healthy controls

In general, the group of elderly healthy participants interrupted fixations more frequently than the young subjects (*Mann-Whitney* $U = 167.000$, $Z = -2.107$, $p = 0.035$).

RH stroke patients: acute and chronic

The two groups of right hemispheric injured patients, acute and chronic, exhibited no significant difference in their fixation behavior, statistical comparison between the groups yielded the following results: *Mann-Whitney* $U = 6$, $Z = -0.577$, p(2-tailed) = 0.564. The two groups were merged together for further comparisons.

Healthy elderly participants vs. RH stroke patients

The group of patients with right-hemispheric stroke interrupted fixations significantly more frequently than the group of healthy young participants (*Mann-Whitney* $U = 16.500$, $Z = -3.509$, p(two-tailed) < 0.001).

Compared to elderly healthy participants, right-hemispheric stroke patients interrupted fixations significantly more frequently as well. Statistical testing yielded the following results: *Mann-Whitney* $U = 39$, $Z = -2.196$, p(2-tailed) = 0.028.

Percentage of fixations loss in neglect: two single cases

Figure 10 exhibits the fraction of lost fixations in each of the tested groups and individual neglect cases.

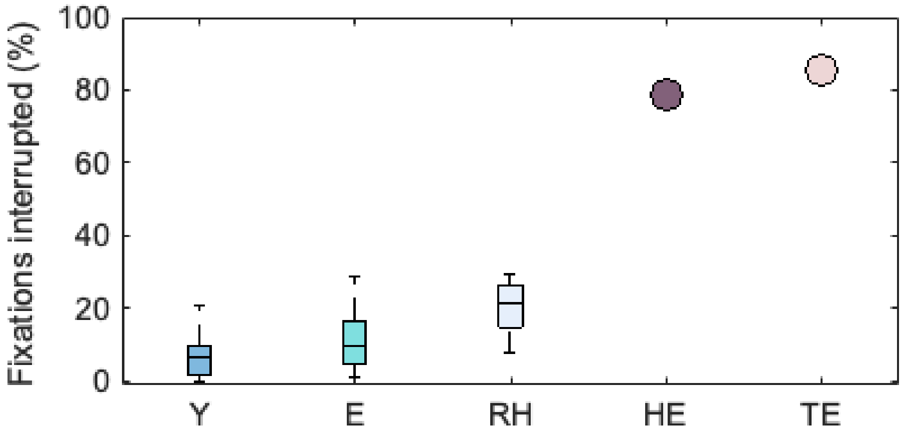


Figure 10: Fraction of lost fixations in each of the tested groups and individual neglect patients. Box plots represent median, minimum and maximum values of the non-parametric data for each of the control groups. Data of individual neglect patients are represented as single points. Y, young healthy subjects; E, elderly healthy subjects; RH, right-hemispheric stroke patients; HE and TE, neglect patients.

Each of the neglect patients interrupted a significantly higher amount of fixations than any of the control groups. HE failed to maintain fixation in ca. 78.5% of the trials, while TE lost fixation in 85.7% of the trials. Each of the neglect patients' results are clearly outside of the 95.0%-confidence interval for the same variable (fraction of lost fixations) in the group of young healthy participants (4.727 – 8.763), of the elderly healthy participants (8.7036 – 18.794) and of the right hemispheric injured subjects without neglect (15.5516 – 38.5836), based on bootstrapping the mean value for each of the groups using 40000 resamples.

Differences in the saccadic directions leading to fixation loss

Table 6 shows frequencies of saccades in the two horizontal directions (left and right), coupled to the sample presentation condition for all tested groups and neglect patient cases. The results of the Wilcoxon signed-rank test for comparisons between the fraction of saccades performed in each horizontal direction under each sample presentation conditions and each group are presented in Table 7.

Table 6: Interrupted fixations.

	Values in %	Conditions Sample left Saccade left	Sample left Saccade right	Sample right Saccade left	Sample right Saccade right
Y	Median	9.0909	12.5	28.5714	20
	SD	23.60670	19.75265	24.10396	23.90499
	Min	0	0	0	0
	Max	100	80	100	70
E	Median	15.6875	17.6470	37.5	20
	SD	17.27199	24.17884	26.78692	18.32157
	Min	0	0	0	0
	Max	66,67	100	100	60
RH	Median	20	32.3910	22.8448	24.4643
	SD	11.20661	14.13842	9.09345	13.57454
	Min	6.67	15	7.14	0
	Max	39.13	57.14	33.33	44.83
HE		19.5	8.18	12.26	60.06
TE		25.44	3.07	6.58	64.91

Variables in the table include median, minimum, maximum, and *SD* values in the control groups. Data given for each control group and individual neglect patients were grouped by sample position and saccade direction, resulting in congruent and incongruent conditions (towards and against the sample position). Y, control group of young healthy participants; E, control group of elderly healthy participants; RH, control group of patients with right hemispheric stroke but without neglect; HE and TE, individual neglect patients.

Young and elderly controls

Saccades were similarly frequent in both horizontal directions (left and right), regardless of the sample presentation position in both groups of healthy participants, young and elderly (Young: sample left: $Z = -0.024$, p(two-tailed) = 0.981; sample right: $Z = -0.871$, p(two-tailed) = 0.384; Elderly: sample left: $Z = -0.710$, p(two-tailed) = 0.478; sample right: $Z = -1.871$, p(two-tailed) = 0.061).

RH stroke patients: acute and chronic

Acute RH stroke patients performed saccades similarly frequently in each of the horizontal directions for both sample presentation positions (sample left: $Z = -1.604$, p (two-tailed) = 0.109; sample right: $Z = -0.730$, p(two-tailed) = 0.465).

No statistically significant difference in the frequencies of saccades in the two horizontal directions were found in the group of chronic RH stroke patients (sample left: $Z = -0.365$, p(two-tailed) = 0.715; sample right: $Z = -0.535$, p(two-tailed) = 0.593).

All RH stroke patients (acute and chronic) were merged into one single group of RH brain-damaged subjects for further comparisons.

Table 7: Results of Wilcoxon signed rank test for comparisons of saccade frequencies in each of the horizontal directions in the control groups.

Group		Conditions Sample left saccade right – Sample left saccade left	Sample right saccade right – sample right saccade left
Y	*Z*	- 0.024	- 0.871
	p(2-tailed)	0.981	0.384
E	*Z*	- 0.710	- 1.871
	p(2-tailed)	0.478	0.061
RH	*Z*	- 1.680	- 0.085
	p(2-tailed)	0.093	0.933

Y, young healthy subjects; E, control group of elderly healthy participants; RH, control group of stroke patients without neglect.

Dissociations between saccadic frequencies related to sample position in neglect

Subjects of the control groups (healthy young and elderly participants as well as right-hemispheric stroke patients without neglect) rarely interrupted fixations and if they did so, no relation between saccade direction and the position of the sample was detected. For the following comparisons with the single neglect patients, the data thus were merged into a single control group (n = 54) (Fig. 11).

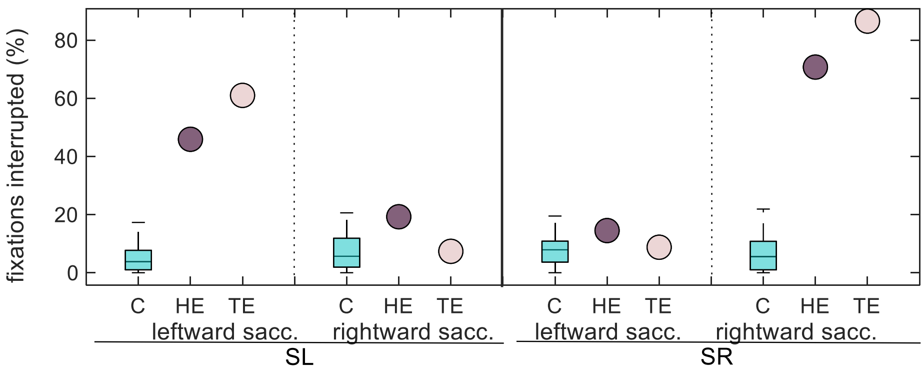


Figure 11: Percentage of interrupted fixations, grouped by the direction of the reflexive saccades. Values were computed for each sample presentation condition: SL, sample presented left and SR, sample presented right. Box plots represent median, minimum and maximum values for each of the control groups, individual data points are given for each of the neglect patients. C, merged control group; HE and TE, individual neglect patients.

Figure 11 shows the frequency of horizontal saccades leading to fixation loss in each of the sample presentation conditions. Both neglect patients performed reflexive saccades toward the sample more frequently than in the inverse direction; this behavior was especially stringent when the sample was presented on the right of the fixation spot. Results are presented in more detail below.

Sample left

In trials with the sample presented on the left, HE performed 11.32% additional leftward saccades, compared to saccades towards the right. TE exhibited an even more extreme result, with an additional 22.37% of leftward eye movements, compared to rightward ones. Both results are outside of the 95.0 %- confidence interval of the same average difference in the control group based on bootstrapping with 40000 resamples (- 12.2815 - 3.68).

Sample right

In trials with the sample placed on the right, HE performed additional 47.8% saccades to the right, compared to the percentage of leftward saccades; for TE the same difference was 58.33%. The 95.0%- confidence interval for the same difference (percentage of rightward saccades – the percentage of leftward saccades) in the merged the control group ranged from - 17.9369 to - 0.2147, based on bootstrapping with 40000 resamples.

Rightward sample-driven saccades in neglect

To investigate whether or not sample-driven saccades to the right were significantly more frequent than sample-driven leftward eye movements, we computed differences between the fraction of saccades in each sample-congruent condition (fraction of rightward sample-driven saccades – fraction of leftward sample-driven saccades). Each of the neglect patients performed roughly 40% (for HE: 40.56%, for TE: 39.47%) of saccades more by performing rightward than leftward sample-driven saccades. In the merged control group, the 95% confidence interval for the same difference ranged from - 4.2933 to 11.9906 based on bootstrapping with 40000 resamples.

4. Discussion

Neglect patients exhibit stereotypical behavior in pencil-and-paper tests, consistently missing targets presented on the left/contralateral side and/or marking the midline of horizontal lines further to the right than individuals without neglect. Their exploratory eye movements consistently show an orientation bias to the right, ipsilateral space. These aspects of pathological behavior can be interpreted both in light of disturbed processing of sensory information, but can equally result from inadequate spatial mapping or directional planning of eye and/or hand movements. In order to disentangle these possible mechanisms, we designed a novel experimental task, presenting important methodological advances compared to previous procedures used in the literature. The present task requires a complex oculomotor search and selection response, after covertly attending to a lateralized stimulus. Consequently, it links the presumably neglected object with the identical match directly, avoiding unclear responses. Apart from that, it includes the control of eye movements, allowing unambiguous interpretations. An important feature of the current design is its applicability both in human and non-human primates, facilitating potential future inter-species experimental investigations.

4.1 Implicit processing of contralesional stimuli

Both neglect patients in the present study exhibited no difference in performance between the left and right sample presentation conditions. Nevertheless, given the low success rates (of 33% or 38%) in the S2S task one might conclude that these patients chose their targets rather by chance. Since the sample was only briefly flashed on the neglected side, how can one be sure that the patient perceived it and knew what particular target to look for in the adjacent exploration period? Hints are provided by the thorough analysis of the exploration and selection behavior. When followed trial-by-trial neglect patients exhibit a clearly intentional choice: when these patients are confronted with different objects they consistently abandon the incorrect one and even return to the appropriate match. Figure 12 demonstrates examples of search and target selection of neglect patients during trials where the sample was found on the left: Figures 12a and b exhibit the process of choosing the correct match, when the patient went back in forth between the two options. Figure 12d shows the exploration pattern of a neglect patient who, while s/he clearly did not find the match in his back-and-forth search between the two objects he discovered (lower corner right and center-left), leading to repeated inspections of the two objects, still did not orient his gaze to the left, where the third and correct target (match) was hidden. Thus, the inability to search further in the leftward direction might explain why neglect patients exhibit a much lower success rate when the match is placed left. Figure 12e and f demonstrate how easily and non-problematic are neglect patients able to find targets on the right side of the screen, discriminating even between the most difficult distractors and the correct match. In each of the cases, the sample was presented left. These examples speak for a clear perception of the contralesionally presented figure.

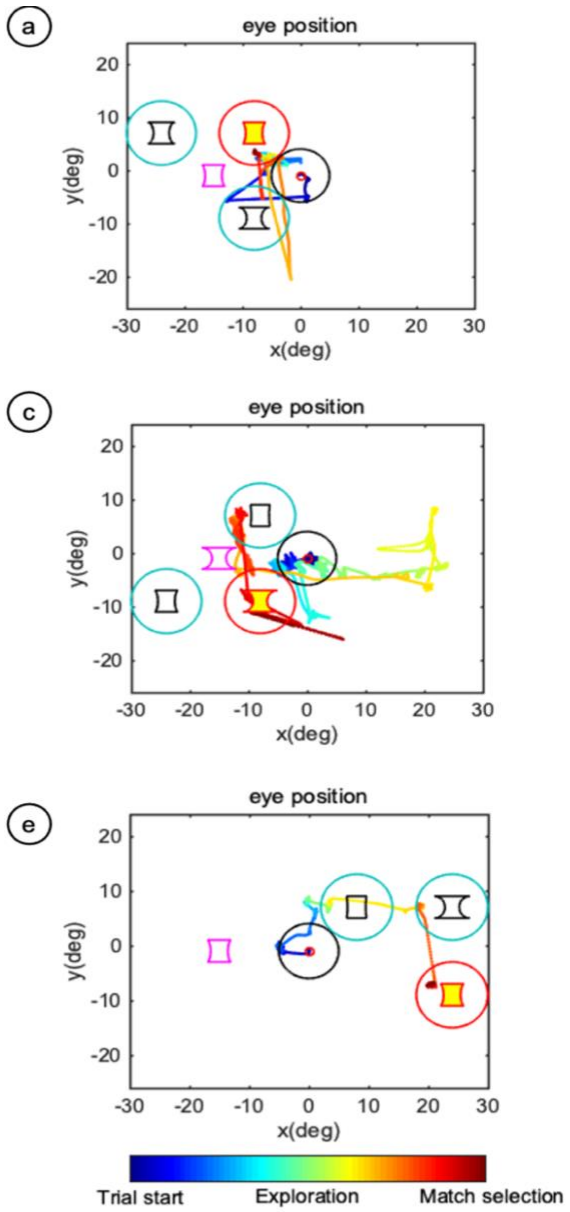


Figure 12: Examples of trials with the sample placed left in neglect patients.
The dotted colored line represents the trajectory of the eyes across the screen, colors (see legend of color gradient) correspond to stages of exploration in the trial: dark blue for the start and dark red for the end of exploration, colors in between represent adjacent stages in exploration. The presented symbols are to be read as follows:

a) both inspected targets are found on the central left, at 8° visual angle from the center, the patient TE inspected the distractor first (blue line), discovered the match but returned to the previous figure for comparison and finally selected the correct target (red circle). b) TE started by inspecting a distractor (blue line), explored to the upper right corner (match), returned to the previously inspected object (green line), and finally decided to select the correct match in the upper right corner of the screen c) initial rightward search behavior (blue, green, and yellow line) of neglect patient HE, despite the lack of placeholders that can bias attention to the right; the patient was still able to return to the left, inspect the targets and choose the correct match.

We thus can infer that perception of the contralateral sample was preserved at least at the shape discrimination level. Such implicit categorical processing of contralesional stimuli was previously demonstrated in neglect/extinction for lexical contents (Ladavas et al., 1993; D'Esposito et al., 1993; Berti et al., 1994; McGlinchey-berroth et al., 1993; Ladavas et al., 1997a; Ladavas et al., 1997b), faces (Vuilleumier et al., 2002), line drawings, figures, or color photographs (Vallar G., 1994; Berti and Rizzolatti, 1992; Doricchi and Galati, 2000; Audet et al., 1991; Volpe et al., 1979; Karnath, 1988; Karnath and Hartje, 1987; Marshall and Halligan, 1988; Esterman et al., 2002), and numbers (Sackur et al., 2008; Rusconi et al., 2006).

At the same time, the methodological approaches in some of the antecedent studies can be questioned. For instance, some experiments asked the participants to perform same-different judgments in bilateral-stimulation settings (Vallar G., 1994; Volpe et al., 1979; Karnath and Hartje, 1987; Karnath, 1988). Rusconi and colleagues have shown that the identification of the contralateral object might be facilitated by the presence of a semantically identical stimulus on the ipsilateral side (Rusconi et al., 2006). When asked to trace the contours of line drawings, neglect patients ignored contralesional details or even entire halves of images and acted as if being confronted with a single object, reconstructed from the right (Bisiach and Rusconi, 1990). Thus, it can’t be excluded that under bilateral stimulation the patient only processes the ipsilateral object and extrapolates from it.

Another strategy, asking patients indirect questions regarding the stimuli(Marshall and Halligan, 1988), is not ideal, since the answers provide no exact measurement of the implicit processing. Bisiach and colleagues (1990) provided convincing results speaking against this procedure. In their attempt of replicating the study of Marshall and Halligan (1988), some patients preferred the burning house, arguing it was “more spacious” and one patient refused to make a choice, reporting no difference between the pictures (Bisiach and Rusconi, 1990). A possible reason is that neglect patients are unable to offer reliable responses about the presence or lack of information on the contralesional side, processing of such stimuli can only be inferred from their behavior (Deouell, 2002; Ladavas et al., 1993).

Our novel experimental design provides clear evidence of perceptual processing of the neglected field. Implicit awareness of contralesional stimuli most likely reflects the intact main visual areas and their neural projections via the ventral visual pathway into the inferior temporal lobe, involved in object identification. Evidence suggests that extinguished stimuli excite the sensory cortices, yet to a lesser degree than the conscious experience of them does (for review see (Deouell, 2002)). More precisely, fMRI and event-related brain potential (ERP) studies of visual extinction in patients with right parietal injury have shown that disregarded visual items in such patients could nevertheless stimulate area V1, striate, extrastriate, and fusiform regions in the injured right hemisphere and demonstrated some intact ERP components (Rees et al., 2000; Driver and Vuilleumier, 2001; Vuilleumier et al., 2001). At the same time emotional stimuli activate the amygdala and orbitofrontal cortex even under lack of awareness (Vuilleumier et al., 2002). Nevertheless, this activation is mostly weaker and noisier than for aware stimuli (Mudrik and Deouell, 2022). Mere processing within the sensory cortices does not suffice for explicit awareness. Instead, it has been proposed that encoding of sensory information in spatial coordinates might constitute the *sine qua non* for explicit awareness (Deouell, 2002; Vuilleumier et al., 2001; Berti et al., 1992).

As mentioned in the introductory chapter of this dissertation, visual information might be processed in two neural networks in the brain: a "dorsal" stream coding the position in space and a "ventral" one, for shape, orientation, and size of an object (Goodale and Milner, 1992; Goodale, 2011). On the functional level, a helpful framework for the interaction of these two neural circuits is the Feature Integration Theory (FIT) (Treisman and Gelade, 1980). It postulates that individual features of an object can be processed pre-attentively and independently of their location but are bound together through spatial attention (Treisman and Gelade, 1980; Cohen et al., 2012; Lamme, 2003; Reynolds and Desimone, 1999). Thus, awareness of an object only becomes possible in the neural integration of the two aforementioned visual processing streams.

In the past, parallels have been drawn between neglect and the phenomenon of "inattentional blindness" in healthy individuals (Humphreys, 2000; Rafal, 1998). Some studies demonstrated, for instance, that healthy subjects can remain unaware of obvious stimuli when attention is engaged elsewhere (Simons and Chabris, 1999; Mack and Rock, 1998; Most et al., 2001). In a seminal experiment, participants were asked to observe various video versions of two teams passing a basketball to each other and count the aerial passes. At some point during the task, a person wearing an umbrella or a gorilla costume walked through the scene for 5 seconds. When, at the end of the experiment, the participants were asked if they had seen anything out of ordinary, 46% of the respondents did not notice this unexpected event (Simons and Chabris, 1999). Such implicit processing in the healthy population has also been shown to correspond to neural activity related to the segregation of stimuli from their backgrounds, analogous to implicit sensory processing in neglect ((Moore and Egeth, 1997; Scholte et al., 2008; Rafal, 1998), for review, see (Nobre et al., 2020)). As we will outline in the following paragraph, results from the current study provide support for the view that the attention of neglect patients is strongly captured by ipsilateral objects, providing more support for this analogy.

4.2 Oculomotor capture by ipsilesional stimuli

Both neglect patients in the present study were unable to resist performing reflexive saccades, especially to ipsilesional samples, even when instructed to maintain fixation and verbally urged to do so. This result supports the hypothesis that one of the central symptoms of spatial neglect is a spontaneous orienting of attention toward the half-space ipsilateral to the lesion (Karnath, 1988). In this early investigation of "attentional capture", neglect patients were asked to name visual stimuli presented simultaneously both to the right and the left visual hemifields. If a free choice of order was given, all patients consistently named the stimuli presented on the ipsilesional right first. This stereotypical covert orientation of attention to the ipsilesional field and the "attentional capture" of suddenly appearing stimuli on that side was identified as one of the core components of neglect (Karnath, 1988). Evidence of the early orientation in neglect has been provided in several studies since (for instance (Pflugshaupt et al., 2004; Mattingley et al., 1994; Azouvi et al., 2006; Toba et al., 2018; Bartolomeo and Chokron, 2002)). Direct clinical observations of reflexive eye movements towards the ipsilesional side in neglect patients have been reported by Gainotti et al (1991). They used the classical neurological confrontation technique to assess the visual field and observed automatic saccades toward the side ipsilateral to the lesion, as soon as the arms of the examiner were outstretched and before the administration of the stimuli. Few recent studies provided eye-tracking evidence for the ipsilateral oculomotor capture in neglect (Bourgeois et al., 2015; Van der Stigchel and Nijboer, 2010).

“Oculomotor capture” might precede the later “disengagement” difficulty from ipsilesional stimuli (Posner, 1987; Gainotti et al., 1991; Ptak and Fellrath, 2013; Bartolomeo and Chokron, 2002; Pflugshaupt et al., 2004). This direction-specific deficit in reorienting attention into the contralateral direction was identified by Karnath (1988) as another core component of neglect. Posner-like spatial cue experiments (Posner et al., 1987) have since repeatedly shown that, when attention is cued to the right in an invalid condition, neglect patients are slower to detect stimuli on the left (D'Erme et al., 1992; Morrow and Ratcliff, 1988). The “disengagement deficit” might explain why neglect symptoms can improve if visual stimulation from the right side is reduced (Mark et al., 1988; Chokron et al., 2004; Wojciulik et al., 2004; Toba et al., 2018).

In healthy individuals oculomotor capture can be induced by highly salient stimuli such as abrupt onsets, color singletons, moving objects, and others, shown to attract attention automatically (Yantis and Nakama, 1998; Yantis and Jonides, 1984; Schreij et al., 2008; Abrams and Christ, 2003; Theeuwes, 2010; Yantis and Jonides, 1990; Adamo et al., 2010). While attentional selection for salient stimuli occurs early in the visual processing (Itti and Koch, 2001; Treisman and Gelade, 1980; Theeuwes, 2010), subjects in the normal population can learn to resist attentional capture through a process of habituation (Gaspelin and Luck, 2018; Gaspelin and Luck, 2019; Vatterott and Vecera, 2012; Luck et al., 2021). In contrast to fast reflexive selection (bottom-up), top-down intentional selection gains traction later in visual processing (Treisman and Gelade, 1980; Theeuwes, 2010).

In the current study, control subjects were able to suppress reflexive saccades and usually became proficient in doing so in a short training period. Automatic capture of eye movements became more frequent with advancing age and cerebral lesions (compare to (Ridderinkhof and Wijnen, 2011)). Age-related failures in undermining oculomotor reflexes might be due to diminishing working memory (de Fockert et al., 2001; Lavie and Fockert, 2005). But while in all control groups of the present study, fixation-interrupting saccades were equally frequent in both horizontal directions, neglect patients exhibited a rightward bias of the reflexive saccades.

Several hypotheses have been put forward to explain the ipsilesional character of attentional and/or oculomotor capture in neglect. For instance, established evidence suggests that the right hemisphere plays a dominant role in spatial attention (f.i. (Heilman and Van Den Abell, 1980; Mattingley, 1999)), leading to an imbalance in attentional functions in case of lesions. More precisely, it has been shown that the right cerebral hemisphere controls stimulus-driven attentional shifts to both left and right visual fields (Shulman et al., 2010; Spagna et al., 2020). Corbetta and colleagues hypothesized that a bilateral dorsal network is necessary for target detection and goal-directed orienting, while a ventral, predominantly right hemispheric network is essential for reorienting toward salient, unexpected, or rare stimuli (Corbetta et al., 1998; Corbetta and Shulman, 2002). The authors suggested that right TPJ lesions might 'functionally' inactivate the right dorsal network, either because of decreased input from the TPJ or because of damage to the underlying white matter. This functional inactivation might be exacerbated by a relative hyperactivation of the left dorsal network, as indicated by hemispheric models of orienting. A stimulus in the right visual half-field thus will have an advantage in capturing attention, on two accounts (i) a decreased contralateral stimulus-driven capture, resulting from damage of the right TPJ, and (ii) a top-down bias against exploring leftward locations, owing to imbalance orienting mechanisms in left and right IPS.

In line with these considerations, evidence supports the hypothesis of a specific impairment of an attentional network implementing exogenous orienting in neglect (Bartolomeo and Chokron, 2002; Bartolomeo et al., 2012). In healthy individuals, temporary inactivation in the SLF II in the right hemisphere was shown to impair the symmetrical distribution of visual attention (Thiebaut de Schotten et al., 2005). Correlations of such lesions of white matter tracts in the RH with attentional deficits in neglect were provided in a number of studies with patients (for instance (Shinoura et al., 2009; Doricchi and Tomaiuolo, 2003; Toba et al., 2018; Kwon et al., 2022)). Bourgeois and colleagues (2015) showed a specific correspondence of the "magnetic ipsilesional capture" to anatomical lesions along the frontoparietal superior longitudinal fasciculus.

SLF connects perisylvian regions and is frequently affected by the right-hemispheric lesions in spatial neglect: TPJ, IPL, the superior/middle temporal cortex and the underlying insula, and the ventrolateral prefrontal cortex (Karnath and Rorden, 2012; Vallar and Bolognini, 2014; Karnath, 2009; Mort et al., 2003; Heilman et al., 1987; Verdon et al., 2010). In addition, subcortical structures have been found to play a substantial role in the etiology of neglect, in particular the putamen, the pulvinar, and the caudate nucleus (Karnath et al., 2002; Vallar and Perani, 1986; Fruhmann Berger et al., 2009; Golay et al., 2008). Some of the mentioned subcortical structures were shown to be involved in oculomotor control (for instance (Munoz and Everling, 2004; Neggers et al., 2012; Wurtz and Hikosaka, 1986; Phillips and Everling, 2012)). In agreement with these findings, in a study involving the intentional inactivation of the dorsal pulvinar in macaque monkeys, Wilke and colleagues have induced a strong oculomotor bias for ipsilateral stimuli (Wilke et al., 2010). Similarly to studies of neglect manipulating the salience of the stimuli (discussed below), the same research group has shown that the induced bias could be reduced when contralateral stimuli received an increased salience (Wilke et al., 2013). It should be noted that, when testing non-human primates with a similar experimental design to the current one, Schneider could not replicate findings of pulvinar inactivation leading to oculomotor ipsilesional bias (Schneider, 2019). Further investigations are needed to elucidate these conflicting accounts.

4.3 Bias of exploration towards the ipsilesional side

Lateralized exploratory deficits were reflected by various measures in the current experiment: the spontaneous orientation of gaze, the divergence in performance related to the match position (left and right) and scan paths (cf. Fig.7). Each of the neglect patients exhibited a strong rightward bias in spontaneous gaze orientation. The results of success rates related to match position were numerically similar in the two neglect patients, but only TE's performance exhibited a significantly higher success rate in trials with the match placed right. Neglect patient HE had generally reduced exploration and "lazy" task-solving strategies, thus diminishing the difference between the two match position-related success rates. Since post-stroke patients frequently suffer, among other deficits, from impairments of motivation (Caeiro et al., 2012) and alertness (Manly et al., 2005; Howes and Boller, 1975), these might have played a role in HE's particular performance. We found that each of the neglect patients exhibited a rather restraint exploration pattern on the left: During the active search demanded by the task, HE consistently inspected the screen up to 18° visual angle to the left, while exhibiting no such limitation on the right hemifield, where she explored up to 26° horizontal eccentricity. TE, a neglect patient that solved the task three days after an ischemic stroke, had an even more profound limitation in his inspection to the left of the screen, stopping at 15° horizontal eccentricity. These exploration patterns are to be contrasted with those of controls, who inspected the

stimulus presentation area symmetrically around 26° visual angle to each horizontal extremity.
These findings are in line with and corroborate evidence of biased exploratory behavior in neglect reported in previous experiments. In the dark, where attention is not modulated by any visual input, patients start exploring on their right and spend less time exploring the contralesional side (Hornak, 1992; Karnath et al., 1998). Also in light and when exploring different scenes, such patients exhibit a strong rightward bias (e.g. (Behrmann et al., 1997; Karnath et al., 1998; Ptak et al., 2009; Machner et al., 2012; Kaufmann et al., 2019; Ohmatsu et al., 2019; Muri et al., 2009; Ptak and Muri, 2013). In extended experimental displays, the pattern of ocular exploration showed a maximum of fixations around 15° to the right in acute neglect patients (Karnath et al., 1998). Moreover, deficits in active search correlate to those in the spontaneous orientation during their recovery (Fruhmann Berger et al., 2008). The fact of their correlation across the time course of recovery suggests common underlying mechanisms.
Since, as shown, exogenous attention is biased to the ipsilesional side, it is not surprising that neglect patients exhibit a corresponding orientation in presence of visual input. Machner and colleagues have recently demonstrated that manipulating salience/attentional priority in a naturalistic salience along a left-right gradient can induce bias in the exploratory eye movements in healthy participants (Machner et al., 2020). Conversely, other authors have shown that manipulating saliency can improve neglect symptoms by increasing the deployment of attention to the contralesional space (Bays et al., 2010; Nardo et al., 2019; Kaufmann et al., 2019). The shifting of salience representations can as well explain the phenomenon of ipsilateral oculomotor capture (Mack and Rock, 1998; Itti and Koch, 2001; Theeuwes, 2010) and it converges well with the evidence for capture by salient features and the previously discussed phenomenon of inattentional blindness in the healthy population.
Nevertheless, disturbed exogenous processing alone does not explain the existing spatial bias in neglect in absence of any visual input (Machner et al., 2020; Hornak, 1992; Karnath et al., 1998). Instead, a model assuming simultaneous neural coding of visual input in two kinds of coordinates might be more fitting (Niemeier and Karnath, 2002). In this publication, salience functions in neglect patients were assumed to show a biased bell shape for the representation of spatial position in egocentric coordinates, while a lateral

gradient was proposed for the representation of spatial position in within-object coordinates. The final saliency of a target was obtained by the multiplication of a linear gradient on the object-based part and a shifted bell curve on the egocentric part. The consequence was a left–right asymmetry that improved with more ipsilesional positions of objects in space in patients with spatial neglect. The salience imbalance always favors the ipsilateral space, while this imbalance/gradient becomes less steep and the width of the salience distribution expands with more ipsilesional egocentric object positions. Indeed, the data of the present as well as of several previous studies fitted well with the predictions by the ISO-map model (e.g. (Karnath et al., 2011a; Li et al., 2014), but are also compatible with other models of spatial attention (Deneve and Pouget, 1998; Pouget and Sejnowski, 2001).

One of the current theories of neglect suggests an imbalance in a “priority map” of the environment, orchestrated by the parietal cortex (Itti and Koch, 2001; Ptak and Fellrath, 2013). Accordingly, fast attentional selection is made possible by a topographical representation of the environment combining stimulus-driven (largely influenced by the saliency of external objects) and endogenous (goal-related) signals and modulating the locus of attention. Selection within the priority map presumably follows a “winner takes it all” principle, while damage to this “map” leads to impairments of focusing attention and consequently to neglect (Ptak, 2012). Importantly, it heavily depends on bodily position, integrating information of egocentric coordinates of space (Ptak and Fellrath, 2013).

Disturbances of the body schema might even be a primary cause of corrupt spatial mapping, leading to the aforementioned shifts in its representation. One of the existing hypotheses postulates that the topographic representation of space might be organized around a center of attention modulated by proprioceptive, vestibular, and retinal information from the periphery (Karnath and Dieterich, 2006). This proposal has support in experimental data, as vestibular or sensory stimulation leads to significant recovery of neglect symptoms (Schindler et al., 2002; Kerkhoff, 2003; Vallar et al., 1990; Pitzalis et al., 2013; Johannsen et al., 2003). Incorrect adjustment of salience functions might result from a shift in egocentric coordinates in relation to the topographic map of external space. This misalignment can lead to exogenous capture and a rightward shift in attention even in absence of sensory input. It might as well explain why, while in some cases tactile/auditive information might even reach awareness in neglect patients, their exact spatial location is often misrepresented (f.i. (Rousseaux et al., 2013; Bisiach and Vallar, 2000)). Nonetheless, the exact relationship between each of the anatomical-functional components of topographical coordination processes and their integration in the central nervous system remains a question of debate.

4.4 Limitations

The current experimental design and its implementation come with several limitations, restricting the possible interpretations. The design of the S2S task is a novel application in the normal population and stroke patients. Several difficulties were encountered, especially when testing post-stroke patients with and without neglect. Post-stroke patients, who usually belong to an older and less technically affine population, had difficulties understanding and performing the task. The training period was significantly longer than in the normal population and frequently frustrating for such subjects. For neglect patients, one of the big challenges was their difficulty in suppressing reflexive saccades. Since such sample-driven saccades led to the abortion of the trial, much of the time spent performing the experiment was dedicated to acquiring correct fixation. Consequently, neglect patients completed a lower number of trials in a much longer amount of time than all other subjects.

The particular design of the objects used in the experiments was sometimes challenging to distinguish from distractors and especially for neglect patients, easily confused. Given the already complex task for such post-stroke patients, it might be reasonable to simplify the stimuli by introducing much larger differences between the individual figures or using more relatable shapes, like line drawings of quotidian items. Nonetheless, such a modification would limit the possibility of inter-species comparisons.

Given the performance of the neglect patients in the S2S task, we concluded that their perception of the neglected space is not affected. This conclusion can be challenged. First, in the design of the experiment, we placed the sample at 15° horizontal eccentricity, a position that might still belong to space that is not neglected, so that it does not reflect particular neglect behavior. The placement of the sample represents a challenging decision, as it requires the object to be placed at a sufficient distance from the center yet, at the same time, far enough from the periphery of the visual field to allow accurate sensory perception. Nevertheless, some researchers appreciate that absolute position is not decisive for the perception of a stimulus in neglect; instead, its relative position in relation to the attentional focus is more important for its access to awareness (Marshall and Halligan, 1989). This criterion was satisfied in our experiment, as it is usually done in such a line of research. Many of the mentioned experiments in this work use, for instance, chimeric pictures of animals in which the left half is modified, without strictly respecting the exact visual degrees of the neglected field of an individual patient (for example (Vallar G., 1994)).

Second, the stimuli, including the samples, were salient red figure onsets on a dark background. A possible effect of this design might be that bottom-up modulation of attention takes place, such that the effect of neglect is compensated (Karnath, 2006).

Another weakness of the experimental design is that the objects were placed in fixed positions. This particular arrangement might have led to stereotypical search behavior and even influence neglect behavior to visit previously inspected locations on the right as a result of their disturbed spatial memory, biased ipsilesionally (Malhotra et al., 2004; Losier and Klein, 2001). Even in the normal population, fixed locations for the objects to be searched might have led to a steep learning curve and, consequently, to reduced overall exploration, rending results hard to interpret.

During the exploration period, we had dark grey placeholders marking the positions of the objects. While the presence of the placeholders helps reduce the cognitive load of the task, it might have biased attention and behavior in a way that interfered with the experimental results: markers on the right visual field can appear more salient and modulate attention exogenously (Losier and Klein, 2001). A setup eliminating any kind of possible modulation of the exploratory behavior might be more adequate to study neglect behavior. Again, such a modification is to be implemented with caution, since it might additionally complicate the design of the task and be less easily applied in patients.

4.5 Future perspectives

By testing various groups of patients with the novel S2S design, we found the task suitable to test for lateralized deficiencies in post-stroke patients. Not only is it applicable for human post-stroke patients, but it is also suitable to be used with non-human primates for further inter-species comparisons. With some improvements, the same task can be implemented for investigating the question of perceptual versus intentional deficits in neglect more thoroughly. One of the applications might consist in analyzing more precisely the implicit perception of the neglected field. For this, possible adjustments of the design can include modifying the placement of the sample on the left, such that the figure appears further away from the center, for instance at 20° visual angle. Varying positions of the sample across the trials might also indicate a precise threshold of perceptual deficiencies if present. If the experimenter is interested in studying the question of aware versus non-aware perception, a control task specifically designed to assess awareness of the perceived stimulus on the left can be introduced.

The design of the targets can be modified to simplify the task for neglect patients. These can include line drawings of particular objects, for instance, different vegetables/fruits that can be more easily distinguished from each other. For future implementations of the task, placeholders could be removed and targets during the exploration period could be placed at varying positions across the screen, such as to prevent learning and stereotypical exploration. To avoid bottom-up modulating of neglect, one might want to make sample objects less salient by presenting them in neutral colors and fading them in. Fading the sample in might as well lead to less sample-driven saccades, such that the task becomes less frustrating for the neglect patients. Finally, if the experimenter is interested in studying perceptual deficits in contrast to (pre)motor impairments with the same task, she could use a touchscreen (to select the matching target) or a movement tracker for the hands with the same task and vary hand positions.

In conclusion, the task has a versatile design that can test for various deficits individually and in parallel. In such a way, it can provide valuable answers about the core characteristics of neglect syndrome. A valuable characteristic of the S2S task is its applicability in humans as well as non-human primates, such that electrode recording and more precise anatomical pinpointing of individual deficits can be achieved in inter-species comparisons. It is imaginable that, given the existing anatomical and conceptual interpretations of neglect, one can test very specific hypotheses and anatomical correlates by using invasive methods (f.i. single-cell recordings) in primates.

4.6 Conclusion

Comparable inter-species designs are a rare opportunity to investigate the exact neural mechanisms of specific behavioral impairments. In the current study, we implemented a novel experimental design, destined for human and non-human primates comparisons, to investigate differential functional impairments in neglect. We showed that pre-attentive processes of object recognition are largely intact, while oculomotor functions, especially the system of exogenous orientation, are impaired in neglect. These dysfunctions reflect, in our view, suboptimal spatial mapping, which might facilitate feature-binding and thus mediate sensory awareness. Further investigations in continuation of the current approach are needed to link behavioral deficits to neural activity or lesions more precisely.

5. Summary

Spatial neglect is a frequent consequence of right-hemispheric brain injury, manifesting itself through difficulties in attending and responding to stimuli contralateral to the cerebral lesion. Patients suffering from such impairments in spatial orientation are slower to recover from post-stroke disabilities and exhibit long-lasting deficits on the functional level. A better understanding of neglect's underlying mechanisms is vital for the future optimization of its clinical management. In the current study, we aimed to investigate in parallel and simultaneously specific functional contributions to neglect: a potentially impaired perception and/or disturbed (oculomotor) exploration of the contralateral space. The hypothesis was that in neglect, the sensory processing of contralesional stimuli is largely intact, while intentional processes, namely search behavior and oculomotor control, are strongly biased to the ipsilesional side.

To quantify the contribution of each of these deficits, we implemented a novel experimental design in three control groups and two individual neglect patients. The so-called search-to-sample task, carried out in the study, consisted of the lateral presentation of a stimulus during central fixation and subsequent search of its match across a darkened exploration area. The stimuli were beamed on a surface in front of the patient by an overhead projector. During the exploration period, objects only appeared when the eyes of the subject fell into their coded field on the screen. Eye movements were registered by an infrared tracking device, while the head was fixed in position by a chinrest. The presented objects were biconcave geometrical figures, suitable for non-human primates to be trained with, as the experiment was intended for (future) inter-species comparisons. In the current work, we present the first results of its implementation in humans and more specifically, in stroke patients. At the end of the experimental session, each participant filled out a self-assessment questionnaire, evaluating their subjective perception and differentiation of the presented stimuli.

We classified success rates by sample position to assess perceptual mechanisms in neglect. We reasoned that, if the sensory processing of the contralateral space was impaired, participants would reach a consistently lower success rate in the sample-left condition. We quantified deficits related to spatial orienting by three different measurements: on the one hand, success rates related to match positions and eye trace recordings reflected potential deficits in active exploration. On the other hand, we

measured the total time the patient spent gazing in each of the hemifields across the inter-trial intervals, during which no stimulus was to be seen. These results were taken to reflect the spontaneous bias in orienting without visual input. We used a final parameter to quantify the interruption of fixations in the stimulus-presentation phase. We classified the resulting values by the saccadic directions leading to the fixation breaks. This last parameter was taken to correspond to attentional/oculomotor disturbances in the exogenous system of attention.

The results were congruent for each of the neglect patients. Each of the neglect patients exhibited no difference in success rates between the two sample presentation conditions, left and right, allowing the interpretation of preserved sensory processing of contralesional stimuli. The eye traces of each neglect patient during the search task illustrated an ipsilesional intentional/oculomotor bias, in which the leftmost areas of the screen remained unvisited. Their hit rates related to match position were significantly lower in conditions with the match placed left, suggesting limited search behavior in this configuration. Another finding was that both neglect patients interrupted fixations significantly more frequently than any of the control groups and did so significantly more often by performing sample-driven saccades to the ipsilesional stimulus than in the opposite horizontal direction.

Taken together, these results provide robust evidence of preserved implicit processing of neglected stimuli on the contralesional side, associated with an asymmetrical exploration pattern, favoring the ipsilesional space, and a strong ipsilesional oculomotor capture of the sample stimulus. These findings are compatible with models of neglect suggesting defective neural integration of spatial mapping processes that might physiologically take place predominantly in the right hemisphere. In absence of adequate spatial processing, no aware perception is possible. In agreement with this interpretation, we hypothesized that the rightward attentional bias in neglect might arise due to a disturbed feeding of body-centered coordinates into the neural map of external space. Such incongruent coding could lead to a shift in salience representations, resulting in an exogenous ipsilesional attentional/oculomotor capture, accompanied by a biased orientation in absence of any visual input.

5.1 Deutsche Zusammenfassung

Räumlicher Neglect ist ein neuropsychologisches Syndrom, das vermehrt nach rechtshemisphärischen Hirnläsionen auftritt und sich durch Defizite in der Raumorientierung und -wahrnehmung äußert. So weisen Neglect-Patienten Verhaltensauffälligkeiten auf, die gravierende Konsequenzen fü ihren Alltag haben: Sie ü ersehen Gegenstände auf der linken Seite, verschätzen sich in der Richtung, aus der sie gerufen werden, oder verpassen sogar, dass sie angesprochen wurden, wenn dies von der kontralateralen Seite zur Hirnläsion geschieht. Sie lassen das Essen auf der linken Seite des Tellers unberüh , sowie die linke Gesichts- oder Körperhälfte beim Waschen. Die Ursachen solcher heterogener Defizite sind bisher nicht vollständig bekannt. Ein besseres Verständnis der Grundlage dieser Symptome wäre jedoch hinsichtlich der weltweit steigenden Inzidenz von Schlaganfall, eine füh ende Ursache von Gehirnläsionen, von großem Nutzen fü die Rehabilitation von Neglect.

Die vorliegende Arbeit untersucht einige gängige Hypothesen, welche Funktions- und Verhaltensmechanismen zu visuellem Neglect füh n. Als Arbeitshypothese legt dieses Manuskript die Auffassung zugrunde, dass die sensorisch-visuellen Verarbeitungsprozesse im Neglect größtenteils intakt sind, während intentionale Prozesse, die zur Explorationssteuerung und der Kontrolle von Augenbewegungen dienen, durch die Hirnläsionen beeinträchtigt werden. Um diese Hypothese zu ü erprüfen, implementieren wir ein neues experimentelles Design, mit dem wir Wahrnehmung und Exploration getrennt voneinander betrachten können. Der aktuelle Versuchsaufbau kann künf ig auch zum experimentellen Vergleich zwischen Menschen und nichtmenschlichen Primaten herangezogen werden.

In diesem Versuch, hatten die Teilnehmer*innen die Aufgabe, einen lateral präsentierten Reiz während der zentralen Fixation zu betrachten und sein identisches Gegenstü k durch eine nachfolgende okuläre Exploration auf einer verdunkelten Fläche wiederzufinden. Die gesuchten Figuren sind nur dann aufgetaucht, wenn die Versuchsperson ihre Augen auf die kodierten Bereiche auf dem Explorationsareal gerichtet haben, wo sich solche Stimuli verdeckt aufgehalten haben. Die Kontrolle der Augenbewegungen erfolgte durch einen Eye-Tracker. Die Reize wurden auf einer Fläche gegenüb r der Versuchsperson durch einen üb r dem Kopf platzierten Projektor zurü kgeworfen und konnten in der Explorationsphase durch Tastendruck selektiert werden. Nach dem

Versuch hat jeder Proband einen Fragebogen zur subjektiven visuellen Wahrnehmung und Differenzierung der Stimuli ausgefü lt.
Fü die Überprüfun der zentralen Hypothese waren folgende Messungen relevant: die Erfolgsraten bezogen auf die zwei Positionen der Samples (links oder rechts) lieferten Hinweise auf mögliche visuell-sensorischen Defizite. Um die Explorationseinschränkungen zu quantifizieren, haben wir die Augenbewegungen während der Suche aufgezeichnet, sowie die Erfolgsraten, bezogen auf die Position der gesuchten Figuren (matches) ausgewertet. Eine zusätzliche Bestimmung war die Zeit, in der der Blick der Versuchsperson spontan, ohne visuellen Reiz, auf eine der Hälften der Projektionsfläche gerichtet war. Eine letzte wichtige Messung war die Anzahl der Fixationsunterbrechungen, aufgeteilt nach der horizontalen Richtung der ursächlichen Sakkaden. Beide Neglect-Patienten in der Studie hatten vergleichbare Erfolgsraten bezogen auf die Position (links oder rechts) der Musterfigur (sample). Gleichzeitig haben beide Neglect-Patienten eine ipsiläsionale Präferenz in ihrem Explorationsverhalten gezeigt: zum einen wurde eine Vernachlässigung der am weitesten gelegenen kontraläsionalen Areale in den Augenbewegungsmustern sichtbar, zum anderen waren die Erfolgsraten bezogen auf das Match signifikant geringer auf der kontraläsionalen Seite. Beide Neglect-Patienten haben vermehrt reflexive Sakkaden zu den ipsiläsionalen Figuren durchgeführ und dadurch ein deutliches Defizit in der Fixation gehabt.
Insgesamt deuten die vorliegenden Ergebnisse darauf hin, dass die visuelle Wahrnehmung in Neglect funktional, wenngleich nicht bewusst ist. Hingegen weisen Neglect-Patienten Defizite in der räumlichen Orientierung sowohl in Suchaufgaben als auch in der spontanen Hinwendung in den Raum auf. Ihre exogene Aufteilung der Aufmerksamkeit zeigt eine üb rmäßige Präferenz fü ipsiläsionale Gegenstände, die dem Training sehr eingeschränkt zugänglich ist. Diese Befunde sind mit der Hypothese einer gestörten topographischen Kodierung des Raumes in Neglect vereinbar und können durch Läsionen der rechten Hemisphäre, die physiologisch fü die Steuerung der räumlichen Aufmerksamkeit in beiden visuellen Feldern zuständig ist, funktional-anatomisch erklärt werden. Die Verschiebung egozentrischer räumlicher Koordinaten in Bezug auf die neuronalen topographischen Salienzkarte der Umgebung kann zu einer inkorrekten spontanen Orientierung, aber auch zu einem verschobenen Aufmerksamkeitsfokus führ n und schließlich das Verhalten der Neglect-Patienten in der vorliegenden Arbeit erklären.

6. Supplementary material

Name: ___________________ Alter: _____________ Händigkeit: □ rechts □ links

SELBSTEINSCHÄTZUNG

Bitte kreuzen Sie das Zutreffende an:

1. Mir war die Aufgabe…

   …von Anfang an klar □
   …nach einigen Versuchen klar □
   …im zweiten Durchgang klar □
   …bis zuletzt unklar □

2. Dier Objekte

   ...konnte ich gut erkennen □
   …konnte ich nur schwer erkennen □
   …konnte ich gut unterscheiden □
   …konnte ich nur schwer unterscheiden □
   …konnte ich mir gut merken □
   …musste ich teilweise durch raten auswählen □

3. Meine Konzentration war

   …durchgehend hoch □
   …im ersten Durchgang höher □
   …im zweiten Durchgang höher □
   …durchgehend niedrig □

4. Mir ist das Erkennen der gezeigten Objekte auf folgender Seite leichter gefallen:

   □ rechts □ links □ kein Unterschied

5. Mir ist die Suche nach Objekten an folgendem Ort leichter gefallen:

   □ rechts □ links
   □ oben □ unten
   □ kein Unterschied

6. Ich schätze, ich habe richtig unterschieden in

   …_____________% der Fälle (1. Durchgang)
   …_____________% der Fälle (2. Durchgang)

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8. Erklärung zum Eigenanteil der Dissertationsschrift

Die Arbeit wurde in der Neurologischen Universitätsklinik, Sektion fü Neuropsychologie, unter Betreuung von Prof. Dr. Dr. Karnath durchgefü rt.

Die Konzeption der Studie erfolgte in Zusammenarbeit mit der Forschungsgruppe „Decision and Awareness“ am DPZ Göttingen und Prof. Dr. Dr. Karnath, Forschungsgruppenleiter in Neuropsychologie um Universitätsklinikum Tüb ngen.

Die Versuche wurden nach Einarbeitung durch Labormitglieder Sophia Nestmann und Daniel Wiesn von mir eigenständig durchgeführ .

Die statistische Auswertung erfolgte nach Beratung durch Prof. Dr. Dr. Karnath und das Institut fü Biometrie durch mich.

Ich versichere, das Manuskript selbständig nach Anleitung durch Prof. Dr. Dr. Karnath verfasst zu haben und keine weiteren als die von mir angegebenen Quellen verwendet zu haben.

Tü ingen, den

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