Lateralization, functional specialization, and dysfunction of attentional networks

Paola Mengotti[a,*], Anne-Sophie Käsbauer[a], Gereon R. Fink[a,b], Simone Vossel[a,c]

[a]Cognitive Neuroscience, Institute of Neuroscience & Medicine (INM-3), Forschungszentrum Jülich, 52425 Jülich, Germany

[b]Department of Neurology, Faculty of Medicine and University Hospital Cologne, University of Cologne, 50937 Cologne, Germany

[c]Department of Psychology, Faculty of Human Sciences, University of Cologne, 50923 Cologne, Germany

***Corresponding author:**

Dr. Paola Mengotti

Cognitive Neuroscience, Institute of Neuroscience and Medicine (INM-3)

Forschungszentrum Jülich

Leo-Brandt-Str. 5, 52425 Jülich, Germany

Phone: +49-2461-61- 85163

Fax:+49-2461-61-1518

Email: p.mengotti@fz-juelich.de

Abstract

The present review covers the latest findings on the lateralization of the dorsal and ventral attention systems, their functional specialization, and their clinical relevance for stroke-induced attentional dysfunction. First, the original assumption of a bilateral dorsal system for top-down attention and a right-lateralized ventral system for stimulus-driven attention is critically reviewed. The evidence for the left parietal cortex's involvement in attentional functions is discussed and findings on putative pathways linking the dorsal and ventral network are presented. In the second part of the review, we focus on the different attentional subsystems and their lateralization, discussing the differences between spatial, feature- and object-based attention, and motor attention. We also review studies based on predictive coding frameworks of attentional functions. Finally, in the third section, we provide an overview of the consequences of specific disruption within the attention networks after stroke. The role of the interhemispheric (im)balance is discussed, and the results of new promising therapeutic approaches employing brain stimulation techniques such as transcranial magnetic stimulation (TMS) or transcranial direct current stimulation (tDCS) are presented.

Keywords: spatial attention; fronto-parietal network; interhemispheric competition; disconnection; spatial neglect.

1. Introduction

Investigating the lateralization and functional specialization of the brain's attentional systems is pivotal for understanding attentional deficits after stroke and developing effective rehabilitation approaches. Right hemisphere stroke often leads to spatial neglect, a syndrome characterized by a failure to process stimuli appearing in the contralateral hemispace (see for a review Corbetta & Shulman, 2011; Halligan, Fink, Marshall, & Vallar, 2003) and which complicates the functional recovery of the patients (Rengachary, He, Shulman, & Corbetta, 2011). Also, stroke can lead to extinction, a phenomenon where patients can detect stimuli presented unilaterally, but fail to detect a contralesional stimulus in bilateral stimulation conditions (i.e., in the presence of an ipsilesional stimulus).

The most influential model of the last 15 years concerning the anatomical and functional organization of attentional systems in the human brain distinguishes two distinct albeit interacting fronto-parietal networks: the dorsal network guiding the voluntary allocation of attention, and the ventral network responding to unexpected but relevant stimuli (Corbetta & Shulman, 2002; 2011; Corbetta, Patel, Shulman, 2008).

In this review, we will first focus on studies investigating the lateralization of these two attentional networks. Here, the results generally confirmed the dorsal system's bilateral organization, whereas the assumption of an exclusive right-lateralization of the ventral system has been challenged. The latter aspect is crucial for developing therapeutic protocols for patients with neglect targeting the undamaged (left) hemisphere. Moreover, in this section, we review findings on the interaction between the dorsal and ventral attentional systems. This aspect is also of high clinical significance. Although the lesions of neglect patients most commonly affect ventral and rarely dorsal fronto-parietal regions, these lesions typically result in impaired voluntary/spontaneous orienting of attention to contralesional space (mediated by the dorsal system) and deficits in reorienting attention (mediated by the ventral system). Hence, the clinical picture of neglect may best be explained by impaired functionality of both attention networks, and recent findings have started to shed light on the critical pathways that may underlie such distributed network effects.

In the second part of the manuscript, we will review the evidence for the functional specialization of dorsal and ventral regions beyond spatial attention. We will discuss recent studies investigating feature-based, object-based, and motor attention in healthy participants and patients with focal brain lesions. Additionally, we will reconsider the ventral system's role for attentional reorienting and discuss recent findings on the involvement of the right temporoparietal junction (TPJ) in predictive coding. This has important implications for our understanding of the pathomechanisms underlying the spatial neglect syndrome and, consequently, therapeutic interventions.

The last part of this review is specifically dedicated to the dysfunction of the attentional systems in stroke patients with spatial neglect. Here, we will review recent neurostimulation approaches aiming at ameliorating symptoms of neglect and associated disability. Whereas these studies offer future perspectives for new therapeutic approaches for neglect, they also serve as a lesion model validating the findings in healthy volunteers.

2. Functional and structural lateralization of the attentional systems

Historically, two competing theoretical frameworks describe the organization of the voluntary allocation of attention: The "hemispatial" theory postulates a dominant role of the right hemisphere in allocating attention to both hemispaces, whereas the left hemisphere allocates attention only to the contralateral hemispace (Heilman & Van Den Abell, 1980; Mesulam, 1981; see Figure 1). In contrast, the "interhemispheric competition" or "interhemispheric rivalry" theory (Kinsbourne, 1977) assumes that both hemispheres allocate attention to the contralateral hemispace and that the balance is maintained through interhemispheric inhibition. The left hemisphere is thought to exert a more substantial rightward bias than the leftward bias of the right hemisphere, thereby leading to a stronger imbalance after right hemispheric damage (Kinsbourne, 1987). A more recent account considering evolutionary factors (Bartolomeo & Seidel Malkinson, 2019) generally postulates a predominant role of the right hemisphere in attentional processes. According to this formulation, the left hemisphere processes familiar patterns of responses in routine situations, whereas the right hemisphere controls responses to novel, unexpected (and potentially dangerous) events. Following this line of thought, the authors speculate that attentional processes might have been shaped primarily in the right hemisphere to detect possibly threatening (i.e., behaviorally relevant) events.

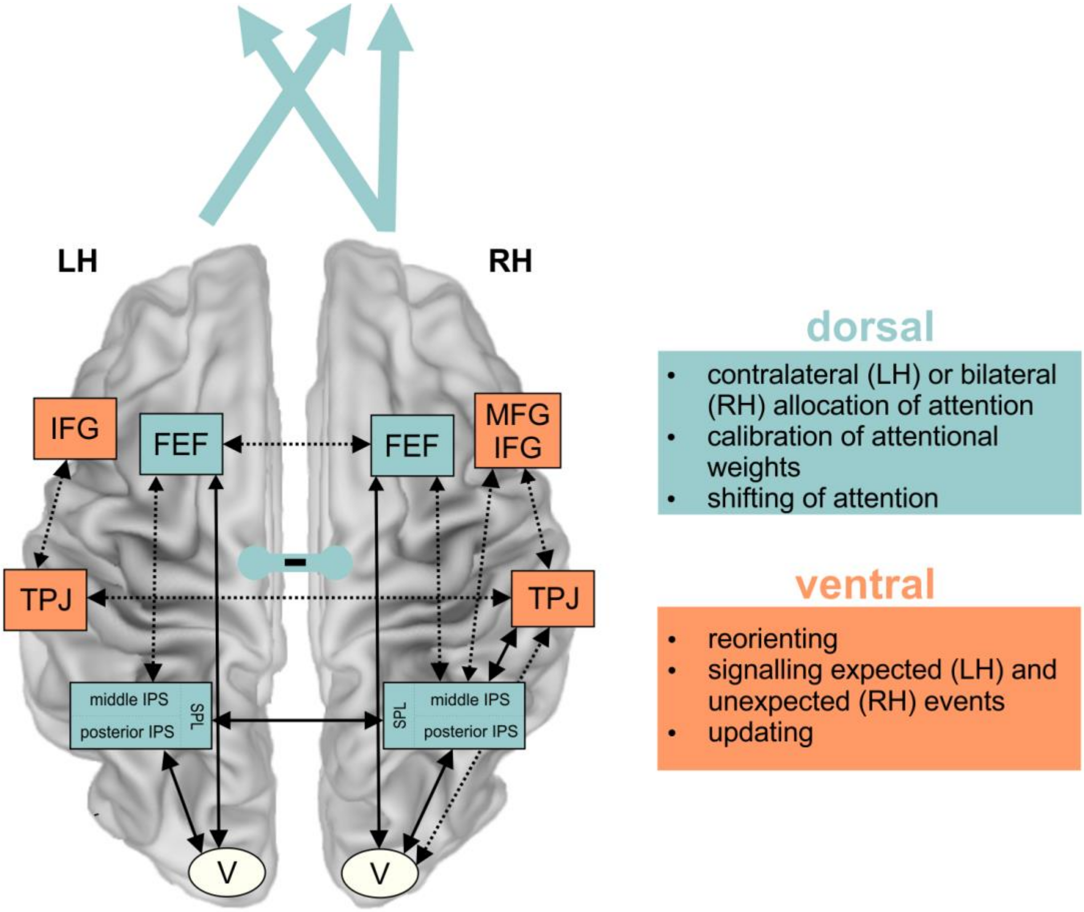

Figure 1. Schematic illustration of the central nodes of the dorsal (light blue) and ventral (orange) attention systems. Bidirectional arrows exemplarily depict connections between the nodes. Solid lines depict connections for which there is evidence from correlational (e.g., fMRI) and causal techniques (e.g., TMS). Dotted lines depict connections with evidence from correlational techniques only. Visual areas are depicted in white. Blue arrows illustrate the organization of the allocation of attention by the dorsal system according to the hemispatial theory, whereas the blue interhemispheric connection indicates interhemispheric inhibition. LH: left hemisphere; RH: right hemisphere; IFG: inferior frontal gyrus; MFG: middle frontal gyrus; FEF: frontal eye fields; TPJ: temporoparietal junction; IPS: intraparietal sulcus; SPL: superior parietal lobule; V: visual cortex.

According to the neuroanatomical model of attention by Corbetta and Shulman (2002; 2011), the dorsal system, mediating attentional orienting, comprises the intraparietal sulcus (IPS) and the frontal eye fields (FEF) and is organized bilaterally. In contrast, the ventral system, responsible for detecting unexpected stimuli and inducing attentional shifts in cooperation with the dorsal system, comprises the right TPJ and the ventral frontal cortex and is deemed more right-lateralized (Corbetta et al., 2008; Corbetta and Shulman, 2011; see Figure 1). Both networks control spatial attention across different sensory modalities (for a review, see, e.g., Macaluso, 2010), although most studies focused on visuospatial attention. The model was initially based on evidence from task-based functional MRI (fMRI) studies, but the two networks have also been distinguished in resting-state studies looking at task-free functional connectivity (Fox, Corbetta, Snyder, Vincent, & Raichle, 2006; He et al., 2007). Structurally, the two networks are connected by the fronto-parietal branches of the superior longitudinal fasciculus (SLF; Thiebaut de Schotten et al., 2011) and the parietal inferior-to-superior tract (PIST; Catani et al., 2017).

2.1 Lateralization of the dorsal network

Neuroimaging work in the visual system has shown that both parietal (i.e., IPS/SPL) and frontal (i.e., FEF) regions of the dorsal network show a topographical organization, responding preferentially to the presence of stimuli in the contralateral visual field (for a review see Silver & Kastner, 2009) and to contralateral shifts of spatial attention (Szczepanski, Konen, & Kastner, 2010; Jeong & Xu, 2016). Szczepanski et al. (2010) found that although asymmetries were observed for some brain areas, the mean strength of the contralateral attentional bias across different fronto-parietal regions did not differ between the two hemispheres. The contralateral attentional bias has also been related to the microstructural integrity of the fronto-parietal white matter (possibly corresponding to SLF), with higher fractional anisotropy in the right parietal white matter being associated with a more substantial leftward attentional bias in healthy participants (Kocsis et al., 2019). Also, subcortical structures, such as the superior colliculus, show lateralized biases in attentional control (Sreenivasana & Sridharana, 2019). The superior colliculus plays a role in target selection for saccades (McPeek & Keller, 2004) and in attentional orienting (Anderson & Rees, 2011; Krauzlis, Lovejoy, & Zénon, 2013). Sreenivasana and Sridharana (2019) analyzed participants' responses in a change detection task with endogenous spatial cueing using signal detection theoretic measures. They observed that the choice bias asymmetry in this task mirrored the asymmetry in white matter connectivity between the superior colliculus and the cortex. Moreover, the subcortical-cortical connectivity's strength predicted the modulation of the choice bias induced by the spatial cues.

For the cortical areas, a more elaborated model of the involvement of dorsal parietal structures in attentional processes has been deduced from a series of fMRI and patient studies by Vandenberghe and colleagues (Molenberghs, Gillebert, Peeters, & Vandenberghe, 2008; Vandenberghe et al., 2005; see Vandenberghe & Gillebert, 2013 for a review; see Figure 1). Here, the contralateral enhancement of stimulus processing is thought to be mediated by the posterior segment of the IPS in both hemispheres. In contrast, the middle segment of the IPS (particularly in the right hemisphere) supposedly calibrates attentional weights of stimuli or objects, irrespective of the direction of attention. The superior parietal lobe is involved in spatial shifts of attention (i.e., in the displacement of attentional weights).

There is now considerable evidence that the attentional enhancement relies on the modulation of sensory areas by IPS and FEF via backward connections. This evidence comes from concurrent online transcranial magnetic stimulation (TMS) fMRI studies, in which activity changes in the visual cortex were caused by the direct spread of activity to interconnected regions from TMS over FEF and IPS (Ruff et al., 2006; 2008; 2009). The TMS-induced modulation of visual areas was restricted to stimulation of the right hemisphere when TMS was applied over IPS, while the lateralization of the TMS effects for the FEF was different for the central and peripheral visual field (Ruff et al., 2008; 2009). Moreover, evidence for top-down modulation of visual cortex activity comes from fMRI studies employing connectivity analyses. Using Granger causality measures, Bressler, Tang, Sylvester, Shulman, and Corbetta (2008) showed that both FEF and IPS modulated activity in the visual cortex and that FEF modulated the activity of IPS. Vossel, Weidner, Driver, Friston, and Fink (2012) employed dynamic causal modeling (DCM) and observed that the most plausible connectivity model contained direct connections from IPS to the visual cortex in both hemispheres, which were modulated by the direction of spatial attention. Interestingly, an fMRI study in two patients with right parietal lesions and spatial neglect showed an asymmetric activation of the retinotopic visual cortex, but this asymmetry was only present in conditions with a high attentional load (Vuilleumier et al., 2008).

Methods with a higher temporal resolution such as magnetoencephalography (MEG) and EEG have provided further insights into the processes underlying lateralized orienting of attention and the interplay between fronto-parietal and visual areas. A MEG study by Simpson et al. (2011) demonstrated that the degree of direction-specificity of brain responses in FEF and IPS is different for different stages of the orienting phase. More specifically, the direction-specific activation of FEF occurred in an early stage of processing and preceded the IPS activity during the anticipatory allocation of attention. EEG and MEG research has also shown that a lateralized focus of attention to the left or the right hemispace induces a contralateral modulation of oscillatory synchronization in different frequency bands (in particular alpha-band activity) along visual areas and the dorsal network (Siegel, Donner, Oostenveld, Fries, & Engel, 2008; Thut, Nietzel, Brandt, & Pascual-Leone, 2006). The strength of the lateralization of the oscillatory activity correlated with task performance (Siegel et al., 2008; Thut et al., 2006), and could be predicted by the volume asymmetry of a subpart of the SLF (SLF II) connecting ventral and dorsal networks (D'Andrea et al., 2019). Using concurrent EEG-TMS, Capotosto, Babiloni, Romani, and Corbetta (2012) revealed that TMS interference with either left or right IPS activity caused a disruption of the contralateral desynchronization of alpha-band activity in the visual cortex during spatial attention. However, only TMS over the right IPS caused bilateral impairments in target identification accompanied by bilateral pre-target synchronization of the alpha-band.

TMS and transcranial direct current (tDCS) studies have also shed light on the role of interhemispheric competition effects for attentional processing. In a seminal study, Hilgetag, Théoret, and Pascual-Leone (2001) showed that low-frequency repetitive TMS (rTMS) over both left and right posterior parietal cortex (PPC) reduced performance in the detection of bilateral stimuli. This effect resembles the behavior of stroke patients with extinction who fail to detect a contralesional stimulus in the presence of ipsilesional stimulation. Interestingly, the detection of unilateral stimuli was enhanced after rTMS in the visual field ipsilateral to the side of the stimulation for both hemispheres, supporting the hypothesis of interhemispheric competition.

Consistent with this, a study using a landmark task (Szczepanski & Kastner, 2013) showed that TMS interference with left and right IPS activity caused a leftward or rightward shift in the participants' judgments ipsilateral to the side of the stimulation. Even more interestingly, performance remained unchanged after concurrent bilateral TMS of left and right IPS, again providing evidence in favor of the interhemispheric competition hypothesis.

Similarly, the results of other neuromodulation and neurostimulation studies are generally supportive of the interhemispheric competition theory. Results showed a separate contribution of both right and left PPC to orienting attention to the contralateral hemispace (Bien, Goebel, & Sack, 2012; Duecker, Schuhmann, Bien, Jacobs, & Sack, 2017; Roy, Sparing, Fink, & Hesse, 2015; Sparing et al., 2009; Zuanazzi & Cattaneo, 2017; see, however, Filmer, Dux, & Mattingley, 2015), even with more consistent effects for the right hemisphere (Bien et al., 2012; Bourgeois, Chica, Valero-Cabré, & Bartolomeo, 2013a; 2013b; Chechlacz, Humphreys, Sotiropoulos, Kennard, and Cazzoli, 2015; Hilgetag et al., 2001). Chechlacz et al. (2015) demonstrated that the consistency of the effect of theta-burst TMS over IPS on attentional shifts is higher for right IPS, while TMS of left IPS leads to variable responses that depend on micro- and macrostructural differences in the corpus callosum. Along the same line are the results of another TMS study (Koch et al., 2011), showing that the right PPC could exert more potent inhibition over the contralateral PPC than the left PPC. Using white matter fiber tracking, this study also showed that the effect was mediated by the posterior part of the corpus callosum.

Fewer TMS studies targeted FEF to modulate attentional processing. Duecker, Formisano, and Sack (2013) showed that theta-burst TMS over right FEF reduced the benefits of the predictive spatial cue when the target appeared in the cued location (i.e., in validly as compared to neutrally cued trials). This reduction was present for targets in both the left and right hemifield, whereas the effect was limited to targets in the contralateral (right) hemifield with TMS over left FEF.

Online TMS over right FEF has been shown to increase perceptual sensitivity (target detection) for targets both in the left and right hemifields (Chanes, Chica, Quentin, & Valero-Cabré 2012). In contrast, TMS over left FEF increased perceptual sensitivity only to left targets (Chica, Valero-Cabré, Paz-Alonso, & Bartolomeo, 2014). To the best of our knowledge, no neurostimulation study has performed concurrent bilateral stimulation of FEF to test for interhemispheric competition directly.

In sum, the studies mentioned above confirm the bilateral organization of the dorsal IPS-FEF network - with each hemisphere controlling perceptual and attentive processing in contralateral space. For regions along the IPS (and for the SPL), there may be functional subdivisions - with different subregions subserving contralateral attentional enhancement, calibration of attentional weights, and spatial shifting, respectively. Despite the bilateral organization of the dorsal system, there is also evidence for asymmetric effects, in that right (but not left) IPS and FEF are involved in attentional control of both hemifields. It remains unclear if this asymmetry is intrinsic to the attentional systems' organization, or if it depends on the specific subregion studied (e.g., posterior versus middle IPS), the time point during attentional orienting, or other factors. Some neurostimulation studies have reported stronger or more consistent TMS effects following stimulation over the right hemisphere, and recent evidence points to a crucial role of transcallosal connectivity for these effects and their interindividual variability.

2.2 Lateralization of the ventral network

The ventral attention network is traditionally considered right-lateralized (Corbetta et al., 2002; 2008; Ingelström, Webb, & Graziano, 2015; see, however, Geng & Vossel, 2013). This system is often studied by contrasting the brain activity in response to invalidly and validly cued trials in spatial cueing paradigms (or Posner tasks; Posner, 1980). In a DCM fMRI study by Vossel et al. (2012), the most plausible connectivity model of the ventral system was characterized by enhanced connectivity from the visual cortex to the right TPJ during invalid cueing, reflecting the pivotal role of this region in signaling unexpected events. Moreover, invalid cueing increased the connectivity from the right TPJ to right IPS, possibly reflecting the signaling of violated expectations from the ventral to the dorsal network.

The involvement of left TPJ in spatial attention allocation is still controversial (Geng & Vossel, 2013). Doricchi, Macci, Silvetti, & Macaluso (2010) showed that whereas right TPJ selectively responded to invalid targets, left TPJ responded to valid and invalid targets compared to a neutral cueing condition. In a more recent study using multivariate pattern recognition analysis (MVPA) of fMRI data in the same task, Silvetti et al. (2017) showed that a different pattern of neural activity characterized the response of left TPJ (and left IFG) to valid and invalid targets. The authors suggested that TPJ might be involved in updating probabilistic expectations concerning the occurrence of events, with right TPJ signaling the 'mismatch' between expected and unexpected events, and left TPJ signaling the 'match' between expected and actual target location. Other studies provided further evidence for the involvement of TPJ in updating contextual information or probabilistic beliefs/expectancies (Di Quattro & Geng, 2010; Mengotti, Dombert, Fink, & Vossel, 2017; Vossel, Mathys, Stephan, & Friston, 2015).

Recent evidence for a bilateral involvement of TPJ is provided by one of our fMRI studies that investigated the link between attentional reorienting, updating of expectancies, and resting-state functional connectivity of right TPJ before and after the performance of a spatial cueing paradigm (Käsbauer, Mengotti, Fink, Vossel, 2020). Here, an increase of the interhemispheric functional connectivity between right TPJ and left TPJ after the task was related to faster attentional reorienting (as well as faster trial-wise updating of expectancies after new observations). Another resting-state study (Kucyi, Hodaie, & Davis, 2012) reported significant functional connectivity of left and right TPJ with the salience resting-state network. The connectivity was stronger for the right TPJ, whereas left TPJ showed stronger connectivity with the executive control network. Further neuroimaging studies reported an additional involvement of left TPJ in signaling relevant unexpected stimuli, attentional reorienting, and distractor filtering (Di Quattro & Geng, 2010; Dugué, Merriam, Heeger, & Carrasco, 2017; Geng & Mangun, 2011; Vossel, Weidner, Moos, & Fink, 2016; Weidner, Krummenacher, Reimann, Müller, & Fink, 2009). Hence, left TPJ might be involved in the processing of relevant features to drive attentional reorienting based on contextual relevance, and not necessarily based on spatial information (Di Quattro & Geng, 2010; Geng & Mangun, 2011; Weidner et al., 2009).

In contrast to the dorsal network, there is currently no evidence for a topographical organization of the ventral network. However, it has been reported that the right TPJ responds to invalid targets in both hemispaces, and left TPJ responds only to contralateral targets (Dragone, Lasaponara, Silvetti, Macaluso, & Doricchi, 2015). A TMS study that applied continuous theta-burst TMS over left and right TPJ in a rapid serial visual presentation task (Chang et al., 2013) observed that the detection of targets was increased for targets in the left visual field and decreased for targets in the right visual field after stimulation of right TPJ. No effects were found when stimulating left TPJ.

Taken together, the original assumption of absolute right-hemispheric lateralization of the ventral system needs to be reconsidered. Left TPJ – as well as the connectivity between left and right TPJ – also seem to be relevant for attentive and expectation-related processing, although the exact functions may differ between the two hemispheres. This finding is of clinical significance, since it may stimulate the development of therapeutic protocols that rely on the spared cognitive resources of the left hemisphere.

2.3 Interaction between dorsal and ventral networks

The dorsal and the ventral networks do not work in isolation. For instance, the contrast of invalid versus valid trials in the spatial cueing paradigm often activates both ventral and dorsal areas (Doricchi et al., 2010; Dragone et al., 2015; Kincade, Abrams, Astafiev, Shulman, & Corbetta, 2005; Vossel et al., 2012; Wen, Yao, Liu, & Ding, 2012), suggesting an interplay between the two systems for efficient deployment of attention. As far as the anatomical connectivity is concerned, frontal and parietal regions of the attentional networks are interconnected by different tracts of the SLF (Thiebaut de Schotten et al., 2011). SLF I connects fronto-parietal regions of the dorsal network and is symmetrically distributed in the left and right hemispheres. SLF III connects fronto-parietal regions of the ventral network and is right-lateralized. SLF II is a middle tract connecting the inferior parietal lobule with superior/middle frontal gyri, including FEF, (i.e., connecting ventral and dorsal networks). SLF II tends to be right-lateralized, and the trend towards stronger right lateralization correlated with the participants' performance in spatial attention tasks (i.e., line bisection and Posner task). Damage to SLF II is a good predictor for spatial neglect (Thiebaut de Schotten et al., 2014). Besides, a recent study combining white matter tractography with a meta-analysis of fMRI studies confirmed the involvement of SLF II in both spatial and non-spatial functions of the dorsal and the ventral networks (Parlatini et al., 2017). Recently, Catani et al. (2017) identified the parietal inferior-to-superior tract (PIST), a white matter tract connecting the inferior parietal lobule (i.e., supramarginal and angular gyri) with the superior parietal lobe, as well as different areas within the intraparietal sulcus. The PIST represents an additional intra-parietal source of connectivity between dorsal and ventral systems.

According to the Corbetta and Shulman model (Corbetta et al., 2008; Corbetta & Shulman, 2011), the right middle frontal gyrus (MFG) is a putative region linking ventral and dorsal networks. Supporting evidence is coming mainly from resting-state functional connectivity studies indicating that the right MFG activity correlated with the ventral and the dorsal attention networks (Fox et al., 2006; He et al., 2007). Another possible interconnection between the dorsal and ventral networks might be between the right TPJ and right IPS. Using Granger causality measures, Wen et al. (2012) showed that performance in a cued spatial attention task correlated with the connectivity between right TPJ and right IPS. This finding is in line with the DCM results by Vossel et al. (2012) described above. Results of online TMS studies (Ahrens, Veniero, Freund, Harvey, & Thut, 2019; Chica, Bartolomeo, Valero-Cabré, 2011) showed that right IPS was causally involved in both top-down (endogenous) and bottom-up (exogenous) attention, while right TPJ TMS exclusively affected bottom-up attention. This observation again highlights the interplay between the dorsal and ventral systems through the connection between right IPS and TPJ. Along the same lines are the results of the TMS study by Leitão, Thielscher, Tünnerhoff, and Noppeney (2015), showing that TMS-induced disruption of the activity of right IPS modulated activity in the right TPJ. The hypothesis of a ventral-dorsal system connection through IPS-TPJ is supported by direct anatomical evidence from structural connectivity (Catani et al., 2017).

In sum, these results provide supporting evidence of functional and structural connectivity between the dorsal and ventral networks through IPS-TPJ. The existence of this pathway may explain why damage to ventral regions such as right TPJ can lead to functional impairments of the dorsal fronto-parietal system. Such indirect functional damage of the IPS after ventral parietal lesions has been reported in neglect patients (Corbetta, Kincade, Lewis, Snyder, & Sapir, 2005; see also section 4).

3. Beyond spatial attention: Functional specialization and lateralization of different attentional subsystems

The attentional selection process is not limited to the spatial location of a stimulus, but can also be based on other characteristics relevant for target detection, such as the target features, specific target objects, or the motor response to the target. In this section, we will focus on the functional specialization of the attentional systems beyond spatial attention. Moreover, we will review findings on the processing and updating of expectancies of events in the attentional systems.

3.1 Feature-based attention

Feature-based attention is the ability to enhance the representation of a specific feature (e.g., color, motion, orientation) throughout the entire visual field to detect a stimulus. When feature-based and spatial cueing tasks are compared, feature-based and spatial attention activate similar fronto-parietal networks during attentional orienting and re-orienting (Dombert, Kuhns, Mengotti, Fink, & Vossel, 2016; Egner et al., 2008; Greenberg, Esterman, Wilson, Serences, & Yantis, 2010; Siemann, Herrmann, & Galashan, 2018; Vandenberghe, Gitelman, Parrish, & Mesulam, 2001; see Figure 2A upper panel). In particular, the anterior IPS, both in the left and right hemisphere, has been highlighted as a pivotal region for both types of attention (Egner et al., 2008; Dombert et al., 2016). This was also confirmed by a TMS study (Schenkluhn, Ruff, Heinen, & Chambers, 2008; see Figure 2B), which showed that TMS over right anterior IPS impaired target detection with spatial and feature-based cues. However, there is also evidence that spatial and feature-based attention rely on partially independent systems. When stimulating the right supramarginal gyrus with TMS, Schenkluhn et al. could impair only spatial attention, but not feature-based attention. Also, MVPA analysis of fMRI data of attentional shifts to spatial locations or features showed that commonly activated regions of PPC show a different pattern of activity, suggesting domain-specific subpopulation of neurons (Greenberg et al., 2010; see Figure 2A lower panels). Stroke patient studies have corroborated the putative segregation of spatial and feature-based attentional systems. Two explorative investigations on small samples of neglect patients (Shaqiri & Anderson, 2012; 2013) showed a reduction of spatial priming effects but preserved color priming.

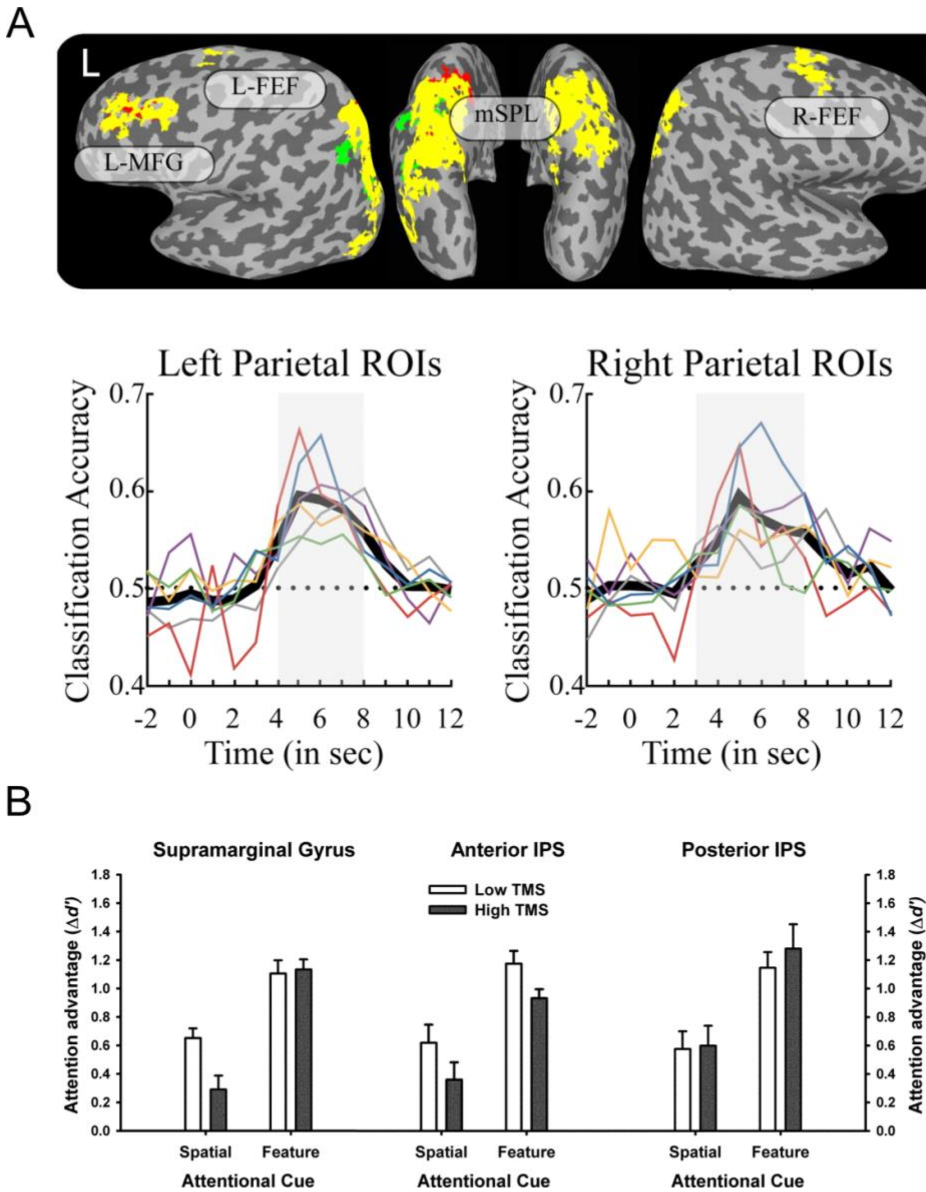

Figure 2. A) Upper panel: Functional fronto-parietal conjunction maps of attentional shifts to spatial locations or features. The joint fronto-parietal network for location and color shifts is shown in yellow. Regions specific to location and color shifts are shown in red and green, respectively. Reprinted with permission of the Society for Neuroscience from Greenberg et al. (2010). Lower panels: Pattern classification results from parietal regions of the conjunction map shown in A). The classifier could classify color and location shifts from the pattern of common activity in the parietal cortices with above-chance accuracy. Gray shading indicates time points of above-chance performance, and colored lines indicate classifier performance for each individual. Modified and reprinted with permission of the Society for Neuroscience from Greenberg et al. (2010). **B)** Results of right parietal TMS on spatial and feature-based

attentional cueing. TMS over the supramarginal gyrus impaired spatial attention but not feature-based attention, whereas TMS over the anterior IPS impaired both types of attention. TMS over the posterior IPS did not affect the attentional allocation of either type. Reprinted with permission from Schenkluhn et al. (2008). Copyright (2008) Society for Neuroscience.

Visual regions processing task-relevant features also show increased activity when attention is focused on a specific feature. However, unlike the lateralized modulation of activity during spatial attention, the enhanced activity spreads throughout the whole visual field (Dombert et al., 2016; Jehee, Brady, & Tong, 2011; Serences & Boynton, 2007; Zhang, Mlynaryk, Ahmed, Japee, & Ungerleider, 2018). The right inferior frontal junction (IFJ) seems to be a critical region for the modulation of activity in the visual areas, but also for the modulation of the activity of regions of the dorsal network, such as IPS and FEF (Zhang et al., 2018). Results of a combined concurrent TMS-fMRI study (Heinen, Feredoes, Weiskopf, Ruff, & Driver, 2014) pointed towards a causal role of right FEF in modulating feature-based attention. TMS over right FEF also induced higher activity in left FEF, possibly pointing towards a bilateral involvement of FEF in feature-based attention.

The presented findings point towards segregated but partially overlapping systems for spatial and feature-based attention, highlighting an involvement of bilateral anterior IPS, but also of IFJ and FEF, in feature-based attention.

3.2 Object-based attention

Attention can also be allocated to entire objects, whereby all parts of the attended object are preferentially processed. Neuroimaging experiments using tasks in which overlapping gratings, dot configurations, or different object categories (faces vs. houses) are presented - and participants have to switch or maintain attention to one of the two objects - have shown that object-based attention recruits fronto-parietal regions, partially overlapping with the spatial attention network (Arrington, Carr, Mayer, & Rao, 2000; Serences, Schwarzbach, Courtney, Golay, & Yantis, 2004; Shomstein & Behrmann, 2006; Stoppel et al., 2013; Wilson, Woldorff, & Mangun, 2005). However, object-based attention additionally recruits regions of the left PPC and IPS (Arrington et al., 2000; Serences et al., 2004; Shomstein & Behrmann, 2006; Wilson et al., 2005). The same pattern was also found in stroke patients, where patients with lesions to the right hemisphere showed spatial attention deficits, and patients with lesions to the left hemisphere showed deficits of object-based attention (Egly, Driver, & Rafal, 1994). A recent fMRI study highlighted the involvement of a bilateral network involving anterior IPS, FEF, and IFJ for object-based attention (Liu, 2016). Like feature-based attention, IFJ seems to be a pivotal region in modulating visual regions' activity during object-based attention (Baldauf & Desimone, 2014). Other studies asking to maintain or switch attention between face or house stimuli showed that object-based attention can modulate the activity of visual areas (from V1 to V4) and higher-order visual regions responding specifically to the object-category presented, such as the fusiform face area and parahippocampal place area (Baldauf & Desimone, 2014; Cohen & Tong, 2015; Davidesco et al., 2013; Shomstein & Behrmann, 2006).

The results presented suggest that similar to feature-based attention, object-based attention recruits a distinct but overlapping network when compared to spatial attention. The additional recruitment of parietal regions of the left hemisphere seems consistent across studies on object-based attention.

3.3 Motor attention

Attention can also be directed towards a specific motor response to the target stimulus. Neuroimaging evidence (Astafiev et al., 2003) highlighted the involvement of overlapping fronto-parietal regions in covert spatial attention, and saccades or pointing movements towards the target. In particular, parts of FEF and IPS in the left hemisphere were recruited during spatial attention and pointing, suggesting an involvement of these regions in motor attentional processes. Along the same lines, motor attention (sometimes also termed motor intention) has been consistently associated with the left parietal cortex, especially its anterior part involving the supramarginal gyrus (Hesse, Thiel, Stephan, & Fink, 2006; Kuhns, Dombert, Mengotti, Fink, Vossel, 2017; Rushworth, Nixon, Renowden, Wade, & Passingham, 1997; Rushworth, Ellison, & Walsh, 2001; Rushworth, Krams, & Passingham, 2001). From this left-hemispheric lateralization, a connection between the disruption of motor attention and limb apraxia has been hypothesized (Rushworth, Johansen-Berg, Göbel, & Devlin, 2003). Despite the partial overlap of spatial and motor attentional areas, apraxic and attentional deficits are uncorrelated in left-hemispheric stroke patients and can be related to differential lesion patterns (Timpert, Weiss, Vossel, Dovern, & Fink, 2015).

The left-lateralization of the motor attention network has been shown to be independent of the hand used for the task. The involvement of the left parietal cortex is present even when participants use their left hand for responses (Rushworth, Krams, & Passingham, 2001; Hesse et al., 2006). However, no study so far has systematically investigated the lateralization of the motor attention network in left-handers. Nevertheless, recent results (Petit et al., 2015) showed that the dorsal attentional network tends to be more strongly right-lateralized in left-handers (especially in the ones who show right-eye dominance), possibly giving these individuals an evolutionary advantage of having control of the dominant hand and visuospatial processes lateralized to the same hemisphere. Differential lateralization of the dorsal fronto-parietal network in left- and right-handers has also been suggested, based on TMS effects over IPS on spatial attention (Cazzoli & Chechlacz, 2017). Moreover, an impact of handedness on the structural asymmetry of the dorsal branch of SLF (SLF I), as well as a relation between this asymmetry and lateralized motor performance, have been reported (Howells et al., 2018).

Left premotor regions are also activated during motor attention (Rushworth, Krams, & Passingham, 2001). The involvement of left frontal regions was supported by a study that used rTMS over the left and right dorsolateral prefrontal cortex (DLPFC) and left and right PPC (Rounis, Yarrow, & Rothwell, 2007). Results showed that TMS over left DLPFC slowed down reaction times in invalidly cued trials during the motor attention task and that TMS over right PPC slowed down reaction times to invalidly cued targets in the spatial attention task.

Taken together, while there is a broad overlap of the activation patterns during the attentional selection of locations, features, objects, and motor responses at first glance, there is also evidence for functional specialization. This becomes evident in a differential hemispheric lateralization, the recruitment of additional brain regions (e.g., IFJ for feature- and object-based attention), and different modulatory influences on visual areas. Different regions of the left parietal cortex are pivotal for feature-based, object-based, and motor attention, in contrast with the more right-hemispheric dominance for spatial attention.

3.4 Attention and expectations

Besides the characterization of different attentional subsystems, recent studies have also focused on the role of expectations (and their violation) for attentional processing. The concepts of expectations/predictions and prediction errors strongly relate to predictive coding frameworks such as the free energy principle (Friston, 2010). Here, the brain is seen as an inference machine, maintaining an internal model of the world to predict percepts, sensations, and events. Crucially, such models are continuously updated after new observations, in particular when events are unexpected (i.e., when they are associated with strong prediction error signals). In Posner's spatial cueing task, where the cue predicts the target location correctly in the majority of the trials, invalidly cued targets require not only a spatial reorienting of attention but also signal an expectancy violation. For instance, the brain response in invalid trials in ventral regions such as the right TPJ is increased with a higher percentage of cue validity (i.e., when invalid trials are more unexpected). Such expectation-dependent effects in right TPJ have been shown by a series of studies looking at either average activity in low probability conditions or the trial-wise modulation of brain responses by probabilities formally derived from computational models (DiQuattro, Sawaki, & Geng, 2014; Dombert et al., 2016; Doricchi et al., 2010; Geng & Mangun, 2011; Kuhns et al., 2017; Mengotti et al., 2017; Vossel et al., 2012; 2015). The activity of right TPJ during spatial attention was shown to be parametrically modulated by the model-derived probability that the cue will be valid, showing stronger activation with increasing cue predictability in invalid trials (i.e., stronger right TPJ activity when invalid trials are less expected) and an inverse pattern for valid trials (Dombert et al., 2016; Kuhns et al., 2017; Vossel et al., 2015). Moreover, an online TMS study interfering with the activity of right TPJ confirmed the involvement of this region in expectation-dependent attention and suggested its involvement in a later stage of stimulus processing, when the updating of predictions may occur (Mengotti et al., 2017). Using DCM in an attentional capture task including feature-based distracters, DiQuattro et al. (2014) suggested that the appearance of the target had an excitatory effect on FEF, but a weakly suppressive effect on TPJ, and that the appearance of the distractor modulated only the connection from FEF to TPJ and not the connection from TPJ to FEF. These results imply that TPJ does not serve the role of informing the dorsal system of the need for reorienting attention. Instead, it is the dorsal system that exerts top-down attentional control over the ventral system during focused attention. TPJ may then instead be involved in post-perceptual updating when relevant unexpected stimuli occur (Stöttinger, Aichhorn, Anderson, & Danckert, 2018). These results are not restricted to the right hemisphere since the left TPJ and IFG have also been shown to be involved in updating expectations (Doricchi et al., 2010; DiQuattro & Geng, 2011). Combined TMS-fMRI evidence (Leitão et al., 2015) showing the influence of right IPS onto right TPJ (and not the other way around) further supports the idea of an involvement of right TPJ for updating in a later stage of processing than the dorsal system.

Additionally, results showed that the right IFG activity and the connectivity between right TPJ and right IFG were modulated by the degree of cue validity (Doricchi et al., 2010; Vossel et al., 2012). Changes in resting-state functional connectivity of right TPJ with right IPS and left TPJ have also been associated with the speed of the updating of predictions about cue validity in a spatial cueing paradigm (Käsbauer et al., 2020).

There is also evidence from fMRI studies (Shulman et al., 2009; Vossel et al., 2015) for an involvement of the basal ganglia in attentional reorienting based on cue-induced expectations, extending the network beyond the cortex.

Taken together, the responses in dorsal and ventral systems are crucially shaped by contextual factors such as probabilistic expectations and prediction errors about the appearance of relevant stimuli. These results are highly relevant for understanding the dynamics of the interaction between both systems and identifying the exact role of the ventral system during the deployment of attention. More specifically, ventral regions such as TPJ may be involved in the mere reorienting of attention to unexpected targets and in updating expectations after new observations. This has important implications for our understanding of the pathomechanisms underlying the spatial neglect syndrome, which may not only be attributed to purely attentional deficits in orienting and reorienting, but also to impairments in updating internal models and learning from recent observations.

4. Dysfunctions of the attentional systems after stroke, hemispheric imbalance, and new approaches for enhancing recovery of function

Spatial neglect is characterized by deficits in attending and responding to events in the contralesional space (for a comprehensive review, see Halligan et al., 2003; Corbetta & Shulman, 2011). While neglect can occur after left- or right-hemispheric lesions, it is more persistent after damage to the right hemisphere (Bowen, McKenna, & Tallis, 1999; Ringman et al., 2004). Since neglect cannot be attributed to a failure of the sensory systems (e.g., hemianopia), many authors regard the syndrome as an attentional disorder. In contrast to hemianopia patients, stimulus detection in contralesional space can be facilitated transiently with spatial cues in patients with neglect. However, in Posner's spatial cueing paradigm, neglect patients are particularly impaired when attention needs to be reoriented from the ipsilesional to the contralesional hemispace after invalid cues (Posner, Walker, Friedrich, & Rafal, 1984). For this reason, neglect has been viewed as a deficit in disengaging attention from ipsilateral stimuli. More recent studies suggest that neglect may also be related to deficits in updating mental models (Danckert, Stöttinger, Quehl, & Anderson, 2012; Shaqiri & Anderson, 2012; Stöttinger et al., 2014; for a review see Shaqiri, Anderson, & Danckert, 2013). The latter would be consistent with the studies mentioned above in healthy volunteers showing that ventral parietal regions such as right TPJ are involved in updating expectations after new observations.

4.1 Neuroanatomy and hemispheric imbalance in spatial neglect

Numerous studies have shown that neglect cannot be ascribed to damage to one circumscribed brain region (for meta-analyses see Chechlacz, Rotshtein, & Humphreys, 2012; Molenberghs, Sale, & Mattingley, 2012). Even lesions confined to subcortical areas such as the basal ganglia (in particular putamen and caudate nucleus) and the thalamus can lead to spatial neglect and attentional orienting deficits (Karnath, Himmelbach, & Rorden, 2002; Maeshima & Osawa, 2018; Rafal & Posner, 1987; Sakashita, 1991).

Regarding the cortical attention networks, lesions to regions of the ventral network, involving the right inferior parietal lobule including right TPJ and surrounding areas, but also superior temporal and ventral frontal cortex, have most consistently and reliably been associated with spatial neglect. In line with the clinical picture of neglect, neuroimaging work in neglect patients has suggested that lesions to the right-lateralized ventral network cause a hemispheric imbalance of brain activity (hyperactivation of the left, hypoactivation of the right hemisphere) of the (unlesioned) dorsal network (Corbetta et al. 2005). This imbalance is also visible in tonic alpha-band activity measured with EEG (Lasaponara, Pinto, Aiello, Tomaiuolo, & Doricchi, 2019). However, an fMRI study of right hemisphere damaged patients with and without neglect has questioned the specificity of the hemispheric imbalance for neglect (Umarova et al., 2011). Also, rare focal lesions to the IPS (Gillebert et al., 2011) or more generally to regions of the dorsal system (Ptak & Schnider, 2010) can lead to reorienting deficits in spatial cueing paradigms.
There is also significant evidence that lesions to white matter fiber tracts such as the SLF connecting the ventral and dorsal fronto-parietal network might contribute to the emergence of neglect symptoms (Corbetta et al., 2015; De Schotten et al., 2014; Doricchi & Tomaiuolo, 2003; He et al., 2007; Leibovitch et al., 1998; Lunven et al., 2015; Ptak & Schnider, 2010; Ramsey et al., 2017; Thiebaut de Schotten et al., 2005). Two longitudinal studies tested stroke patients in their acute, subacute (< 3 months from stroke onset), and chronic phase (one year from onset; Lunven et al., 2015; Ramsey et al., 2017). Results indicated that damage to the SLF, especially the SLF II and SLF III branches, was consistently associated with symptoms of spatial neglect and attention deficits. In the study by Lunven et al. (2015), damage to SLF II-III was related to spatial neglect and correlated with its severity. In contrast, microstructural alterations of the white matter of the splenium of the corpus callosum were associated with a poor recovery in the chronic phase, highlighting the importance of interhemispheric connectivity. Along the same line, damage to SLF II-III and the arcuate fasciculus further predicted worse recovery from attentional deficits (Ramsey et al., 2017). Additionally, there is evidence that microstructural alterations of the white matter of the (undamaged) left hemisphere are associated with worse recovery of spatial neglect symptoms in the acute phase (Umarova et al., 2014).

Recent theoretical computational modeling work within predictive coding frameworks (Parr & Friston, 2018) successfully simulated the behavior of neglect patients (saccadic behavior in cancellation tasks), improving our understanding of the disorder. In particular, these simulations showed how different functional lesions to the model (corresponding anatomically to different white matter connections) could lead to the same pattern of deficits in the exploration of the contralesional hemispace. However, simulated lesions to SLF II produced a specific behavioral pattern that could be distinguished from other types of simulated lesions based on synthetic saccade data.

Furthermore, lesions to the parietal inferior-to-superior tract (PIST) might be related to neglect symptoms, together with reduced functioning of regions of the intact dorsal system in the superior parietal lobe after ventral parietal lesions (Corbetta et al., 2005). This intraparietal disconnection presumably disrupts the interplay between dorsal and ventral systems within the right parietal cortex, preventing the ventral system from signaling salient information to the dorsal system. Lesions to PIST could also explain neglect cases caused by focal lesions to the intraparietal sulcus (Gillebert et al., 2011).

In addition to structural imaging, resting-state functional connectivity and other connectivity-based approaches have been widely used to investigate the disruption of functional network brain activity and its correlation with behavioral deficits following stroke (Adhikari et al., 2017; Baldassarre et al., 2014, 2016; Carter et al., 2010; He et al., 2007; Siegel et al., 2016; for reviews Grefkes & Fink, 2014; Corbetta, Siegel, & Shulman, 2018). As mentioned above, focal lesions also have remote effects on other structurally intact brain regions. Particularly for higher-order integrative cognitive functions, such as attention or memory, the amount of variance of the behavioral deficit explained by lesion location or lesion size was smaller than for motor functions (Corbetta et al., 2015). Siegel et al. (2016) showed that different cognitive deficits could be predicted by either functional connectivity measures or lesion location. Memory deficits could be better predicted by functional connectivity, whereas motor and visual deficits could be better predicted by lesion location. Attention and language deficits could be equally predicted by both variables, with a tendency in favor of functional connectivity as a better predictor for attention deficits. Besides, this study showed that stroke patients had decreased interhemispheric functional connectivity compared to healthy controls and that this decrease predicted cognitive deficits, supporting the interhemispheric competition hypothesis.

Further studies showed that attention deficits and the severity of spatial neglect were associated with reduced interhemispheric functional connectivity in different attentional and sensory-motor networks (Baldassarre et al., 2014; Ramsey et al., 2016; see Figure 3A), but particularly in the dorsal network (Baldassarre et al., 2016; Carter et al., 2010). Moreover, some studies have highlighted the role of intrahemispheric connectivity (Baldassarre et al., 2014; Siegel et al., 2016). Changes in functional connectivity after stroke can also predict recovery (He et al., 2007; Ramsey et al., 2016; Umarova et al., 2016). Recovery of attentional functions was accompanied by a restoration of interhemispheric connectivity in the dorsal network, but not in the ventral network (He et al., 2007). More recent results from a longitudinal study (Ramsey et al., 2016; see Figure 3B) showed that improvement of attentional deficits during the first year after stroke was associated with increased interhemispheric connectivity in the dorsal network (but also in visual, auditory and motor networks), as well as with reduced intrahemispheric connectivity between the dorsal and the default mode network.

These results suggest that spatial neglect is caused by widespread dysfunction and disconnection of the fronto-parietal attentional networks. Disrupted structural and functional interhemispheric and intrahemispheric connectivity can predict neglect as well as its recovery. However, it should be noted that most of the research has focused on neglect caused by lesions to the right hemisphere. Therefore, it is still unclear how these effects would look like in patients with neglect after left-hemisphere damage (but see Beume et al., 2017 for a recent study).

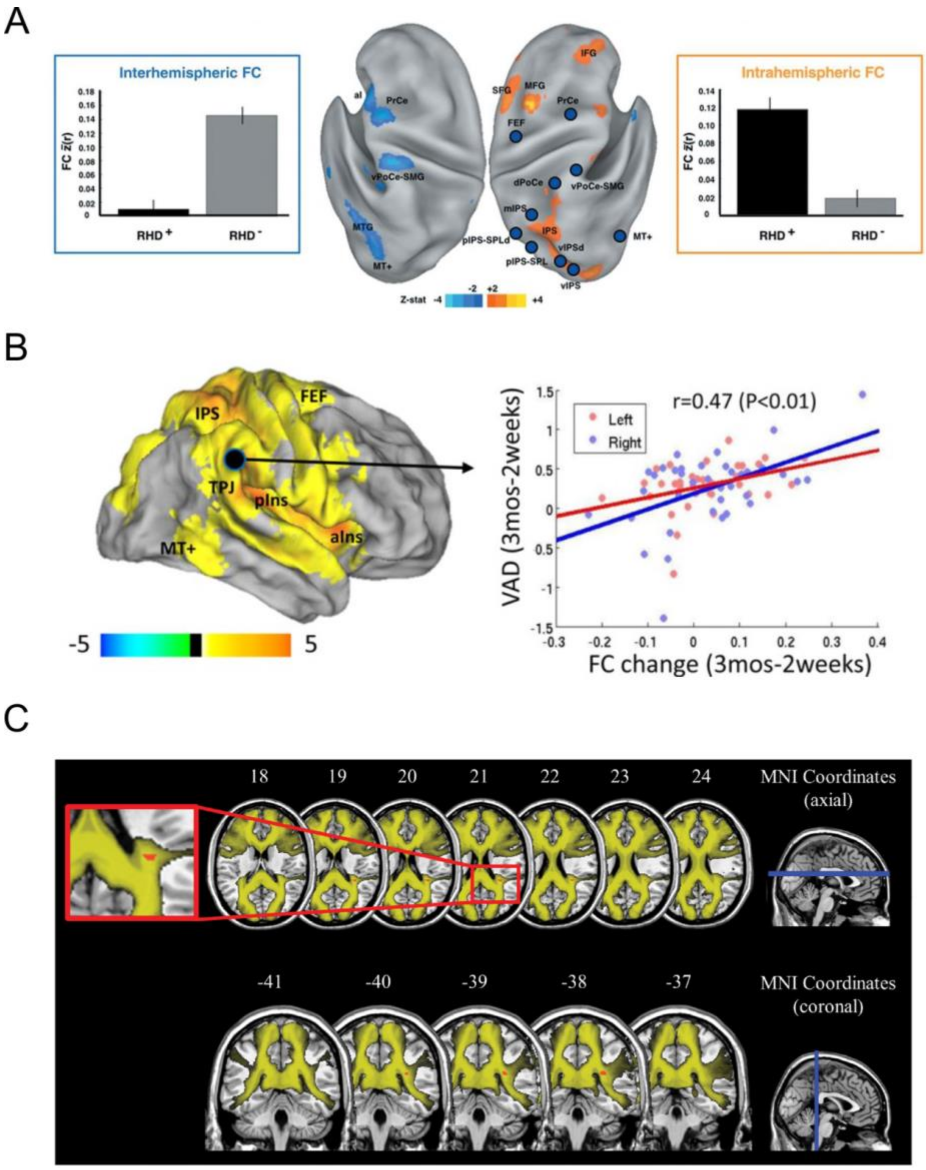

Figure 3. A) Functional connectivity (FC) of the dorsal attention network in the right-hemisphere damaged patients with (RHD+) and without (RHD-) neglect. The blue circles indicate the nodes of the dorsal attention network (DAN) used to compute the functional connectivity. Surface regions in blue-cyan (orange-yellow) color indicate lower (higher) functional connectivity in patients with neglect. The left bar graph (blue frame) depicts the interhemispheric functional connectivity between the dorsal network nodes in the right hemisphere and the blue-cyan regions in the left hemisphere. Patients with neglect showed reduced interhemispheric functional connectivity. The right bar graph (orange frame) depicts the intrahemispheric functional connectivity between the dorsal network nodes in the right hemisphere and the orange-yellow regions in the right hemisphere. Patients with neglect showed increased intrahemispheric functional connectivity. vIPSd: ventral intraparietal sulcus dorsal portion; MT+: middle temporal area; MTG: middle temporal gyrus; pIPS-SPL: posterior intraparietal sulcus-superior parietal lobule; pIPS-SPLd: posterior intraparietal sulcus-superior parietal lobule dorsal portion; mIPS: middle intraparietal sulcus; dPoCe: dorsal post-central gyrus; vPoCe-SMG: ventral post-central gyrus- supramarginal gyrus; PrCe: precentral gyrus; FEF: frontal eye fields; MFG: middle frontal gyrus; SFG: superior frontal gyrus; IFG: inferior frontal gyrus; aI: anterior insula. Modified and reprinted with permission of Oxford University Press from Baldassarre et al. (2014). **B)** Functional connectivity (FC) change and recovery of

the visual attention deficit (VAD) in patients from 2 weeks to 3 months after stroke. The change in interhemispheric functional connectivity between selected nodes in the dorsal attention/motor networks of the left hemisphere and regions of the right hemisphere was computed and correlated with the change in the severity of the visual attention deficit (significant regions are shown in yellow-orange, indicating a positive correlation). The scatterplot depicts the correlation of the change in the average interhemispheric functional connectivity (i.e., the connectivity between the right TPJ region (black circle) and selected nodes in the left hemisphere (not shown)) and the improvement in visual attention deficit. Higher VAD scores indicate better behavioral performance. Blue dots indicate single patients with right-hemisphere damage and red dots patients with left-hemisphere damage. FEF: frontal eye fields; IPS: intraparietal sulcus; TPJ: temporoparietal junction; pIns: posterior insula; aIns: anterior insula; MT+: middle temporal complex. Modified and reprinted with permission from Ramsey et al. (2016). Copyright (2016) American Neurological Association. **C)** Lesion correlates of individual differences in the responsiveness to TMS treatment in right-hemisphere damaged patients. Voxel-based lesion-symptom mapping indicated that the posterior part of the corpus callosum was significantly more often lesioned in patients who did not respond to TMS treatment. Modified and reprinted with permission of Oxford University Press from Nyffeler et al. (2019).

4.2 Noninvasive brain stimulation approaches for recovery

The interhemispheric competition framework also provides the rationale for studies aiming at ameliorating neglect symptoms with neurostimulation or neuromodulation. The idea is that techniques such as continuous theta-burst TMS or cathodal tDCS can reduce the hyperactivation of the contralesional (left) hemisphere (or increase the activity of the hypoactivated ipsilesional (right) hemisphere) and thereby improve neglect. Overall, these studies were generally successful in enhancing or accelerating recovery from spatial neglect and promoting daily living abilities (Cazzoli et al., 2012; 2015; Koch et al., 2008; 2012; Sparing et al., 2009; Nyffeler et al., 2019).

First direct physiological evidence of the hyperexcitability of the left parietal cortex in patients with neglect came from a paired-pulse TMS study (Koch et al., 2008). In paired-pulse protocols, a conditioning TMS pulse is delivered to a brain region shortly before a second TMS pulse is delivered to another brain region. Based on the timing between the two pulses and the intensity of the stimulation, it is possible to record changes in the excitability of the second stimulated region. Koch et al. (2008) applied the conditioning TMS pulse to the left PPC and recorded the motor evoked potentials (MEPs) after stimulating the left motor cortex. Patients with spatial neglect had higher MEP amplitudes after delivery of the conditioning pulse to left PPC than patients without neglect and healthy controls, indicating hyperexcitability of the left parietal cortex. In a second experiment, repetitive TMS was administered to inhibit the left PPC activity before the paired-pulse protocol. Results showed a normalization of left PPC activity in spatial neglect patients, together with an improvement of neglect symptoms after TMS.

Concerning the duration of the TMS-induced improvement from spatial neglect, studies reported long-lasting effects from three to six weeks (Cazzoli et al., 2012; Koch et al., 2012; Nyffeler et al., 2019) with subsequent stabilization of the improvement achieved. In a recent study, Nyffeler et al. (2019; see Figure 3C) showed that the application theta-burst TMS accelerated the recovery in patients with spatial neglect so that most of them reached the level of performance and disability of less impaired patients without neglect in about six weeks after the TMS protocol administration. In this study, two critical issues were addressed: the amount of stimulation and the individual differences in the responsiveness to the TMS protocol. Results showed that doubling the number of sessions and TMS trains administered did not lead to better results. However, not all patients showed the same level of improvement following TMS administration. Almost one-third of the patients were classified as non-responders, as their recovery speed was not distinguishable from that of patients who did not receive TMS. A lesion analysis comparing responders and non-responders showed that lesions to the posterior part of the corpus callosum (connecting the superior parietal lobules) were associated with non-responsiveness to the TMS protocol. This result, in line with Lunven et al. (2015) mentioned above, highlights the importance of intact transcallosal fibers for better and faster recovery. However, it also suggests that the cTBS effect might go beyond reducing the hyperactive left parietal activity by additionally boosting the post-lesional depressed interhemispheric communication (see also Bartolomeo, 2019).

From the results of these studies, we conclude that neurostimulation and neuromodulation protocols reducing contralesional hyperactivity ameliorate spatial neglect. These protocols constitute a new and promising approach to boost recovery and reduce disabilities associated with spatial neglect. Almost all the studies discussed above stimulated the spared contralesional hemisphere. In contrast, data concerning the neurostimulation or neuromodulation of the ipsilesional hemisphere is lacking (but see Sparing et al., 2009). However, for the stimulation studies, we cannot exclude the possibility of a spread of activation to other regions of the network or the contralateral hemisphere. Data suggest that the efficacy of these approaches may critically depend on the integrity of transcallosal fibers connecting both parietal cortices. The findings in stroke patients also mostly confirm the crucial role of inter- and intrahemispheric connectivity shown in neuroimaging and neurostimulation studies with healthy subjects.

5. Conclusions

Traditional views, substantially influenced by lesion and neuroimaging studies, considered the brain's spatial attention systems - and especially the ventral system - right-lateralized. Indeed, evidence for a right-hemispheric dominance can be found even for the bilaterally organized dorsal fronto-parietal attention system. However, more recent work has shown that left-hemispheric regions also play a crucial role in attentional functions, particularly for non-spatial and motor attention. Furthermore, recent studies have demonstrated that both interhemispheric and intrahemispheric connectivity, as well as balanced hemispheric activity, are critical for efficient and flexible deployment of attention. Disconnection and activity imbalances give rise to spatial neglect and impact on its recovery. These network dysfunctions can be ameliorated with neurostimulation techniques, thereby offering new promising therapeutic approaches for stroke-induced disorders such as spatial neglect. However, interindividual variability in the responsiveness to these interventions is high and may crucially be related to the integrity of structural inter- and intrahemispheric connections. These novel findings will motivate further investigations and eventually lead to the development of personalized treatment protocols for stroke-induced attentional deficits.

Acknowledgements

We are grateful to our colleagues from the INM-3 for valuable support and discussions.

Funding

This work was supported by funding from the Federal Ministry of Education and Research to SV (BMBF, 01GQ1401).

References

Adhikari, M. H., Hacker, C. D., Siegel, J. S., Griffa, A., Hagmann, P., Deco, G., & Corbetta, M. (2017). Decreased integration and information capacity in stroke measured by whole brain models of resting state activity. *Brain*, *140*(4), 1068–1085. https://doi.org/10.1093/brain/awx021

Ahrens, M.-M., Veniero, D., Freund, I. M., Harvey, M., & Thut, G. (2019). Both dorsal and ventral attention network nodes are implicated in exogenously driven visuospatial anticipation. *Cortex*, *117*, 168–181.

Anderson E.J., & Rees G. (2011) Neural correlates of spatial orienting in the human superior colliculus. *Journal of Neurophysiol*ogy, 106(5):2273-2284. doi:10.1152/jn.00286.2011

Arrington, C. M., Carr, T. H., Mayer, A. R., & Rao, S. M. (2000). Neural Mechanisms of Visual Attention: Object-Based Selection of a Region in Space. *Journal of Cognitive Neuroscience*, *12*, 106–117. https://doi.org/10.1016/j.jval.2014.08.1939

Astafiev, S. V, Shulman, G. L., Stanley, C. M., Snyder, A. Z., Van Essen, D. C., & Corbetta, M. (2003). Functional Organization of Human Intraparietal and Frontal Cortex for Attending, Looking, and Pointing. The Journal of Neuroscience, 23(11), 4689–4699. https://doi.org/10.1177/0011128702048003001

Baldassarre, A., Ramsey, L., Hacker, C. L., Callejas, A., Astafiev, S. V., Metcalf, N. V., … Corbetta, M. (2014). Large-scale changes in network interactions as a physiological signature of spatial neglect. *Brain*, *137*(12), 3267–3283. https://doi.org/10.1093/brain/awu297

Baldassarre, A., Ramsey, L., Rengachary, J., Zinn, K., Siegel, J. S., Metcalf, N. V., … Shulman, G. L. (2016). Dissociated functional connectivity profiles for motor and attention deficits in acute right-hemisphere stroke. *Brain*, *139*(7), 2024–2038. https://doi.org/10.1093/brain/aww107

Baldauf, D., & Desimone, R. (2014). Neural Mechanisms of Object-Based Attention. *Science*, *1268*(April), 424–428.

Bartolomeo, P. (2019). Visual neglect: getting the hemispheres to talk to each other. *Brain*, *142*(4), 834–846. https://doi.org/10.1093/brain/awz068

Bartolomeo, P., & Seidel Malkinson, T. (2019). Hemispheric lateralization of attention processes in the human brain. *Current Opinion in Psychology*, *29*(January), 90–96. https://doi.org/10.1016/j.copsyc.2018.12.023

Beume, L. A., Martin, M., Kaller, C. P., Klöppel, S., Schmidt, C. S. M., Urbach, H., … Umarova, R. M. (2017). Visual neglect after left-hemispheric lesions: a voxel-based lesion–symptom mapping study in 121 acute stroke patients. *Experimental Brain Research*, *235*(1), 83–95. https://doi.org/10.1007/s00221-016-4771-9

Bien, N., Goebel, R., & Sack, A. T. (2012). Extinguishing extinction: Hemispheric differences in the modulation of TMS-induced visual extinction by directing covert spatial attention. *Journal of Cognitive Neuroscience*, *24*(4), 809–818. https://doi.org/10.1162/jocn_a_00179

Bourgeois, A., Chica, A. B., Valero-Cabré, A., & Bartolomeo, P. (2013a). Cortical control of inhibition of return: causal evidence for task-dependent modulations by dorsal and ventral parietal regions. Cortex, 49(8), 2229-2238. doi: 10.1016/j.cortex.2012.10.017

Bourgeois, A., Chica, A. B., Valero-Cabré, A., & Bartolomeo, P. (2013b). Cortical control of Inhibition of Return: exploring the causal contributions of the left parietal cortex. Cortex, 49(10), 2927-2934. doi: 10.1016/j.cortex.2013.08.004

Bowen, A., McKenna, K., & Tallis, R. C. (1999). Reasons for variability in the reported rate of occurrence of unilateral spatial neglect after stroke. *Stroke*, *30*(6), 1196–1202. https://doi.org/10.1161/01.STR.30.6.1196

Bressler, S. L., Tang, W., Sylvester, C. M., Shulman, G. L., & Corbetta, M. (2008). Top-Down Control of Human Visual Cortex by Frontal and Parietal Cortex in Anticipatory Visual Spatial Attention. *Journal of Neuroscience*, *28*(40), 10056–10061. https://doi.org/10.1523/jneurosci.1776-08.2008

Capotosto, P., Babiloni, C., Romani, G. L., & Corbetta, M. (2012). Differential contribution of right and left parietal cortex to the control of spatial attention: A simultaneous EEG-rTMS study. *Cerebral Cortex*, *22*(2), 446–454. https://doi.org/10.1093/cercor/bhr127

Carter, A. R., Astafiev, S. V., Lang, C. E., Connor, L. T., Rengachary, J., Strube, M. J., … Corbetta, M. (2010). Resting interhemispheric functional magnetic resonance imaging connectivity predicts performance after stroke. *Annals of Neurology*, *67*(3), 365–375. https://doi.org/10.1002/ana.21905

Catani, M., Robertsson, N., Beyh, A., Huynh, V., de Santiago Requejo, F., Howells, H., … Dell'Acqua, F. (2017). Short parietal lobe connections of the human and monkey brain. *Cortex*, *97*, 339–357. https://doi.org/10.1016/j.cortex.2017.10.022

Cazzoli, D., & Chechlacz, M. (2017). A matter of hand: Causal links between hand dominance, structural organization of fronto-parietal attention networks, and variability in behavioural responses to transcranial magnetic stimulation. *Cortex*, *86*, 230–246. https://doi.org/10.1016/j.cortex.2016.06.015

Cazzoli, D., Müri, R. M., Schumacher, R., Von Arx, S., Chaves, S., Gutbrod, K., … Nyffeler, T. (2012). Theta burst stimulation reduces disability during the activities of daily living in spatial neglect. *Brain*, *135*(11), 3426–3439. https://doi.org/10.1093/brain/aws182

Cazzoli, D., Rosenthal, C. R., Kennard, C., Zito, G. A., Hopfner, S., Mueri, R. M., & Nyffeler, T. (2015). Theta burst stimulation improves overt visual search in spatial neglect independently of attentional load. *Cortex*, *73*, 317–329.

Chanes, L., Chica, A. B., Quentin, R., & Valero-Cabré, A. (2012). Manipulation of pre-target activity on the right frontal eye field enhances conscious visual perception in humans. *PloS One*, *7*(5), 1–9. https://doi.org/10.1371/journal.pone.0036232

Chang, C. F., Hsu, T. Y., Tseng, P., Liang, W. K., Tzeng, O. J. L., Hung, D. L., & Juan, C. H. (2013). Right temporoparietal junction and attentional reorienting. *Human Brain Mapping*, *34*(4), 869–877. https://doi.org/10.1002/hbm.21476

Chechlacz, M., Humphreys, G. W., Sotiropoulos, S. N., Kennard, C., & Cazzoli, D. (2015). Structural Organization of the Corpus Callosum Predicts Attentional Shifts after Continuous Theta Burst Stimulation. *Journal of Neuroscience*, *35*(46), 15353–15368. https://doi.org/10.1523/jneurosci.2610-15.2015

Chechlacz, M., Rotshtein, P., & Humphreys, G. W. (2012). Neuroanatomical Dissections of Unilateral Visual Neglect Symptoms: ALE Meta-Analysis of Lesion-Symptom Mapping. *Frontiers in Human Neuroscience*, *6*(August), 1–20. https://doi.org/10.3389/fnhum.2012.00230

Chica, A. B., Bartolomeo, P., & Valero-Cabré, A. (2011). Dorsal and ventral parietal contributions to spatial orienting in the human brain. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *31*(22), 8143–8149. https://doi.org/10.1523/JNEUROSCI.5463-10.2010

Chica, A. B., Valero-Cabré, A., Paz-Alonso, P. M., & Bartolomeo, P. (2014). Causal contributions of the left frontal eye field to conscious perception. *Cerebral Cortex*, *24*(3), 745–753. https://doi.org/10.1093/cercor/bhs357

Cohen, E. H., & Tong, F. (2015). Neural mechanisms of object-based attention. *Cerebral Cortex*, *25*(4), 1080–1092. https://doi.org/10.1093/cercor/bht303

Corbetta, M., Kincade, M. J., Lewis, C., Snyder, A. Z., & Sapir, A. (2005). Neural basis and recovery of spatial attention deficits in spatial neglect. *Nature Neuroscience*, *8*(11), 1603–1610. https://doi.org/10.1038/nn1574

Corbetta, M., Patel, G., & Shulman, G. L. (2008). The Reorienting System of the Human Brain: From Environment to Theory of Mind. *Neuron*, *58*(3), 306–324. https://doi.org/10.1016/j.neuron.2008.04.017

Corbetta, M., Ramsey, L., Callejas, A., Baldassarre, A., Hacker, C. D., Siegel, J. S., … Shulman, G. L. (2015). Common behavioral clusters and subcortical anatomy in stroke. *Neuron*, *85*(5), 927–941. https://doi.org/10.1016/j.neuron.2015.02.027

Corbetta, M., & Shulman, G. L. (2011). *Spatial neglect and attention networks. Annual review of neuroscience* (Vol. 34). https://doi.org/10.1146/annurev-neuro-061010-113731

Corbetta, M., & Shulman, G. L. (2002). Control of Goal-Directed and Stimulus-Driven Attention in the Brain. *Nature Reviews Neuroscience*, *3*(3), 215–229. https://doi.org/10.1038/nrn755

Corbetta, M., Siegel, J. S., & Shulman, G. L. (2018). On the low dimensionality of behavioral deficits and alterations of brain network connectivity after focal injury. *Cortex*, *107*, 229–237. https://doi.org/10.1016/j.cortex.2017.12.017

Danckert, J., Stöttinger, E., Quehl, N., & Anderson, B. (2012). Right hemisphere brain damage impairs strategy updating. *Cerebral Cortex*, *22*(12), 2745–2760. https://doi.org/10.1093/cercor/bhr351

D'Andrea, A., Chella, F., Marshall, T. R., Pizzella, V., Romani, G. L., Jensen, O., & Marzetti, L. (2019). Alpha and alpha-beta phase synchronization mediate the recruitment of the visuospatial attention network through the Superior Longitudinal Fasciculus. *NeuroImage*, *188*(December 2018), 722–732. https://doi.org/10.1016/j.neuroimage.2018.12.056

Davidesco, I., Ramot, M., Harel, M., Malach, R., Kramer, U., Kipervasser, S., … Fried, I. (2013). Spatial and object-based attention modulates broadband high-frequency responses across the human visual cortical hierarchy. *Journal of Neuroscience*, *33*(3), 1228–1240. https://doi.org/10.1523/JNEUROSCI.3181-12.2013

DiQuattro, N. E., & Geng, J. J. (2011). Contextual Knowledge Configures Attentional Control Networks. *Journal of Neuroscience*, *31*(49), 18026–18035. https://doi.org/10.1523/jneurosci.4040-11.2011

Diquattro, N. E., Sawaki, R., & Geng, J. J. (2014). Effective connectivity during feature-based attentional capture: Evidence against the attentional reorienting hypothesis of TPJ. *Cerebral Cortex*, *24*(12), 3131–3141. https://doi.org/10.1093/cercor/bht172

Dombert, P. L., Kuhns, A., Mengotti, P., Fink, G. R., & Vossel, S. (2016). Functional mechanisms of probabilistic inference in feature-and space-based attentional systems. *NeuroImage*, *142*, 553–564. https://doi.org/10.1016/j.neuroimage.2016.08.010

Doricchi, F., Macci, E., Silvetti, M., & Macaluso, E. (2010). Neural correlates of the spatial and expectancy components of endogenous and stimulus-driven orienting of attention in the posner task. *Cerebral Cortex*, *20*(7), 1574–1585. https://doi.org/10.1093/cercor/bhp215

Doricchi, F., & Tomaiuolo, F. (2003). The anatomy of neglect without hemianopia: a key role for parietal-frontal disconnection? NeuroReport, 14(17), 2239-2243.

Dragone, A., Lasaponara, S., Silvetti, M., Macaluso, E., & Doricchi, F. (2015). Selective reorienting response of the left hemisphere to invalid visual targets in the right side of space: Relevance for the spatial neglect. *Cortex*, *65*, 31–35.

Duecker, F., Formisano, E., & Sack, A. T. (2013). Hemispheric Differences in the Voluntary Control of Spatial Attention: Direct Evidence for a Right-Hemispheric Dominance within Frontal Cortex. *Journal of Cognitive Neuroscience*, *25*(8), 1332–1342. https://doi.org/10.1162/jocn

Duecker, F., Schuhmann, T., Bien, N., Jacobs, C., & Sack, A. T. (2017). Moving Beyond Attentional Biases: Shifting the Interhemispheric Balance between Left and Right Posterior Parietal Cortex Modulates Attentional Control Processes. *Journal of Cognitive Neuroscience*, *26*(3), 194–198. https://doi.org/10.1162/jocn

Dugué, L., Merriam, E. P., Heeger, D. J., & Carrasco, M. (2017). Specific Visual Subregions of TPJ Mediate Reorienting of Spatial Attention. *Cerebral Cortex*, (Table 1), 1–16. https://doi.org/10.1093/cercor/bhx140

Egly, R., Driver, J., & Rafal, R. D. (1994). Shifting Visual Attention Between Objects and Locations: Evidence From Normal and Parietal Lesion Subjects. *Journal of Experimental Psychology: General*, *123*(2), 161–177. https://doi.org/10.1037/0096-3445.123.2.161

Egner, T., Monti, J. M. P., Trittschuh, E. H., Wieneke, C. A., Hirsch, J., & Mesulam, M.-M. (2008). Neural Integration of Top-Down Spatial and Feature-Based Information in Visual Search. *Journal of Neuroscience*, *28*(24), 6141–6151. https://doi.org/10.1523/JNEUROSCI.1262-08.2008

Feldman, H., & Friston, K. J. (2010). Attention, Uncertainty, and Free-Energy. *Frontiers in Human Neuroscience*, *4*(December), 1–23. https://doi.org/10.3389/fnhum.2010.00215

Filmer, H. L., Dux, P. E., & Mattingley, J. B. (2015). Dissociable effects of anodal and cathodal tDCS reveal distinct functional roles for right parietal cortex in the detection of single and competing stimuli. *Neuropsychologia*, *74*, 120–126. https://doi.org/10.1016/j.neuropsychologia.2015.01.038

Fox, M. D., Corbetta, M., Snyder, A. Z., Vincent, J. L., & Raichle, M. E. (2006). Spontaneous neuronal activity distinguishes human dorsal and ventral attention systems. *Proceedings of the National Academy of Sciences*, *103*(25), 9381–9386.

Geng, J. J., & Vossel, S. (2013). Re-evaluating the role of TPJ in attentional control: Contextual updating? *Neuroscience and Biobehavioral Reviews*, *37*(10), 2608–2620. https://doi.org/10.1016/j.neubiorev.2013.08.010

Gillebert, C. R., Mantini, D., Thijs, V., Sunaert, S., Dupont, P., & Vandenberghe, R. (2011). Lesion evidence for the critical role of the intraparietal sulcus in spatial attention. *Brain*, *134*(6), 1694–1709. https://doi.org/10.1093/brain/awr085

Greenberg, A. S., Esterman, M., Wilson, D., Serences, J. T., & Yantis, S. (2010). Control of Spatial and Feature-Based Attention in Frontoparietal Cortex. *Journal of Neuroscience*, *30*(43), 14330–14339. https://doi.org/10.1523/jneurosci.4248-09.2010

Grefkes, C., & Fink, G. R. (2014). Connectivity-based approaches in stroke and recovery of function. *Lancet Neurology*, *13*, 206–216.

Halligan, P. W., Fink, G. R., Marshall, J. C., & Vallar, G. (2003). Spatial cognition: Evidence from visual neglect. *Trends in Cognitive Sciences*, *7*(3), 125–133. https://doi.org/10.1016/S1364-6613(03)00032-9

He, B. J., Snyder, A. Z., Vincent, J. L., Epstein, A., Shulman, G. L., & Corbetta, M. (2007). Breakdown of Functional Connectivity in Frontoparietal Networks Underlies Behavioral Deficits in Spatial Neglect. *Neuron*, *53*(6), 905–918. https://doi.org/10.1016/j.neuron.2007.02.013

Heilman, K. M., & Van den Abell, T. (1980). Right hemisphere dominance for attention: The mechanism underlying hemispheric asymmetries of inattention (neglect). *Neurology*, *30*, 327–330.

Heinen, K., Feredoes, E., Weiskopf, N., Ruff, C. C., & Driver, J. (2014). Direct evidence for attention-dependent influences of the frontal eye-fields on feature-responsive visual cortex. *Cerebral Cortex*, *24*(11), 2815–2821. https://doi.org/10.1093/cercor/bht157

Hesse, M. D., Thiel, C. M., Stephan, K. E., & Fink, G. R. (2006). The left parietal cortex and motor intention: An event-related functional magnetic resonance imaging study. *Neuroscience*, *140*(4), 1209–1221. https://doi.org/10.1016/j.neuroscience.2006.03.030

Hilgetag, C. C., Théoret, H., & Pascual-Leone, A. (2001). Enhanced visual spatial attention ipsilateral to rTMS-induced “virtual lesions” of human parietal cortex. *Nature Neuroscience*, *4*(9), 953–957. https://doi.org/10.1038/nn0901-953

Howells, H., De Schotten, M. T., Dell’Acqua, F., Beyh, A., Zappalà, G., Leslie, A., … Catani, M. (2018). Frontoparietal tracts linked to lateralized hand preference and manual specialization. *Cerebral Cortex*, *28*(7), 1–13. https://doi.org/10.1093/cercor/bhy040

Igelström, K. M., Webb, T. W., & Graziano, M. S. A. (2015). Neural Processes in the Human Temporoparietal Cortex Separated by Localized Independent Component Analysis. *Journal of Neuroscience*, *35*(25), 9432–9445. https://doi.org/10.1523/JNEUROSCI.0551-15.2015

Jehee, J. F. M., Brady, D. K., & Tong, F. (2011). Attention Improves Encoding of Task-Relevant Features in the Human Visual Cortex. *Journal of Neuroscience*, *31*(22), 8210–8219. https://doi.org/10.1523/jneurosci.6153-09.2011

Jeong, S. K., & Xu, Y. (2016). The impact of top-down spatial attention on laterality and hemispheric asymmetry in the human parietal cortex. *Journal of Vision*, *16*, 1–21. https://doi.org/10.1167/16.10.2.doi

Käsbauer, A.S., Mengotti, P., Fink, G.R., Vossel, S. (2020). Resting-state Functional Connectivity of the Right Temporoparietal Junction Relates to Belief Updating and Reorienting during Spatial Attention. *Journal of Cognitive Neuroscience, Feb 6*: 1-13.

Karnath, H. O., Himmelbach, M., & Rorden, C. (2002). The subcortical anatomy of human spatial neglect: Putamen, caudate nucleus and pulvinar. *Brain*, *125*(2), 350–360. https://doi.org/10.1093/brain/awf032

Karnath, H. O., & Rorden, C. (2012). The anatomy of spatial neglect. *Neuropsychologia*, *50*(6), 1010–1017. https://doi.org/10.1016/j.neuropsychologia.2011.06.027

Kincade, J. M., Abrams, R. A., Astafiev, S. V., Shulman, G. L., & Corbetta, M. (2005). An Event-Related Functional Magnetic Resonance Imaging Study of Voluntary and Stimulus-Driven Orienting of Attention. *Journal of Neuroscience*, *25*(18), 4593–4604. https://doi.org/10.1523/jneurosci.0236-05.2005

Kinsbourne, M., (1977). Hemi-neglect and hemisphere rivalry. *Adv. Neurol*. 18, 41–49.

Kinsbourne, M. (1987). Mechanisms of unilateral neglect. In *Advances in psychology* (Vol. 45, pp. 69-86). North-Holland.

Koch, G., Bonnì, S., Giacobbe, V., Bucchi, G., Basile, B., Lupo, F., … Caltagirone, C. (2012). Theta-burst stimulation of the left hemisphere accelerates recovery of hemispatial neglect. *Neurology*, *78*(1), 24–30. https://doi.org/10.1212/WNL.0b013e31823ed08f

Koch, G., Cercignani, M., Bonni, S., Giacobbe, V., Bucchi, G., Versace, V., … Bozzali, M. (2011). Asymmetry of Parietal Interhemispheric Connections in Humans. *Journal of Neuroscience*, *31*(24), 8967–8975. https://doi.org/10.1523/jneurosci.6567-10.2011

Koch, G., Oliveri, M., Cheeran, B., Ruge, D., Gerfo, E. Lo, Salerno, S., … Caltagirone, C. (2008). Hyperexcitability of parietal-motor functional connections in the intact left-hemisphere of patients with neglect. *Brain*, *131*(12), 3147–3155. https://doi.org/10.1093/brain/awn273

Kocsis, K., Csete, G., Erdei, Z., Király, A., Szabó, N., Vécsei, L., & Kincses, Z. T. (2019). Lateralisation of the white matter microstructure associated with the hemispheric spatial attention dominance. *PLoS ONE*, *14*(4), 1–15. https://doi.org/10.1371/journal.pone.0216032

Krauzlis, R. J., Lovejoy, L. P., & Zénon, A. (2013). Superior Colliculus and Visual Spatial Attention. *Annual Review of Neuroscience*, *36*(1), 165–182. https://doi.org/10.1146/annurev-neuro-062012-170249

Kucyi, A., Hodaie, M., & Davis, K. D. (2012). Lateralization in intrinsic functional connectivity of the temporoparietal junction with salience- and attention-related brain networks. *Journal of Neurophysiology*, *108*(12), 3382–3392. https://doi.org/10.1152/jn.00674.2012

Kuhns, A. B., Dombert, P. L., Mengotti, P., Fink, G. R., & Vossel, S. (2017). Spatial Attention, Motor Intention, and Bayesian Cue Predictability in the Human Brain. *Journal of Neuroscience*, *37*(21), 5334–5344. https://doi.org/10.1523/JNEUROSCI.3255-16.2017

Lasaponara, S., Pinto, M., Aiello, M., Tomaiuolo, F., & Doricchi, F. (2019). The Hemispheric Distribution of α-Band EEG Activity During Orienting of Attention in Patients with Reduced Awareness of the Left Side of Space (Spatial Neglect). *The Journal of Neuroscience*, *39*(22), 4332–4343. https://doi.org/10.1523/jneurosci.2206-18.2019

Leibovitch, F. S., Black, S. E., Caldwell, C. B., Ebert, P. L., Ehrlich, L. E., & Szalai, J. P. (1998). Brain-behavior correlations in hemispatial neglect using CT and SPECT: the Sunnybrook Stroke Study. Neurology, 50(4), 901-908.

Leitão, J., Thielscher, A., Tünnerhoff, J., & Noppeney, U. (2015). Concurrent TMS-fMRI Reveals Interactions between Dorsal and Ventral Attentional Systems. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *35*(32), 11445–11457. https://doi.org/10.1523/JNEUROSCI.0939-15.2015

Liu, T. (2016). Neural representation of object-specific attentional priority. *NeuroImage*, *129*, 15–24. https://doi.org/10.1016/j.neuroimage.2016.01.034

Lunven, M., & Bartolomeo, P. (2017). Attention and spatial cognition: Neural and anatomical substrates of visual neglect. *Annals of Physical and Rehabilitation Medicine*, *60*(3), 124–129. https://doi.org/10.1016/j.rehab.2016.01.004

Lunven, M., De Schotten, M. T., Bourlon, C., Duret, C., Migliaccio, R., Rode, G., & Bartolomeo, P. (2015). White matter lesional predictors of chronic visual neglect: A longitudinal study. *Brain*, *138*(3), 746–760. https://doi.org/10.1093/brain/awu389

Macaluso, E., & Doricchi, F. (2013). Attention and predictions: control of spatial attention beyond the endogenous-exogenous dichotomy. *Frontiers in Human Neuroscience*, *7*(October), 685. https://doi.org/10.3389/fnhum.2013.00685

Macaluso, E. (2010). Orienting of spatial attention and the interplay between the senses. *Cortex*, *46*(3), 282–297. https://doi.org/10.1016/j.cortex.2009.05.010

Maeshima, S., & Osawa, A. (2018). Thalamic Lesions and Aphasia or Neglect. *Current Neurology and Neuroscience Reports*, *18*(7), 1–6. https://doi.org/10.1007/s11910-018-0844-4

McPeek, R. M., & Keller, E. L. (2004). Deficits in saccade target selection after inactivation of superior colliculus. *Nature Neuroscience*, *7*(7), 757–763. https://doi.org/10.1038/nn1269

Mengotti, P., Dombert, P. L., Fink, G. R., & Vossel, S. (2017). Disruption of the Right Temporoparietal Junction Impairs Probabilistic Belief Updating. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *37*(22), 5419–5428. https://doi.org/10.1523/JNEUROSCI.3683-16.2017

Mesulam, M. M. (1981). A cortical network for directed attention. *Annals of Neurology*, *10*(4), 309–325.

Molenberghs, P., Gillebert, C. R., Peeters, R., & Vandenberghe, R. (2008). Convergence between Lesion-Symptom Mapping and Functional Magnetic Resonance Imaging of Spatially Selective Attention in the Intact Brain. *Journal of Neuroscience*, *28*(13), 3359–3373. https://doi.org/10.1523/jneurosci.5247-07.2008

Molenberghs, P., Sale, M. V., & Mattingley, J. B. (2012). Is there a critical lesion site for unilateral spatial neglect? A meta-analysis using activation likelihood estimation. *Frontiers in Human Neuroscience*, *6*(April), 1–10. https://doi.org/10.3389/fnhum.2012.00078

Nyffeler, T., Vanbellingen, T., Kaufmann, B. C., Pflugshaupt, T., Bauer, D., Frey, J., … Cazzoli, D. (2019). Theta burst stimulation in neglect after stroke: functional outcome and response variability origins. *Brain*, 992–1008. https://doi.org/10.1093/brain/awz029

Parlatini, V., Radua, J., Dell'Acqua, F., Leslie, A., Simmons, A., Murphy, D. G., … Thiebaut de Schotten, M. (2017). Functional segregation and integration within fronto-parietal networks. *NeuroImage*, *146*(January 2016), 367–375. https://doi.org/10.1016/j.neuroimage.2016.08.031

Parr, T., & Friston, K. J. (2018). The Computational Anatomy of Visual Neglect. *Cerebral Cortex*, (December), 1–14. https://doi.org/10.1093/cercor/bhx316

Pascual-Leone, A., Walsh, V., & Rothwell, J. (2000). Transcranial magnetic stimulation in cognitive neuroscience--virtual lesion, chronometry, and functional connectivity. *Current Opinion in Neurobiology*, *10*(2), 232–237. https://doi.org/10.1016/S0959-4388(00)00081-7

Petit, L., Zago, L., Mellet, E., Jobard, G., Crivello, F., Joliot, M., … Tzourio-Mazoyer, N. (2015). Strong rightward lateralization of the dorsal attentional network in left-handers with right sighting-eye: An evolutionary advantage. *Human Brain Mapping*, *36*(3), 1151–1164. https://doi.org/10.1002/hbm.22693

Pilz, K. S., Roggeveen, A. B., Creighton, S. E., Bennett, P. J., & Sekuler, A. B. (2012). How prevalent is object-based attention? *PLoS ONE*, *7*(2). https://doi.org/10.1371/journal.pone.0030693

Posner, M. I. (1980). Orienting of attention. Quarterly journal of experimental psychology, 32(1), 3-25.

Posner, M. I., Walker, J. A., Friedrich, F. J., & Rafal, R. D. (1984). Effects of parietal injury on covert orienting of attention. Journal of neuroscience, 4(7), 1863-1874.

Ptak, R., & Schnider, A. (2010). The Dorsal Attention Network Mediates Orienting toward Behaviorally Relevant Stimuli in Spatial Neglect. *Journal of Neuroscience*, *30*(38), 12557–12565. https://doi.org/10.1523/jneurosci.2722-10.2010

Rafal, R. D., & Posner, M. I. (1987). Deficits in human visual spatial attention following thalamic lesions. *Proceedings of the National Academy of Sciences of the United States of America*, *84*(20), 7349–7353. https://doi.org/10.1073/pnas.84.20.734

Ramsey, L. E., Siegel, J. S., Lang, C. E., Strube, M., Shulman, G. L., & Corbetta, M. (2017). Behavioural clusters and predictors of performance during recovery from stroke. *Nature Human Behaviour*, *1*(3), 1–10. https://doi.org/10.1038/s41562-016-0038

Ramsey, L. E., Siegel, J. S., Baldassarre, A., Metcalf, N. V., Zinn, K., Shulman, G. L., & Corbetta, M. (2016). Normalization of network connectivity in hemispatial neglect recovery. *Annals of Neurology*, *80*(1), 127–141. https://doi.org/10.1002/ana.24690

Rengachary, J., He, B. J., Shulman, G., & Corbetta, M. (2011). A behavioral analysis of spatial neglect and its recovery after stroke. *Frontiers in Human Neuroscience*, *5*, 29.

Reppa, I., Schmidt, W. C., & Leek, E. C. (2012). Successes and failures in producing attentional object-based cueing effects. *Attention, Perception, and Psychophysics*, *74*(1), 43–69. https://doi.org/10.3758/s13414-011-0211-x

Ringman, J. M., Saver, J. L., Woolson, R. F., Clarke, W. R., & Adams, H. P. (2004). Frequency, risk factors, anatomy, and course of unilateral neglect in an acute stroke cohort. *Neurology*, *63*(3), 468-474.

Rounis, E., Yarrow, K., & Rothwell, J. C. (2007). Effects of rTMS conditioning over the fronto-parietal network on motor versus visual attention. *Journal of Cognitive Neuroscience*, *19*(3), 513–524. https://doi.org/10.1162/jocn.2007.19.3.513

Roy, L. B., Sparing, R., Fink, G. R., & Hesse, M. D. (2015). Modulation of attention functions by anodal tDCS on right PPC. *Neuropsychologia*, *74*, 96–107. https://doi.org/10.1016/j.neuropsychologia.2015.02.028

Ruff, C. C., Bestmann, S., Blankenburg, F., Bjoertomt, O., Josephs, O., Weiskopf, N., … Driver, J. (2008). Distinct causal influences of parietal versus frontal areas on human visual cortex: Evidence from concurrent TMS-fMRI. *Cerebral Cortex*, *18*(4), 817–827. https://doi.org/10.1093/cercor/bhm128

Ruff, C. C., Blankenburg, F., Bjoertomt, O., Bestmann, S., Freeman, E., Haynes, J. D., … Driver, J. (2006). Concurrent TMS-fMRI and Psychophysics Reveal Frontal Influences on Human Retinotopic Visual Cortex. *Current Biology*, *16*(15), 1479–1488. https://doi.org/10.1016/j.cub.2006.06.057

Ruff, C. C., Blankenburg, F., Bjoertomt, O., Bestmann, S., Weiskopf, N., & Driver, J. (2009). Hemispheric differences in frontal and parietal influences on human occipital cortex: Direct confirmation with concurrent TMS-fMRI. *Journal of Cognitive Neuroscience*, *21*(6), 1146–1161. https://doi.org/10.1162/jocn.2009.21097

Rushworth, M. F. S., Nixon, P. D., Renowden, S., Wade, D. T., & Passingham, R. E. (1997). The left parietal cortex and attention to action. *Neuropsychologia*, *35*(9), 1261–1273.

Rushworth, M. F., Ellison, A., & Walsh, V. (2001). Complementary localization and lateralization of orienting and motor attention. *Nature Neuroscience*, *4*(6), 656–661. https://doi.org/10.1038/88492

Rushworth, M. F. S., Krams, M., & Passingham, R. E. (2001). The attentional role of the left parietal cortex: the distinct lateralization and localization of motor attention in the human brain. *Journal of Cognitive Neuroscience*, *13*(5), 698–710. https://doi.org/10.1162/089892901750363244

Rushworth, M. F. S., Johansen-Berg, H., Göbel, S. M., & Devlin, J. T. (2003). The left parietal and premotor cortices: Motor attention and selection. *NeuroImage*, *20*(SUPPL. 1). https://doi.org/10.1016/j.neuroimage.2003.09.011

Sakashita, Y. (1991). Visual attentional disturbance with unilateral lesions in the basal ganglia and deep white matter. *Annals of Neurology*, *30*(5), 673–677. https://doi.org/10.1002/ana.410300507

Schenkluhn, B., Ruff, C. C., Heinen, K., & Chambers, C. D. (2008). Parietal Stimulation Decouples Spatial and Feature-Based Attention. *Journal of Neuroscience*, *28*(44), 11106–11110. https://doi.org/10.1523/JNEUROSCI.3591-08.2008

Serences, J. T., & Boynton, G. M. (2007). Feature-Based Attentional Modulations in the Absence of Direct Visual Stimulation. *Neuron*, *55*(2), 301–312. https://doi.org/10.1016/j.neuron.2007.06.015

Serences, J. T., Schwarzbach, J., Courtney, S. M., Golay, X., & Yantis, S. (2004). Control of object-based attention in human cortex. *Cerebral Cortex*, *14*(12), 1346–1357. https://doi.org/10.1093/cercor/bhh095

Shaqiri, A., & Anderson, B. (2013). Priming and statistical learning in right brain damaged patients. *Neuropsychologia*, *51*(13), 2526–2533. https://doi.org/10.1016/j.neuropsychologia.2013.09.024

Shaqiri, A., & Anderson, B. (2012). Spatial probability cuing and right hemisphere damage. *Brain and Cognition*, *80*(3), 352–360. https://doi.org/10.1016/j.bandc.2012.08.006

Shaqiri, A., Anderson, B., & Danckert, J. (2013). Statistical learning as a tool for rehabilitation in spatial neglect. Frontiers in Human Neuroscience, 7(May), 1–15. https://doi.org/10.3389/fnhum.2013.00224

Shomstein, S., & Behrmann, M. (2006). Cortical systems mediating visual attention to both objects and spatial locations. *Proceedings of the National Academy of Sciences*, *103*(30), 11387–11392. https://doi.org/10.1073/pnas.0601813103

Shulman, G. L., Astafiev, S. V., Franke, D., Pope, D. L. W., Snyder, A. Z., McAvoy, M. P., & Corbetta, M. (2009). Interaction of Stimulus-driven reorienting and expectation in ventral and dorsal frontoparietal and basal Ganglia-cortical networks. *Journal of Neuroscience*, *29*(14), 4392–4407. https://doi.org/10.1523/JNEUROSCI.5609-08.2009

Siegel, J. S., Ramsey, L. E., Snyder, A. Z., Metcalf, N. V., Chacko, R. V., Weinberger, K., … Corbetta, M. (2016). Disruptions of network connectivity predict impairment in multiple behavioral domains after stroke. *Proceedings of the National Academy of Sciences*, *113*(30), E4367–E4376. https://doi.org/10.1073/pnas.1521083113

Siegel, M., Donner, T. H., Oostenveld, R., Fries, P., & Engel, A. K. (2008). Neuronal Synchronization along the Dorsal Visual Pathway Reflects the Focus of Spatial Attention. *Neuron*, *60*(4), 709–719. https://doi.org/10.1016/j.neuron.2008.09.010

Siemann, J., Herrmann, M., & Galashan, D. (2018). The effect of feature-based attention on flanker interference processing: An fMRI-constrained source analysis. *Scientific Reports*, *8*(1), 1–18. https://doi.org/10.1038/s41598-018-20049-1

Silver, M. A., & Kastner, S. (2009). Topographic maps in human frontal and parietal cortex. *Trends in Cognitive Sciences*, *13*(11), 488–495. https://doi.org/10.1016/j.tics.2009.08.005

Silvetti, M., Lasaponara, S., Lecce, F., Dragone, A., Macaluso, E., & Doricchi, F. (2017). The Response of the Left Ventral Attentional System to Invalid Targets and its Implication for the Spatial Neglect Syndrome: a Multivariate fMRI Investigation. *Cerebral Cortex*, *27*(8), 3962–3969. https://doi.org/10.1093/cercor/bhw208

Simpson, G. V, Weber, D. L., Dale, C. L., Pantazis, D., Bressler, S. L., Leahy, R. M., & Luks, T. L. (2011). Dynamic activation of frontal, parietal, and sensory regions underlying anticipatory visual spatial attention. *Journal of Neuroscience*, *31*(39), 13880–13889. https://doi.org/10.1523/JNEUROSCI.1519-10.2011

Sparing, R., Thimm, M., Hesse, M. D., Küst, J., Karbe, H., & Fink, G. R. (2009). Bidirectional alterations of interhemispheric parietal balance by non-invasive cortical stimulation. *Brain*, *132*(11), 3011–3020. https://doi.org/10.1093/brain/awp154

Sreenivasana, V., & Sridharana, D. (2019). Subcortical connectivity correlates selectively with attention's effects on spatial choice bias. *Proceedings of the National Academy of Sciences of the United States of America*, *116*(39), 19711–19716. https://doi.org/10.1073/pnas.1902704116

Stöttinger, E., Aichhorn, M., Anderson, B., & Danckert, J. (2018). The neural systems for perceptual updating. *Neuropsychologia*, 112, 86-94.

Stöttinger, E., Filipowicz, A., Marandi, E., Quehl, N., Danckert, J., & Anderson, B. (2014). Statistical and perceptual updating: Correlated impairments in right brain injury. *Experimental Brain Research*, *232*(6), 1971–1987. https://doi.org/10.1007/s00221-014-3887-z

Stoppel, C. M., Boehler, C. N., Strumpf, H., Krebs, R. M., Heinze, H. J., Hopf, J. M., & Schoenfeld, M. A. (2013). Distinct representations of attentional control during voluntary and stimulus-driven shifts across objects and locations. *Cerebral Cortex*, *23*(6), 1351–1361. https://doi.org/10.1093/cercor/bhs116

Szczepanski, S. M., Konen, C. S., & Kastner, S. (2010). Mechanisms of Spatial Attention Control in Frontal and Parietal Cortex. *Journal of Neuroscience*, *30*(1), 148–160. https://doi.org/10.1523/JNEUROSCI.3862-09.2010

Szczepanski, S. M., & Kastner, S. (2013). Shifting attentional priorities: Control of spatial attention through hemispheric competition. *The Journal of Neuroscience*, *33*(12), 5411–5421. https://doi.org/10.1523/JNEUROSCI.4089-12.2013

Thiebaut de Schotten, M., Dell'Acqua, F., Forkel, S. J., Simmons, A., Vergani, F., Murphy, D. G., & Catani, M. (2011). A lateralized brain network for visuospatial attention. *Nat Neurosci*, *14*(10), 1245–1246. https://doi.org/10.1038/nn.2905

Thiebaut De Schotten, M., Tomaiuolo, F., Aiello, M., Merola, S., Silvetti, M., Lecce, F., … Doricchi, F. (2014). Damage to white matter pathways in subacute and chronic spatial neglect: A group study and 2 single-case studies with complete virtual "in vivo" tractography dissection. *Cerebral Cortex*, *24*(3), 691–706. https://doi.org/10.1093/cercor/bhs351

Thiebaut de Schotten, M., Urbanski, M., Duffau, H., Volle, E., Levy, R., Dubois, B., & Bartolomeo, P. (2005). Direct evidence for a parietal-frontal pathway subserving spatial awareness in humans. Science, 309(5744), 2226-2228. doi: 10.1126/science.1116251

Timpert, D.C., Weiss, P.H., Vossel, S., Dovern, A. & Fink, G.R. (2015). Apraxia and spatial inattention dissociate in left hemisphere stroke. Cortex, 71, 349-358.

Thut, G., Nietzel, A., Brandt, S. A., & Pascual-Leone, A. (2006). Alpha-Band Electroencephalographic Activity over Occipital Cortex Indexes Visuospatial Attention Bias and Predicts Visual Target Detection. *Journal of Neuroscience*, *26*(37), 9494–9502. https://doi.org/10.1523/jneurosci.0875-06.2006

Umarova, R. M., Nitschke, K., Kaller, C. P., Klöppel, S., Beume, L., Mader, I., … Weiller, C. (2016). Predictors and signatures of recovery from neglect in acute stroke. *Annals of Neurology*, *79*(4), 673–686. https://doi.org/10.1002/ana.24614

Umarova, R. M., Saur, D., Kaller, C. P., Vry, M. S., Glauche, V., Mader, I., … Weiller, C. (2011). Acute visual neglect and extinction: Distinct functional state of the visuospatial attention system. *Brain*, *134*(11), 3310–3325. https://doi.org/10.1093/brain/awr220

Vandenberghe, R., Geeraerts, S., Molenberghs, P., Lafosse, C., Vandenbulcke, M., Peeters, K., … Orban, G. A. (2005). Attentional responses to unattended stimuli in human parietal cortex. *Brain*, *128*(12), 2843–2857. https://doi.org/10.1093/brain/awh522

Vandenberghe, R., Gitelman, D., Parrish, T., & Mesulam, M.-M. (2001). Location- or Feature-Based Targeting of Peripheral Attention. *NeuroImage*, *144*, 37–47. https://doi.org/10.1006/n

Vandenberghe, R., & Gillebert, C. R. (2013). Dissociations between spatial-attentional processes within parietal cortex: insights from hybrid spatial cueing and change detection paradigms. *Frontiers in Human Neuroscience*, *7*(July), 1–11. https://doi.org/10.3389/fnhum.2013.00366

Vossel, S., Mathys, C., Stephan, K. E., & Friston, K. J. (2015). Cortical Coupling Reflects Bayesian Belief Updating in the Deployment of Spatial Attention. *The Journal of Neuroscience*, *35*(33), 11532–11542. https://doi.org/10.1523/JNEUROSCI.1382-15.2015

Vossel, S., Weidner, R., Driver, J., Friston, K. J., & Fink, G. R. (2012). Deconstructing the architecture of dorsal and ventral attention systems with dynamic causal modelling. *Journal of Neuroscience*, *32*(31), 10637–10648. https://doi.org/10.1523/JNEUROSCI.0414-12.2012

Vossel, S., Weidner, R., Moos, K., & Fink, G. R. (2016). Individual attentional selection capacities are reflected in interhemispheric connectivity of the parietal cortex. *NeuroImage*, *129*, 148–158. https://doi.org/10.1016/j.neuroimage.2016.01.054

Vuilleumier, P., Schwartz, S., Verdon, V., Maravita, A., Hutton, C., Husain, M., & Driver, J. (2008). Abnormal attentional modulation of retinotopic cortex in parietal patients with spatial neglect. *Current Biology*, *18*(19), 1525-1529.

Weidner, R., Krummenacher, J., Reimann, B., Müller, H. J., & Fink, G. R. (2009). Sources of top-down control in visual search. *Journal of Cognitive Neuroscience*, *21*(11), 2100–2113. https://doi.org/10.1162/jocn.2008.21173

Wen, X., Yao, L., Liu, Y., & Ding, M. (2012). Causal Interactions in Attention Networks Predict Behavioral Performance. *Journal of Neuroscience*, *32*(4), 1284–1292. https://doi.org/10.1523/jneurosci.2817-11.2012

Wilson, K. D., Woldorff, M. G., & Mangun, G. R. (2005). Control networks and hemispheric asymmetries in parietal cortex during attentional orienting in different spatial reference frames. *NeuroImage*, *25*(3), 668–683. https://doi.org/10.1016/j.neuroimage.2004.07.075

Zhang, X., Mlynaryk, N., Ahmed, S., Japee, S., & Ungerleider, L. G. (2018). The role of inferior frontal junction in controlling the spatially global effect of feature-based attention in human visual areas. *PLoS Biology*, *16*(6), 1–28. https://doi.org/10.1371/journal.pbio.2005399

Zuanazzi, A., & Cattaneo, L. (2017). The right hemisphere is independent from the left hemisphere in allocating visuospatial attention. *Neuropsychologia*, *102*(November 2016), 197–205. https://doi.org/10.1016/j.neuropsychologia.2017.06.005