SI: Facets of Human Attention

Modulation of visual attention by prismatic adaptation

Running title: **Prismatic adaptation and attention**

Stephanie Clarke & Sonia Crottaz-Herbette

Service de Neuropsychologie et de Neuroréhabilitation, Centre Hospitalier Universitaire Vaudois and
Université de Lausanne, Lausanne, Switzerland.

Corresponding author:

Prof. Stephanie Clarke

Service de Neuropsychologie et de Neuroréhabilitation,
CHUV, Université de Lausanne,
1011 Lausanne, Switzerland.

Stephanie.Clarke@chuv.ch

29 pages

Word count: Text (without references and figure legends) = 5990

2 figures (both in color)

Conflict of interest: none

Acknowledgments: [The authors thank Dr. Laure Pisella and Dr. Janet Bultitude for their discerning and accurate comments on the manuscript.](#) This work was supported by Swiss National Science Foundation grants 320030-159708 to S.C. and Marie-Heim-Vögtlin fellowship FNS PMPDP3_129028 to S. C.-H., as well as support from the Biaggi de Blasys Foundation.

.

Abstract

Visuo-motor adaptation via rightward-deviating prisms has been repeatedly shown to alleviate lateralized deficits in neglect, including detection of targets as well as endogenous and exogenous orienting of attention. We review here evidence relevant to the underlying neural mechanisms. Rightward prismatic adaptation was shown to shift visual field representation from right to left inferior parietal lobule, changing thus hemispheric dominance within the ventral attentional system. This change is likely to redirect visual input to the dorsal attentional system and to re-install balance between its left- and right-hemispheric components in neglect. We propose a model based on the shift in hemispheric dominance within the ventral attentional system (SHD-VAS), which offers a parsimonious explanation for the effect of rightward prismatic adaptation on spatial bias in neglect and on behavioral data in normal subjects.

Keywords: dorsal and ventral attentional system; visual representations; hemispatial neglect; fMRI; inferior parietal lobule; human

Abbreviations

FEF = frontal eye field

IPL = inferior parietal lobule

IPS = intraparietal sulcus

PA = prismatic adaptation

SPL = superior parietal lobule

STG = superior temporal gyrus

TPJ = temporoparietal junction

Introduction

Rightward prismatic adaptation (PA) was introduced to neglect rehabilitation at the end of the last century (Rossetti et al., 1998). It was repeatedly shown to decrease lateralized deficits in neglect and is believed to alleviate attentional bias in neglect; however, its underlying neural mechanisms remain poorly understood (Barrett et al., 2012; Newport and Schenk, 2012; Redding and Wallace, 2006; Rode et al., 2003). The overall effect of rightward PA in neglect was interpreted as modulation of visual spatial attention, modification of spatial representations and/or changes in visually guided motor behaviours (Pisella et al., 2006; Striemer and Danckert, 2010; Jacquin-Courtois et al., 2013).

We review the current evidence and discuss the putative mechanisms by which rightward PA affects the attentional systems. After a brief introduction to rightward PA and neglect (sections 1 and 2) we outline the effects of PA on endogenous and exogenous orienting of attention and on target detection (sections 3-4). We then formulate a model that explains how rightward PA is likely to modulate spatial and attentional representations (section 5).

1. Rightward prismatic adaptation: a brief intervention that changes visuo-motor realignment and visual representations

PA is based on early experiments that were published 130 years ago (Stratton, 1896). In its most used version today it requires the subject to point toward a visual target with his hand while wearing prismatic goggles that deviate the visual field unilaterally to the right or left. During the first trials of pointing toward the target, the visuo-proprioceptive conflict produced by the prisms induces a pointing error in the same direction as the optical deviation. Usually within 10-15 trials, subjects adapt their pointing responses, and the pointing errors disappear. If the prisms produce a deviation of the visual field toward the right, the subject has to orient his movements to the left to compensate for the deviation, thereby inducing a leftward drift of the sensori-motor coordinates (Jacquin-Courtois et al., 2013; Redding et al., 2005; Rossetti et al., 1998). [When the goggles are removed, the after-effects of such adaptation can be observed, for example, a leftward shift of the perceived](#)

proprioceptive midline (evaluated by pointing straight-ahead without visual feedback). These after-effects compensate for the visuo-proprioceptive discrepancy introduced by the prisms.

In normal subjects, two types of activation studies have been carried out. First, neural activity has been investigated during the actual adaptation to prisms, showing differential activation patterns during the initial phase of the adaptation to right- or leftward deviating prisms (i.e., during the error pointing and its correction), while the adaptation is stable, and during the de-adaptation phase. During the adaptation phase, activation has been reported in the parieto-temporal cortex and the cerebellum, subserving a mechanism of spatial realignment (leftward PA: Chapman et al., 2010; Luauté et al., 2009; rightward PA: Danckert et al., 2008; either: Clower et al., 1996). Second, the effects of PA on tasks that are known to depend on the posterior parietal cortex have been assessed by comparing pre- and post-PA activation patterns to i) visual targets presented in the left, right or central visual field; ii) visuo-spatial short-term memory; and iii) verbal short-term memory (Crottaz-Herbette et al., 2014). A brief exposure to rightward PA modulated the representation of visual space in the inferior parietal lobule (IPL) bilaterally; it increased the representation of the left, central and right visual field within the left IPL and decreased the representation of the right and central visual field within the right IPL (Fig. 1A). No hemispheric shift in the neural activity associated with either of the short-term memory tasks was noted. Thus, in normal subjects, rightward PA changes hemispheric dominance of visuo-spatial representation within the ventral attentional system in favor of left hemispheric competence.

2. *Unilateral neglect: alleviation of the spatial attentional deficit by rightward prismatic adaptation*

Unilateral neglect is defined as difficulty or inability to respond to or to orient towards stimuli in the space contralateral to damage that cannot be explained by primary sensory (e.g., hemianopia) or motor deficit (e.g., hemiparesis) (Bisiach and Vallar, 1988; Brain, 1941; Heilman et al., 2000). Neglect most often involves the left hemispace following right hemispheric lesions and subsists into

the chronic stage in approximately 40-60% of patients (Cassidy et al., 1998; Nijboer et al., 2013; Stone et al., 1993).

Unilateral neglect can affect one or several sensory modalities (tactile, visual, or auditory), with or without motor-intentional involvement. Visual imagery can be affected by neglect, as illustrated in patients who failed to report items in the left half of an imagined scene or map (Bisiach and Luzzatti, 1978; Rode et al., 2010, 2007). Neglect can impair reading of the left part of a text or of individual words (Siéroff, 2015).

Early studies identified the right parietal lobe as key region in left neglect (Brain, 1941; Critchley, 1953; McFie et al., 1950; Paterson and Zangwill, 1944). Its role has been confirmed by imaging studies (Mort et al., 2003; Perani et al., 1993). Current evidence from large series of patients points to the critical roles of the superior temporal gyrus (STG) and the temporo-parietal junction (TPJ)¹ (Karnath et al., 2011; Karnath and Rorden, 2012) as well as the frontal convexity and basal ganglia (Farnè et al., 2004; Maguire and Ogden, 2002) in neglect that persists into the chronic stage. Anatomical (Bartolomeo et al., 2007; Doricchi and Tomaiuolo, 2003; Leibovitch et al., 1998), neurosurgical (Shinoura et al., 2009; Thiebaut de Schotten et al., 2005) and functional fMRI evidence (He et al., 2007) has revealed the contribution of damage to white matter fiber tracts and in particular to the superior longitudinal fasciculus, which links which links parietal and frontal areas (Doricchi et al., 2008).

A single exposure to rightward PA has been shown to alleviate neglect symptoms for a few hours (Farnè et al., 2002; Rode et al., 2001; Rossetti et al., 1998). The improvement can, however, last up to 6 months after 2 weeks of daily rightward PA training (Frassinetti et al., 2002; Serino et al., 2007, 2006). Rightward PA has also been reported to improve performance on several standard neuropsychological tests, such as line bisection, copying a simple drawing, and drawing of a daisy from memory and reading (Rossetti et al., 1998). Further studies have demonstrated positive effects

¹ Temporoparietal junction refers to the part of hemispheric convexity where the temporal and parietal lobes meet. Without fixed anatomical landmark, the term is used to designate the gathering of IPL and STG (e. g. Corbetta and Shulman 2011) or the part of IPL next to the junction with the temporal lobe (i. e. without STG; e. g. Karnath et al. 2009, Karnath and Rorden 2012).

on wheel-chair navigation (Jacquin-Courtois et al., 2008), postural control (Nijboer et al., 2014), mental imagery (Rode et al., 2001, 1998), haptic spatial judgments (McIntosh et al., 2002), accuracy and response times in pre-attentive visual search (Saevarsson et al., 2009), tactile attention (Maravita et al., 2003), and auditory extinction (Jacquin-Courtois et al., 2010) as well as activities much closer to daily living, such as picture scanning, telephone dialing, and coin and card sorting (Frassinetti et al., 2002). Visuo-constructive disorders and spatial dysgraphia have also been improved by rightward PA (Rode et al., 2006), as was temporal order judgment (Berberovic et al., 2004). Overall, these studies show that in addition to having positive effects on neglect symptoms, rightward PA yields improvement in non-trained tasks in the motor domain, such as wheelchair driving (Jacquin-Courtois et al., 2008; Watanabe and Amimoto, 2010) and postural control (Nijboer et al., 2014). Taken together, the evidence from these studies suggests that rightward PA affects general visuo-spatial functions attributed to the right hemisphere and improves general spatial cognition in patients with right hemispheric damage. There are, however, exceptions, which we discuss in detail in Section 5.4; rightward PA does not affect spatial bias in lateral preference tasks (Ferber et al., 2003; Sarri et al., 2011, 2006), size estimation (Dijkerman et al., 2003), or visual search (Morris et al., 2004). Furthermore, several clinical studies reported promising, albeit not conclusive effects of rightward PA (Keane et al., 2006; Nys et al., 2008), possibly because not all types of neglect respond equally well to this treatment (Clarke et al., 2015).

The first neuroimaging study involving neglect patients showed that the improvement in neglect symptoms following rightward PA was correlated with an increase in activation in the right cerebellum, left globus pallidus, left thalamus, and left temporo-occipital cortex, and with a decrease in activation in the left medial temporal lobe and right posterior parietal lobe (Luauté et al., 2006). Altogether, lesions studies (Pisella et al., 2005, 2004), as well as neuroimaging studies on normal subjects (Clower et al., 1996; Danckert et al., 2008) and patients (Luauté et al., 2006), confirm the major involvement of the right cerebellum and left hemisphere in rightward PA. The mechanisms of rightward PA were proposed to be related to an enhanced plasticity of spatial representations and

thus contribute to the recovery of patients with right hemispheric damage. It has been hypothesized that rightward PA enlarges the representation of space in the spared hemisphere and that this effect is mediated by left hemispheric pathways that are functionally homologous to those involved in spatial cognition in the damaged hemisphere (Pisella et al., 2006; Rode et al., 2006).

3. Endogenous and exogenous orienting of attention is modulated by rightward prismatic adaptation

Covert shifts of attention direct attention to specific locations without an accompanying shift of gaze. They can be generated voluntarily and are thus described as endogenous, or they can be stimulus-driven and referred to as exogenous. Most paradigms in psychophysical and imaging studies of endogenous and exogenous attention used variations of the paradigm developed by Posner and colleagues (Posner, 1980; Posner et al., 1984). Briefly, targets are presented on the right or left and are preceded by spatial cues. The cues indicate correctly (as valid cues) or incorrectly (as invalid cues) the location of the forthcoming target. When they are at the presumed location of the target, the paradigm investigates exogenous orienting. When they are centrally placed and indicate the presumed location of the target with an arrow, the paradigm investigates endogenous orienting. Three types of cues can be used: valid, invalid or neutral.

Initial studies of endogenous and exogenous spatial orienting used 1.5 T fMRI and revealed largely overlapping bilateral fronto-parietal networks (Rosen et al., 1999), albeit with more pronounced involvement of the right parietal cortex (Kim et al., 1999). Subsequent studies highlighted neural correlates for specific aspects of spatial attention. Endogenous allocation and maintenance of spatial attention was shown to be sustained bilaterally by the IPS and the frontal eye field (FEF), whereas the right TPJ and inferior frontal gyrus were activated by the detection of targets at unattended locations, independent of whether they occurred in the left or right visual field (Corbetta et al., 2002). The two partially segregated networks were referred to as the dorsal and ventral attentional systems. The former is bilateral and is involved in top-down selection of stimuli,

whereas the latter is largely lateralized to the right hemisphere and specialized in the detection of behaviourally relevant stimuli (Corbetta and Shulman, 2002).

Further studies refined the understanding of the organization of the two attentional systems. In the core regions of the dorsal attentional system, IPS and FEF, voluntary shifts of spatial attention yielded greater preparatory activity than stimulus-driven shifts (Kincade et al., 2005). The core region of the ventral attentional system, the right TPJ, was strongly activated by stimulus-driven attentional shifts to behaviorally relevant stimuli, such as targets at unattended locations. Right hemispheric dominance was repeatedly confirmed for TPJ activation by stimulus-driven shifts of spatial attention to left or right visual fields; however, no notable hemispheric asymmetries were reported for shifts of attention or target detection in the dorsal attentional system (Shulman et al., 2010, 2009). The different steps of endogenous orienting appear to rely on distinct parts of the attentional networks, as demonstrated by activation patterns yielded by the Posner paradigm (Thiel et al., 2004). The effect of general alerting by a cue was assessed by comparing conditions with neutral vs no cues; the resulting activation involved the extrastriate cortex bilaterally. The orientation towards a location, which was assessed by comparing the effect of valid vs neutral cues, involved the cingulate cortex. Reorienting of spatial attention from an invalidly cued location to the target was assessed by comparing activation in trials with invalid vs valid cues. In doing so it was shown to involve bilaterally IPS and middle frontal gyrus, as well as the right TPJ. Thus, reorienting of attention involves also the right-lateralized ventral system, possibly by stimulus-driven breach of spatial expectation (Shulman et al., 2009). The involvement of TPJ in endogenous attention was further investigated by varying the predictive value of cues (Doricchi et al., 2010). A left-right asymmetry appeared as a function of the attentional context. The right TPJ sustained a deactivation during endogenous orienting when the cues had a high predictive value. Independent of the predictive value of the orienting cues, the left TPJ tended to be more activated by targets that were preceded by valid rather than neutral cues, and both the left and the right TPJ, by targets preceded by invalid

rather than neutral cues. The authors concluded that the TPJ on either side plays a crucial role in updating the statistical contingency between cues and targets.

The dorsal system, which controls endogenous attention, has been shown to be sensitive to bottom-up influences. The activity within the anterior part of the IPS (but not within the FEF) was modulated by the perceptual salience of stimuli, independent of whether they constituted the target or not (Geng and Mangun, 2009). The architecture of the dorsal and ventral attentional systems was investigated by dynamic causal modeling of effective connectivity during lateralized orienting and reorienting of attention (Vossel et al., 2012). In the location-cueing Posner paradigm, the direction of attention modulated top-down connections from the left and right IPS to the left and right visual cortex. Strong influence was demonstrated from the bilateral IPS to the FEF and between FEFs in either hemisphere. Invalid cueing was shown to enhance connections from visual areas to the right TPJ and from there to the right IPS and inferior frontal gyrus. Taken together with the above quoted evidence from activation studies, the connectivity data support a bilateral top-down mediation of endogenous attentional orienting and bottom-up effects of invalid cueing toward the right TPJ.

In their seminal paper Posner and colleagues reported the effect of parietal, but not frontal or temporal lesions, on covert orienting of attention (Posner et al., 1984). Contralateral targets yielded significantly longer response times than ipsilateral ones, and this difference was greater when the preceding cue was invalid rather than valid. Both peripheral and central cues, testing, respectively, exogenous and endogenous orienting of attention, presented the invalid vs valid effect. Subsequent studies have shown that this impairment tends to improve from the acute to the chronic stage and that recovery correlates with the restoration of activity within attentional networks (Corbetta et al., 2005).

In normal subjects, rightward PA was shown to modulate differentially endogenous and exogenous generated shifts of attention (Striemer et al., 2006). Following rightward PA, exogenous reorienting of attention from invalid cues was faster for targets on the right side. For endogenous re-

orienting, rightward PA decreased the efficiency of voluntary attention in both right and left space in subjects who presented a large cueing effect before PA.

Rightward PA was shown to reduce the deficit in reorienting attention from an ipsilesional cue to the contralesional target in patients with right hemispheric damage. Striener and Danckert (Striener and Danckert, 2007) investigated the effect of peripheral cues in four patients with right hemispheric damage, of whom two presented unilateral neglect. Irrespective of neglect, rightward PA reduced both the rightward attentional bias and the reorienting deficit. Nijboer and colleagues (Nijboer et al., 2008) examined two patients with right hemispheric damage, of whom one presented left visual extinction, but no longer neglect, at the time of testing, and the second left visual neglect. In both patients, rightward PA improved leftward endogenous orienting independent of the validity of the cue. Interestingly, the effect was greater for invalid cues. No effect was observed for exogenous cues. Schindler and colleagues (Schindler et al., 2009) investigated the effect of rightward PA on disengage deficits between hemifields and between objects in normal controls and in 20 patients with right hemispheric damage, of whom 10 presented neglect. As also reported previously (Egly et al., 1994), normal subjects and patients without neglect presented a greater effect of valid vs. invalid cues for attentional shifts within objects than for attentional shifts between objects. The neglect patients in this study were deficient in disengaging attention from the right to left, but only between objects. This disengage deficit was abolished by rightward PA.

4. Target detection: rightward prismatic adaptation induces a shift in target-driven activity from right to left inferior parietal lobule

By analyzing event-related activity during the Posner paradigm, Corbetta and colleagues (Corbetta et al., 2000) demonstrated that target detection and voluntary orienting of attention involve partially different parts of the posterior parietal cortex. The presentation of visual targets yielded activation in occipital areas with a contralateral bias, bilaterally in IPS and precuneus, as well as in the right TPJ. The right TPJ responded to right and left targets, and neural activity was stronger

when the target was invalidly rather than validly cued. When a location was attended before target presentation, neural activation occurred mainly in the IPS. Conversely, the right TPJ was activated when the target actually appeared, especially at an unattended location. Subsequent studies have confirmed that the right, but not the left, inferior parietal region carries the presentation of both the left and right visual hemifield (Beume et al., 2015; Corbetta and Shulman, 2002; Shulman et al., 2010; Thiel et al., 2004). The right IPL was shown to have a strong functional interaction with the retinotopically organized visual areas of either hemisphere (Ruff et al., 2008).

In patients with right hemispheric lesions and neglect (but without visual field defects) target detection tends to be less accurate and slower within the left than right visual field (e. g. (Butler et al., 2004; Crottaz-Herbette et al., Submitted; Deouell et al., 2005; Eramudugolla et al., 2010; van Kessel et al., 2010). A brief session of rightward PA was shown to improve performance within the left space in easy (Crottaz-Herbette et al., Submitted) and in demanding tasks. In the latter tasks, the performance in the whole field improved without changing the spatial gradient of attention (Eramudugolla et al., 2010). In a single case study of chronic neglect repetitive long-term rightward PA was reported to permanently improve the detection of contralesional targets (Nijboer et al., 2011).

A single brief exposure to rightward PA was shown to change the activation pattern elicited by left, right, and central visual targets. In normal subjects, PA-related modulation occurred in the IPL, with a significant increase of the ipsilateral representation in left IPL and a significant decrease in the right IPL (Crottaz-Herbette et al., 2014). It is noteworthy that rightward PA did not alter other types of visuo-spatial processing in a similar way. For visuo-spatial working memory, tested with a delayed match-to sample design, it yielded a bilateral decrease in activation (Crottaz-Herbette et al., 2014) within regions known to be specifically involved in this task (Ackerman and Courtney, 2012; Awh et al., 1995; Chang et al., 2007; Corbetta et al., 2002; Courtney et al., 1998; Crottaz-Herbette et al., 2004; Sala and Courtney, 2007). This is of interest, because the spatial working memory network was shown to be coextensive with the dorsal attentional network, which sustains voluntary

attentional orienting (Corbetta et al., 2002; LaBar et al., 1999) and is often impaired in neglect (Husain et al., 2001; Striemer et al., 2013). Comparing fMRI activation patterns yielded by a target detection task before and after a single brief session of prismatic adaptation in 15 neglect patients highlighted a very similar PA-related modulation (Fig. 1B). Rightward PA enhanced the neural response to left and central stimuli within the left, spared, hemisphere, predominantly in the superior temporal region (Crottaz-Herbette et al., Submitted), which is known for its involvement in visuo-attentional and multisensory representations (e. g. Beauchamp et al., 2004; Thiel et al., 2004). The PA-related change in visual representation in the left temporal regions of neglect patients correlated with the improvement in target detection.

5. *Shift in hemispheric dominance within the ventral attentional system*

The shift in hemispheric dominance within the ventral attentional system (SHD-VAS), as induced by rightward PA (Crottaz-Herbette et al., 2014), offers a parsimonious explanation for effects reported in normal subjects and in neglect. We present here the key aspects of this model.

5.1. *Organization of the dorsal and ventral attentional systems and its disruption in neglect*

The dorsal and ventral attentional systems contribute differently to visual orienting. Endogenous allocation and maintenance of visuo-spatial attention is mainly mediated by the dorsal attentional network, which comprises the SPL, IPS and the superior frontal cortex of both hemispheres (Corbetta et al., 2002). As highlighted in a metaanalysis of activation studies, the IPS consists of several functional areas, which are topographically organized and encode the contralateral visual space (Silver and Kastner, 2009; Fig. 2A). These areas were shown to be involved in orienting and re-orienting of spatial attention, spatial working memory, and saccadic eye movements, as well as feature and conjunction search (Corbetta et al., 2002; Leonards et al., 2000; Müller et al., 2003; Silver and Kastner, 2009; Thiel et al., 2004). The detection of targets that appear at unattended locations is mediated by the ventral attentional network, which comprises the right

TPJ, IPL and posterior part of the STG and which receives visual information from both hemifields (Corbetta et al., 2002). This region was also shown to be involved non-spatial attention, as demonstrated in paradigms of tonic and phasic alertness (Sturm et al., 1999; Sturm and Willmes, 2001). The top-down attentional control by the dorsal system and the stimulus-driven control by the ventral system interact closely. In particular, the interconnections between the right TPJ/IPL and the IPS/SPL are believed to warrant unattended stimuli access to the dorsal orienting system and to enable voluntary top-down modulation of the ventral system (Corbetta and Shulman, 2002). [A series of activation and TMS studies demonstrated very elegantly that the left and right dorsal regions are interconnected \(Corbetta and Shulman, 2011\) and that the right, but not left posterior parietal cortex exerts a strong inhibitory effect on the contralateral homologous region \(Koch et al., 2011, 2008\).](#)

Lasting unilateral neglect is more often than not associated with lesions of the right TPJ (Karnath et al., 2011; Karnath and Rorden, 2012; Fig. 2B) and a breakdown of functional connections within the attentional networks (He et al., 2007). The stimulus-driven input from the ventral to the dorsal system in the right hemisphere is disrupted, which is believed to decrease the activity within the right dorsal system. [The inhibition that the right dorsal systems exerts on the left is disturbed, resulting in an overactive left dorsal system and an ensuing attentional bias toward the right side \(Corbetta and Shulman, 2011; Koch et al., 2011, 2008\).](#)

5.2. Effects of rightward prismatic adaptation in normal subjects

SHD-VAS is characterized by the emergence of a bilateral visual field representation within the left IPL, whereas the representation within the right IPL is reduced to the left visual field (Crottaz-Herbette et al., 2014). This shift impacts functionally on the attentional and visual systems (Fig. 2C). The dorsal attentional system on either side (Corbetta et al., 2002) receives stimulus-driven activation from the left IPL. As demonstrated in connectivity studies, the left IPL receives visual information from right and left visual field, but in attention tasks the effective connectivity is stronger for right than left stimuli. Resting- state connectivity revealed bilateral connections between

the left posterior IPS and the superior lateral occipital cortex (Uddin et al., 2010). Post-mortem anterograde tracing visualized crossed monosynaptic connections from the right inferior temporal cortex to the left IPL (Di Virgilio and Clarke, 1997). These heterotopic crossed connections, which originate in a region known to carry the representation of the left visual field (as established by comparison with Arcaro et al., 2009), are less dense than the crossed homotopic or the intrahemispheric occipital connections (Clarke, 1994; Clarke and Miklossy, 1990). Effective connectivity, as analyzed during shifts of exogenous visuo-spatial attention, was shown to be asymmetrical; the left TPJ increased its connectivity to the left but not right ventral occipital cortex, whereas the right TPJ did so bilaterally (Indovina and Macaluso, 2004). The crossed connections from right visual cortex to left IPL are crucial for the SHD-VAS to occur rapidly after a brief PA session. The lack of their involvement in shifts of visuo-spatial attention (Indovina and Macaluso, 2004) may accounts for the failure of rightward PA to restore spatial bias in a series of tasks which depend on ventral visual areas (see below).

The rapidity of PA-related changes in visual field representation within the left and right IPL suggests that rightward PA may help to uncover preexisting ipsilateral field representations within the left parietal cortex. Interestingly, a recent study of target detection in multi-target environments hints at such a possibility. When analyzing neural responses within regions with a preference for uncued over cued targets, de Haan and colleagues (de Haan et al., 2015) reported equal levels of activity for ipsilateral and contralateral (unilateral) targets within a large right TPJ region and within a small left TPJ cluster. It is likely that the bilateral visual representation within the left TPJ, which went unreported in a series of previous studies, was revealed here due to the high attentional load of the complex paradigm. [Alternatively, it is possible that rightward PA taps into the motor attentional system, which is located in the left supramarginal gyrus and which concerns the preparation and the redirection of movements and movement intentions within the right and left space \(Rushworth et al., 2003, 2001\).](#)

In normal subjects rightward PA was shown to affect attention in only a few studies. Striemer and colleagues investigated the effects of rightward and leftward PA on reflexive and voluntary reorienting of attention (Striemer et al., 2006). Following rightward PA, a subgroup of subjects, who had large cueing effects before PA, became faster at reorienting reflexively attention from invalid cues on the left to targets on the right side. In the same subgroup, rightward PA led to a slight decrease of cueing effects in voluntary reorienting. Our model offers several leads for the mechanisms, which may account for these highly interesting, but complex results. For the interpretation of results pertaining to reflexive reorienting we need to consider that the dorsal system is known to be sensitive to bottom-up influences and is modulated by the perceptual salience of stimuli, independently of whether they constitute targets or not (Geng and Mangun, 2009). In case of SHD-VAS, visual stimuli which reach the left IPL are more salient when coming from the right than left visual field (cf. gray and black visual-VAS connections in Fig. 2C; Indovina and Macaluso 2004). In a paradigm of exogenous reorienting of attention from invalid cues this means that right targets are more salient than preceding invalid (left) cues, and right invalid cues more than the following (left) targets. Thus, rightward PA can be expected to yield faster response times for right, but not left targets in exogenous reorienting of attention from invalid cues; this is precisely what has been reported by Striemer et al. (2006). Voluntary reorienting of attention was shown to depend bilaterally on IPS and middle frontal gyrus and on the right TPJ (Thiel et al., 2004; section 4). The SHD-VAS decreases the representation of the right and central visual stimuli within the right IPL, depriving this region of essential visual information (the cueing information being presented in the central visual field). This change is bound to decrease cueing effects in voluntary orienting, as reported by Striemer et al. (2006).

Berberovic and Mattingley investigated the effects of rightward and leftward PA on judgments of spatial extent in peri- and extrapersonal space (Berberovic and Mattingley, 2003). Rightward PA led to rightward shift in visual midpoint judgments in extrapersonal, but not peripersonal space. These results can be partially understood in the framework of the SHD-VAS

model. Awareness of the extrapersonal space is known to depend critically on the right frontal and superior temporal regions, whereas awareness of the peripersonal space on the right inferior parietal region (Committeri et al., 2007). In case of SHD-VAS the latter receives less information from the right and central visual field, whereas frontal and temporal regions are likely to receive visual information from the whole visual field via the left IPL. These differences in access to visual information may account for the differential effects of rightward PA on extrapersonal and peripersonal space. The rightward shift in visual midpoint judgment may reflect a lesser salience of left visual field components, which may be due, in case of SHD-VAS, to a functionally weaker connection between the left IPL and right visual areas (Indovina and Macaluso, 2004).

Bultitude and colleagues investigated the effect of rightward and leftward PA on spatial remapping with a double-step saccade paradigm (Bultitude et al., 2013). Rightward PA did not affect spatial remapping; there was an overall leftward shift in the endpoints of the second saccade, which was similar in both visual fields and which was not independent of the endpoint of the first saccade. These changes are suggestive of an effect of PA on oculomotor performance, consistent with low-level adaptation aftereffects, but not spatial remapping. Spatial remapping was shown to depend critically on right posterior parietal cortex (Heide et al., 1995; van Koningsbruggen et al., 2010). The SHD-VAS model does not offer an explanation for the lack of effect on spatial remapping, which may depend on IPL modules that are not affected by rightward PA. Other examples of IPL modules that are not affected by rightward PA are those involved in visuo-spatial or verbal short-term memory (Crottaz-Herbette et al., 2014).

In summary, the SHD-VAS represents major reorganization within the attentional systems. Due to their connectivity pattern, VAS and DAS maintain, however, many of their functional properties. The relatively minor attentional effects, which rightward PA yields in normal subjects, can be accounted for by functionally asymmetric afferents to VAS. The SHD-VAS was shown not to affect the neural underpinning of verbal or visuo-spatial short-term memory and it may not affect other functional modules within the IPL.

5.3. *Effects of rightward prismatic adaptation in neglect*

In neglect rightward PA was shown to reduce the spatial bias in a several tasks, whereas others remained unaffected (section 2). The SHD-VAS model offers a parsimonious explanation for both the positive effects and for absence of effects. The key feature of tasks that are improved by rightward PA is the involvement of the dorsal attentional system (Striemer and Danckert, 2010). Following rightward PA, the left IPL relays left and right visual stimuli to the dorsal system bilaterally (Fig. 2D). This new stimulus-driven input from the left IPL to the right dorsal system is likely to restore right-to-left inhibition. This may explain several positive effects which were reported for rightward PA (see sections 2-4) and, in particular, i) the reduction in the rightward attentional bias and the reorienting deficit (Striemer and Danckert, 2007), ii) the improvement of leftward endogenous orienting (Nijboer et al., 2008) and iii) the alleviation of the disengage deficit (Egly et al., 1994; Schindler et al., 2009).

Our model can account for the effect of rightward PA on the interaction between local and global processing. The processing of global and local aspects engages a complex network (Fink et al., 1997, 1996). Focusing attention on global aspects activates the right lingual gyrus, focusing it on local aspects the left inferior occipital cortex, whereas sustained attention to global or to local aspects involves the temporo-parietal cortex bilaterally, as well as additional parts of the right fronto-parietal cortex including its dorsal parts. Normal subjects are faster identifying global than local information and have difficulties ignoring global information when focusing on local level; rightward PA did not change this bias (Bultitude and Woods, 2010; Reed and Dassonville, 2014). Right hemispheric damage, and neglect in particular, have been found to be associated with hyperattention to local details and with a deficit in perceiving the global structure of stimuli (Delis et al., 1986; Marshall and Halligan, 1995; Robertson et al., 1988). Rightward PA was reported to reduce the local processing bias and to increase the global interference (Bultitude et al., 2009). This effect can be accounted for

by the SHD-VAS model, which predicts that the global processing module in the right lingual gyrus (Fink et al. 1997) gains access, via the left IPL, to the extensive global-local processing network.

Our model predicts two conditions in which spatial bias in neglect should fail to respond to rightward PA. First, this is likely to be the case if a key structure within the right hemisphere is damaged. Lesions associated with neglect often include and/or disconnect the right IPS (Bartolomeo et al., 2007), which has been identified as key structure for pre-attentive and serial search (Donner et al., 2002; Nobre et al., 2003). Thus, it is not surprising that the spatial bias in preattentive and in serial search, which is often observed in neglect, fails to respond to rightward PA (Morris et al., 2004; Saevarsson et al., 2009)². Second, failure to respond to rightward PA may be due to differences in connectivity between the left IPL and visual areas on either side. As discussed above (see 5.1), the left IPL has weaker effective connectivity during attentional tasks to ventral occipital cortex on the right than left side (Indovina and Macaluso, 2004). In case of SHD-VAS, this means that left visual targets appear less salient, in particular in tasks which depend critically on ventral visual areas. Thus, rightward PA should fail to restore the spatial bias in such tasks, as indeed demonstrated in a series of elegant studies. Neglect patients were reported to present lateral preference for right space in tasks involving chimeric stimuli; this preference was proposed to reflect a difference in salience for stimuli on either side (Mattingley et al., 2004; Sarri et al., 2011). The spatial bias on lateral preference tasks involving faces or gray contrasts was repeatedly shown not to be alleviated by rightward PA (Ferber et al., 2003; Sarri et al., 2011, 2006), as predicted by the SHD-VAS model. The same mechanism, namely lack of salience for left stimuli, may also explain why size underestimation of left stimuli persists in neglect after rightward PA (Dijkerman et al., 2003).

6. Concluding remarks

The shift in hemispheric dominance within the ventral attentional system (SHD-VAS), which was demonstrated in normal subjects and in neglect patients following rightward PA (Crottaz-

² Rightward PA was shown to improve accuracy and response time in pre-attentive search, but not to restore the spatial bias, which is typically present in neglect (Saeversson et al. 2009).

Herbette et al., Submitted), offers a parsimonious explanation for the effect on attentional bias in neglect. Furthermore, it offers a framework within which specific hypotheses can be tested concerning the relationship between rightward PA and different aspects of attention. First, the bilateral visual representation, which is uncovered by rightward PA within the left IPL, may be the same as recruited in paradigms of high attentional load (de Haan et al., 2015) or it may be related to the motor attentional system (Rushworth et al., 2003, 2001). Second, seminal studies have revealed fine-tuned interactions between the ventral and the dorsal systems and their breakdown following damage to the ventral system (Corbetta and Shulman, 2011; Koch et al., 2011). The competence of the left IPL for the detection of targets within the whole visual field, induced by rightward PA, is likely to activate the left and right dorsal systems and to restore the functional balance between them. Third, rightward PA changes the visual field representation within the ventral attentional system and may thereby modulate non-spatial visual attention. Further studies need, however, to establish whether the shift of bilateral visual representations to the left IPL serves as simple relay for visual information to the dorsal system or whether non-spatial attention, such as tonic and phasic alertness (Sturm and Willmes, 2001), switch dominance as well. Last, the SHD-VAS model applies to rightward PA. [Changes in higher-level visual representations due to leftward PA have not been so far investigated in normal subjects and we cannot comment on their putative influence on attentional systems.](#)

References

- Ackerman, C.M., Courtney, S.M., 2012. Spatial relations and spatial locations are dissociated within prefrontal and parietal cortex. *J. Neurophysiol.* 108, 2419–2429. doi:10.1152/jn.01024.2011
- Arcaro, M.J., McMains, S.A., Singer, B.D., Kastner, S., 2009. Retinotopic organization of human ventral visual cortex. *J. Neurosci. Off. J. Soc. Neurosci.* 29, 10638–10652. doi:10.1523/JNEUROSCI.2807-09.2009
- Awh, E., Smith, E.E., Jonides, J., 1995. Human rehearsal processes and the frontal lobes: PET evidence. *Ann. N. Y. Acad. Sci.* 769, 97–117.
- Barrett, A.M., Goedert, K.M., Basso, J.C., 2012. Prism adaptation for spatial neglect after stroke: translational practice gaps. *Nat. Rev. Neurol.* 8, 567–577. doi:10.1038/nrneurol.2012.170
- Bartolomeo, P., Thiebaut de Schotten, M., Doricchi, F., 2007. Left unilateral neglect as a disconnection syndrome. *Cereb. Cortex N. Y. N 1991* 17, 2479–2490. doi:10.1093/cercor/bhl181

- Beauchamp, M.S., Lee, K.E., Argall, B.D., Martin, A., 2004. Integration of auditory and visual information about objects in superior temporal sulcus. *Neuron* 41, 809–823.
- Berberovic, N., Mattingley, J.B., 2003. Effects of prismatic adaptation on judgements of spatial extent in peripersonal and extrapersonal space. *Neuropsychologia* 41, 493–503.
- Berberovic, N., Pisella, L., Morris, A.P., Mattingley, J.B., 2004. Prismatic adaptation reduces biased temporal order judgements in spatial neglect. *Neuroreport* 15, 1199–1204.
- Beume, L.-A., Kaller, C.P., Hoeren, M., Klöppel, S., Kuemmerer, D., Glauche, V., Köstering, L., Mader, I., Rijntjes, M., Weiller, C., Umarova, R., 2015. Processing of bilateral versus unilateral conditions: evidence for the functional contribution of the ventral attention network. *Cortex J. Devoted Study Nerv. Syst. Behav.* 66, 91–102. doi:10.1016/j.cortex.2015.02.018
- Bisiach, E., Luzzatti, C., 1978. Unilateral neglect of representational space. *Cortex J. Devoted Study Nerv. Syst. Behav.* 14, 129–133.
- Bisiach, E., Vallar, G., 1988. Hemineglect in humans, in: Boller, F., Grafman, J., Rizzolatti, G., Goodglass, H. (Eds.), *Handbook of Neuropsychology*, Vol. 1. Elsevier Science, New York, NY, US, pp. 195–222.
- Brain, W.R., 1941. Visual Disorientation with Special Reference to Lesions of the Right Cerebral Hemisphere. *Brain* 64, 244–272. doi:10.1093/brain/64.4.244
- Bultitude, J.H., Rafal, R.D., List, A., 2009. Prism adaptation reverses the local processing bias in patients with right temporo-parietal junction lesions. *Brain J. Neurol.* 132, 1669–1677. doi:10.1093/brain/awp096
- Bultitude, J.H., Van der Stigchel, S., Nijboer, T.C.W., 2013. Prism adaptation alters spatial remapping in healthy individuals: evidence from double-step saccades. *Cortex J. Devoted Study Nerv. Syst. Behav.* 49, 759–770. doi:10.1016/j.cortex.2012.01.008
- Bultitude, J.H., Woods, J.M., 2010. Adaptation to leftward-shifting prisms reduces the global processing bias of healthy individuals. *Neuropsychologia* 48, 1750–1756. doi:10.1016/j.neuropsychologia.2010.02.024
- Butler, B.C., Eskes, G.A., Vandorpe, R.A., 2004. Gradients of detection in neglect: comparison of peripersonal and extrapersonal space. *Neuropsychologia* 42, 346–358.
- Cassidy, T.P., Lewis, S., Gray, C.S., 1998. Recovery from visuospatial neglect in stroke patients. *J. Neurol. Neurosurg. Psychiatry* 64, 555–557.
- Chang, C., Crottaz-Herbette, S., Menon, V., 2007. Temporal dynamics of basal ganglia response and connectivity during verbal working memory. *NeuroImage* 34, 1253–1269. doi:10.1016/j.neuroimage.2006.08.056
- Chapman, H.L., Eramudugolla, R., Gavrilescu, M., Strudwick, M.W., Loftus, A., Cunnington, R., Mattingley, J.B., 2010. Neural mechanisms underlying spatial realignment during adaptation to optical wedge prisms. *Neuropsychologia* 48, 2595–2601. doi:10.1016/j.neuropsychologia.2010.05.006
- Clarke, S., 1994. Association and intrinsic connections of human extrastriate visual cortex. *Proc. Biol. Sci.* 257, 87–92. doi:10.1098/rspb.1994.0098
- Clarke, S., Bindschaedler, C., Crottaz-Herbette, S., 2015. Impact of cognitive neuroscience on stroke rehabilitation. *Stroke J. Cereb. Circ.* 46, 1408–1413. doi:10.1161/STROKEAHA.115.007435
- Clarke, S., Miklossy, J., 1990. Occipital cortex in man: organization of callosal connections, related myelo- and cytoarchitecture, and putative boundaries of functional visual areas. *J. Comp. Neurol.* 298, 188–214. doi:10.1002/cne.902980205
- Clower, D.M., Hoffman, J.M., Votaw, J.R., Faber, T.L., Woods, R.P., Alexander, G.E., 1996. Role of posterior parietal cortex in the recalibration of visually guided reaching. *Nature* 383, 618–621. doi:10.1038/383618a0
- Committeri, G., Pitzalis, S., Galati, G., Patria, F., Pelle, G., Sabatini, U., Castriota-Scanderbeg, A., Piccardi, L., Guariglia, C., Pizzamiglio, L., 2007. Neural bases of personal and extrapersonal neglect in humans. *Brain J. Neurol.* 130, 431–441. doi:10.1093/brain/awl265

- Corbetta, M., Kincade, J.M., Ollinger, J.M., McAvoy, M.P., Shulman, G.L., 2000. Voluntary orienting is dissociated from target detection in human posterior parietal cortex. *Nat. Neurosci.* 3, 292–297. doi:10.1038/73009
- Corbetta, M., Kincade, J.M., Shulman, G.L., 2002. Neural systems for visual orienting and their relationships to spatial working memory. *J. Cogn. Neurosci.* 14, 508–523. doi:10.1162/089892902317362029
- Corbetta, M., Kincade, M.J., Lewis, C., Snyder, A.Z., Sapir, A., 2005. Neural basis and recovery of spatial attention deficits in spatial neglect. *Nat. Neurosci.* 8, 1603–1610. doi:10.1038/nn1574
- Corbetta, M., Shulman, G.L., 2011. Spatial neglect and attention networks. *Annu. Rev. Neurosci.* 34, 569–599. doi:10.1146/annurev-neuro-061010-113731
- Corbetta, M., Shulman, G.L., 2002. Control of goal-directed and stimulus-driven attention in the brain. *Nat. Rev. Neurosci.* 3, 201–215. doi:10.1038/nrn755
- Courtney, S.M., Petit, L., Maisog, J.M., Ungerleider, L.G., Haxby, J.V., 1998. An area specialized for spatial working memory in human frontal cortex. *Science* 279, 1347–1351.
- Critchley, M., 1953. Tactile thought, with special reference to the blind. *Brain J. Neurol.* 76, 19–35.
- Crottaz-Herbette, S., Anagnoson, R.T., Menon, V., 2004. Modality effects in verbal working memory: differential prefrontal and parietal responses to auditory and visual stimuli. *NeuroImage* 21, 340–351.
- Crottaz-Herbette, S., Bindschaedler, C., Manzoni, L., Fornari, E., Clarke, S., Submitted. Left hemisphere provides compensatory mechanisms in neglect: fMRI evidence from prismatic adaptation intervention.
- Crottaz-Herbette, S., Fornari, E., Clarke, S., 2014. Prismatic Adaptation Changes Visuospatial Representation in the Inferior Parietal Lobule. *J. Neurosci.* 34, 11803–11811. doi:10.1523/JNEUROSCI.3184-13.2014
- Danckert, J., Ferber, S., Goodale, M.A., 2008. Direct effects of prismatic lenses on visuomotor control: an event-related functional MRI study. *Eur. J. Neurosci.* 28, 1696–1704. doi:10.1111/j.1460-9568.2008.06460.x
- De Haan, B., Bither, M., Brauer, A., Karnath, H.-O., 2015. Neural Correlates of Spatial Attention and Target Detection in a Multi-Target Environment. *Cereb. Cortex N. Y. N 1991* 25, 2321–2331. doi:10.1093/cercor/bhu046
- Delis, D.C., Robertson, L.C., Efron, R., 1986. Hemispheric specialization of memory for visual hierarchical stimuli. *Neuropsychologia* 24, 205–214.
- Deouell, L.Y., Sacher, Y., Soroker, N., 2005. Assessment of spatial attention after brain damage with a dynamic reaction time test. *J. Int. Neuropsychol. Soc. JINS* 11, 697–707. doi:10.1017/S1355617705050824
- Dijkerman, H.C., McIntosh, R.D., Milner, A.D., Rossetti, Y., Tilikete, C., Roberts, R.C., 2003. Ocular scanning and perceptual size distortion in hemispatial neglect: effects of prism adaptation and sequential stimulus presentation. *Exp. Brain Res. Exp. Hirnforsch. Expérimentation Cérébrale* 153, 220–230. doi:10.1007/s00221-003-1595-1
- Di Virgilio, G., Clarke, S., 1997. Direct interhemispheric visual input to human speech areas. *Hum. Brain Mapp.* 5, 347–354. doi:10.1002/(SICI)1097-0193(1997)5:5<347::AID-HBM3>3.0.CO;2-3
- Donner, T.H., Kettermann, A., Diesch, E., Ostendorf, F., Villringer, A., Brandt, S.A., 2002. Visual feature and conjunction searches of equal difficulty engage only partially overlapping frontoparietal networks. *NeuroImage* 15, 16–25. doi:10.1006/nimg.2001.0951
- 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. *Cereb. Cortex N. Y. N 1991* 20, 1574–1585. doi:10.1093/cercor/bhp215
- Doricchi, F., Thiebaut de Schotten, M., Tomaiuolo, F., Bartolomeo, P., 2008. White matter (dis)connections and gray matter (dys)functions in visual neglect: gaining insights into the brain networks of spatial awareness. *Cortex J. Devoted Study Nerv. Syst. Behav.* 44, 983–995. doi:10.1016/j.cortex.2008.03.006

- Doricchi, F., Tomaiuolo, F., 2003. The anatomy of neglect without hemianopia: a key role for parietal-frontal disconnection? *Neuroreport* 14, 2239–2243.
doi:10.1097/01.wnr.0000091132.75061.64
- Egely, R., Driver, J., Rafal, R.D., 1994. Shifting visual attention between objects and locations: evidence from normal and parietal lesion subjects. *J. Exp. Psychol. Gen.* 123, 161–177.
- Eramudugolla, R., Boyce, A., Irvine, D.R.F., Mattingley, J.B., 2010. Effects of prismatic adaptation on spatial gradients in unilateral neglect: A comparison of visual and auditory target detection with central attentional load. *Neuropsychologia* 48, 2681–2692.
doi:10.1016/j.neuropsychologia.2010.05.015
- Farnè, A., Buxbaum, L.J., Ferraro, M., Frassinetti, F., Whyte, J., Veramonti, T., Angeli, V., Coslett, H.B., Làdavas, E., 2004. Patterns of spontaneous recovery of neglect and associated disorders in acute right brain-damaged patients. *J. Neurol. Neurosurg. Psychiatry* 75, 1401–1410.
doi:10.1136/jnnp.2002.003095
- Farnè, A., Rossetti, Y., Toniolo, S., Làdavas, E., 2002. Ameliorating neglect with prism adaptation: visuo-manual and visuo-verbal measures. *Neuropsychologia* 40, 718–729.
- Ferber, S., Danckert, J., Joanisse, M., Goltz, H.C., Goodale, M.A., 2003. Eye movements tell only half the story. *Neurology* 60, 1826–1829.
- Fink, G.R., Halligan, P.W., Marshall, J.C., Frith, C.D., Frackowiak, R.S., Dolan, R.J., 1997. Neural mechanisms involved in the processing of global and local aspects of hierarchically organized visual stimuli. *Brain J. Neurol.* 120 (Pt 10), 1779–1791.
- Fink, G.R., Halligan, P.W., Marshall, J.C., Frith, C.D., Frackowiak, R.S., Dolan, R.J., 1996. Where in the brain does visual attention select the forest and the trees? *Nature* 382, 626–628.
doi:10.1038/382626a0
- Frassinetti, F., Angeli, V., Meneghello, F., Avanzi, S., Làdavas, E., 2002. Long-lasting amelioration of visuospatial neglect by prism adaptation. *Brain J. Neurol.* 125, 608–623.
- Geng, J.J., Mangun, G.R., 2009. Anterior intraparietal sulcus is sensitive to bottom-up attention driven by stimulus salience. *J. Cogn. Neurosci.* 21, 1584–1601. doi:10.1162/jocn.2009.21103
- 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, 905–918. doi:10.1016/j.neuron.2007.02.013
- Heide, W., Blankenburg, M., Zimmermann, E., Kömpf, D., 1995. Cortical control of double-step saccades: implications for spatial orientation. *Ann. Neurol.* 38, 739–748.
doi:10.1002/ana.410380508
- Heilman, K.M., Valenstein, E., Watson, R.T., 2000. Neglect and Related Disorders. *Semin. Neurol.* 20, 463–470. doi:10.1055/s-2000-13179
- Husain, M., Mannan, S., Hodgson, T., Wojciulik, E., Driver, J., Kennard, C., 2001. Impaired spatial working memory across saccades contributes to abnormal search in parietal neglect. *Brain J. Neurol.* 124, 941–952.
- Indovina, I., Macaluso, E., 2004. Occipital-parietal interactions during shifts of exogenous visuospatial attention: trial-dependent changes of effective connectivity. *Magn. Reson. Imaging* 22, 1477–1486. doi:10.1016/j.mri.2004.10.016
- Jacquin-Courtois, S., O'Shea, J., Luauté, J., Pisella, L., Revol, P., Mizuno, K., Rode, G., Rossetti, Y., 2013. Rehabilitation of spatial neglect by prism adaptation: a peculiar expansion of sensorimotor after-effects to spatial cognition. *Neurosci. Biobehav. Rev.* 37, 594–609.
doi:10.1016/j.neubiorev.2013.02.007
- Jacquin-Courtois, S., Rode, G., Pavani, F., O'Shea, J., Giard, M.H., Boisson, D., Rossetti, Y., 2010. Effect of prism adaptation on left dichotic listening deficit in neglect patients: glasses to hear better? *Brain J. Neurol.* 133, 895–908. doi:10.1093/brain/awp327
- Jacquin-Courtois, S., Rode, G., Pisella, L., Boisson, D., Rossetti, Y., 2008. Wheel-chair driving improvement following visuo-manual prism adaptation. *Cortex J. Devoted Study Nerv. Syst. Behav.* 44, 90–96. doi:10.1016/j.cortex.2006.06.003

- Karnath, H.-O., Rennig, J., Johannsen, L., Rorden, C., 2011. The anatomy underlying acute versus chronic spatial neglect: a longitudinal study. *Brain J. Neurol.* 134, 903–912. doi:10.1093/brain/awq355
- Karnath, H.-O., Rorden, C., 2012. The anatomy of spatial neglect. *Neuropsychologia* 50, 1010–1017. doi:10.1016/j.neuropsychologia.2011.06.027
- Keane, S., Turner, C., Sherrington, C., Beard, J.R., 2006. Use of fresnel prism glasses to treat stroke patients with hemispatial neglect. *Arch. Phys. Med. Rehabil.* 87, 1668–1672. doi:10.1016/j.apmr.2006.08.322
- Kim, Y.H., Gitelman, D.R., Nobre, A.C., Parrish, T.B., LaBar, K.S., Mesulam, M.M., 1999. The large-scale neural network for spatial attention displays multifunctional overlap but differential asymmetry. *NeuroImage* 9, 269–277. doi:10.1006/nimg.1999.0408
- 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. *J. Neurosci. Off. J. Soc. Neurosci.* 25, 4593–4604. doi:10.1523/JNEUROSCI.0236-05.2005
- Koch, G., Cercignani, M., Bonni, S., Giacobbe, V., Bucchi, G., Versace, V., Caltagirone, C., Bozzali, M., 2011. Asymmetry of parietal interhemispheric connections in humans. *J. Neurosci. Off. J. Soc. Neurosci.* 31, 8967–8975. doi:10.1523/JNEUROSCI.6567-10.2011
- Koch, G., Oliveri, M., Cheeran, B., Ruge, D., Lo Gerfo, E., Salerno, S., Torriero, S., Marconi, B., Mori, F., Driver, J., Rothwell, J.C., Caltagirone, C., 2008. Hyperexcitability of parietal-motor functional connections in the intact left-hemisphere of patients with neglect. *Brain J. Neurol.* 131, 3147–3155. doi:10.1093/brain/awn273
- LaBar, K.S., Gitelman, D.R., Parrish, T.B., Mesulam, M., 1999. Neuroanatomic overlap of working memory and spatial attention networks: a functional MRI comparison within subjects. *NeuroImage* 10, 695–704. doi:10.1006/nimg.1999.0503
- 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, 901–908.
- Leonards, U., Sunaert, S., Van Hecke, P., Orban, G.A., 2000. Attention mechanisms in visual search -- an fMRI study. *J. Cogn. Neurosci.* 12 Suppl 2, 61–75. doi:10.1162/089892900564073
- Luauté, J., Michel, C., Rode, G., Pisella, L., Jacquin-Courtois, S., Costes, N., Cotton, F., le Bars, D., Boisson, D., Halligan, P., Rossetti, Y., 2006. Functional anatomy of the therapeutic effects of prism adaptation on left neglect. *Neurology* 66, 1859–1867. doi:10.1212/01.wnl.0000219614.33171.01
- Luauté, J., Schwartz, S., Rossetti, Y., Spiridon, M., Rode, G., Boisson, D., Vuilleumier, P., 2009. Dynamic changes in brain activity during prism adaptation. *J. Neurosci. Off. J. Soc. Neurosci.* 29, 169–178. doi:10.1523/JNEUROSCI.3054-08.2009
- Maguire, A.M., Ogden, J.A., 2002. MRI brain scan analyses and neuropsychological profiles of nine patients with persisting unilateral neglect. *Neuropsychologia* 40, 879–887.
- Maravita, A., McNeil, J., Malhotra, P., Greenwood, R., Husain, M., Driver, J., 2003. Prism adaptation can improve contralesional tactile perception in neglect. *Neurology* 60, 1829–1831.
- Marshall, J.C., Halligan, P.W., 1995. Seeing the forest but only half the trees? *Nature* 373, 521–523. doi:10.1038/373521a0
- Mattingley, J.B., Berberovic, N., Corben, L., Slavin, M.J., Nicholls, M.E.R., Bradshaw, J.L., 2004. The greyscales task: a perceptual measure of attentional bias following unilateral hemispheric damage. *Neuropsychologia* 42, 387–394.
- McFie, J., Piercy, M.F., Zangwill, O.L., 1950. Visual-spatial agnosia associated with lesions of the right cerebral hemisphere. *Brain J. Neurol.* 73, 167–190.
- McIntosh, R.D., Rossetti, Y., Milner, A.D., 2002. Prism adaptation improves chronic visual and haptic neglect: a single case study. *Cortex J. Devoted Study Nerv. Syst. Behav.* 38, 309–320.
- Milner, A.D., McIntosh, R.D., 2004. Reaching between obstacles in spatial neglect and visual extinction. *Prog. Brain Res.* 144, 213–226. doi:10.1016/S0079-6123(03)14415-9

- Morris, A.P., Kritikos, A., Berberovic, N., Pisella, L., Chambers, C.D., Mattingley, J.B., 2004. Prism adaptation and spatial attention: a study of visual search in normals and patients with unilateral neglect. *Cortex J. Devoted Study Nerv. Syst. Behav.* 40, 703–721.
- Mort, D.J., Malhotra, P., Mannan, S.K., Rorden, C., Pambakian, A., Kennard, C., Husain, M., 2003. The anatomy of visual neglect. *Brain J. Neurol.* 126, 1986–1997. doi:10.1093/brain/awg200
- Müller, N.G., Donner, T.H., Bartelt, O.A., Brandt, S.A., Villringer, A., Kleinschmidt, A., 2003. The functional neuroanatomy of visual conjunction search: a parametric fMRI study. *NeuroImage* 20, 1578–1590.
- Newport, R., Schenk, T., 2012. Prisms and neglect: what have we learned? *Neuropsychologia* 50, 1080–1091. doi:10.1016/j.neuropsychologia.2012.01.023
- Nijboer, T.C.W., Kollen, B.J., Kwakkel, G., 2013. Time course of visuospatial neglect early after stroke: a longitudinal cohort study. *Cortex J. Devoted Study Nerv. Syst. Behav.* 49, 2021–2027. doi:10.1016/j.cortex.2012.11.006
- Nijboer, T.C.W., McIntosh, R.D., Nys, G.M.S., Dijkerman, H.C., Milner, A.D., 2008. Prism adaptation improves voluntary but not automatic orienting in neglect. *Neuroreport* 19, 293–298. doi:10.1097/WNR.0b013e3282f4cb67
- Nijboer, T.C.W., Nys, G.M.S., van der Smagt, M.J., van der Stigchel, S., Dijkerman, H.C., 2011. Repetitive long-term prism adaptation permanently improves the detection of contralesional visual stimuli in a patient with chronic neglect. *Cortex J. Devoted Study Nerv. Syst. Behav.* 47, 734–740. doi:10.1016/j.cortex.2010.07.003
- Nijboer, T.C.W., Olthoff, L., Van der Stigchel, S., Visser-Meily, J.M.A., 2014. Prism adaptation improves postural imbalance in neglect patients. *Neuroreport* 25, 307–311. doi:10.1097/WNR.0000000000000088
- Nobre, A.C., Coull, J.T., Walsh, V., Frith, C.D., 2003. Brain activations during visual search: contributions of search efficiency versus feature binding. *NeuroImage* 18, 91–103.
- Nys, G.M.S., de Haan, E.H.F., Kunneman, A., de Kort, P.L.M., Dijkerman, H.C., 2008. Acute neglect rehabilitation using repetitive prism adaptation: a randomized placebo-controlled trial. *Restor. Neurol. Neurosci.* 26, 1–12.
- Paterson, A., Zangwill, O.L., 1944. Disorders of Visual Space Perception Associated with Lesions of the Right Cerebral Hemisphere. *Brain* 67, 331–358. doi:10.1093/brain/67.4.331
- Perani, D., Vallar, G., Paulesu, E., Alberoni, M., Fazio, F., 1993. Left and right hemisphere contribution to recovery from neglect after right hemisphere damage—an [18F]FDG pet study of two cases. *Neuropsychologia* 31, 115–125.
- Pisella, L., Michel, C., Gréa, H., Tilikete, C., Vighetto, A., Rossetti, Y., 2004. Preserved prism adaptation in bilateral optic ataxia: strategic versus adaptive reaction to prisms. *Exp. Brain Res. Exp. Hirnforsch. Expérimentation Cérébrale* 156, 399–408. doi:10.1007/s00221-003-1746-4
- Pisella, L., Rode, G., Farnè, A., Tilikete, C., Rossetti, Y., 2006. Prism adaptation in the rehabilitation of patients with visuo-spatial cognitive disorders. *Curr. Opin. Neurol.* 19, 534–542. doi:10.1097/WCO.0b013e328010924b
- Pisella, L., Rossetti, Y., Michel, C., Rode, G., Boisson, D., Pélisson, D., Tilikete, C., 2005. Ipsidirectional impairment of prism adaptation after unilateral lesion of anterior cerebellum. *Neurology* 65, 150–152. doi:10.1212/01.wnl.0000167945.34177.5e
- Posner, M.I., 1980. Orienting of attention. *Q. J. Exp. Psychol.* 32, 3–25.
- Posner, M.I., Walker, J.A., Friedrich, F.J., Rafal, R.D., 1984. Effects of parietal injury on covert orienting of attention. *J. Neurosci. Off. J. Soc. Neurosci.* 4, 1863–1874.
- Redding, G.M., Rossetti, Y., Wallace, B., 2005. Applications of prism adaptation: a tutorial in theory and method. *Neurosci. Biobehav. Rev.* 29, 431–444. doi:10.1016/j.neubiorev.2004.12.004
- Redding, G.M., Wallace, B., 2006. Prism adaptation and unilateral neglect: review and analysis. *Neuropsychologia* 44, 1–20. doi:10.1016/j.neuropsychologia.2005.04.009
- Reed, S.A., Dassonville, P., 2014. Adaptation to leftward-shifting prisms enhances local processing in healthy individuals. *Neuropsychologia* 56, 418–427. doi:10.1016/j.neuropsychologia.2014.02.012

- Robertson, L.C., Lamb, M.R., Knight, R.T., 1988. Effects of lesions of temporal-parietal junction on perceptual and attentional processing in humans. *J. Neurosci. Off. J. Soc. Neurosci.* 8, 3757–3769.
- Rode, G., Cotton, F., Revol, P., Jacquin-Courtois, S., Rossetti, Y., Bartolomeo, P., 2010. Representation and disconnection in imaginal neglect. *Neuropsychologia* 48, 2903–2911. doi:10.1016/j.neuropsychologia.2010.05.032
- Rode, G., Klos, T., Courtois-Jacquín, S., Rossetti, Y., Pisella, L., 2006. Neglect and prism adaptation: a new therapeutic tool for spatial cognition disorders. *Restor. Neurol. Neurosci.* 24, 347–356.
- Rode, G., Pisella, L., Rossetti, Y., Farné, A., Boisson, D., 2003. Bottom-up transfer of sensory-motor plasticity to recovery of spatial cognition: visuomotor adaptation and spatial neglect. *Prog. Brain Res.* 142, 273–287. doi:10.1016/S0079-6123(03)42019-0
- Rode, G., Revol, P., Rossetti, Y., Boisson, D., Bartolomeo, P., 2007. Looking while imagining The influence of visual input on representational neglect. *Neurology* 68, 432–437. doi:10.1212/01.wnl.0000252936.54063.b0
- Rode, G., Rossetti, Y., Boisson, D., 2001. Prism adaptation improves representational neglect. *Neuropsychologia* 39, 1250–1254.
- Rode, G., Rossetti, Y., Li, L., Boisson, D., 1998. Improvement of mental imagery after prism exposure in neglect: a case study. *Behav. Neurol.* 11, 251–258.
- Rosen, A.C., Rao, S.M., Caffarra, P., Scaglioni, A., Bobholz, J.A., Woodley, S.J., Hammeke, T.A., Cunningham, J.M., Prieto, T.E., Binder, J.R., 1999. Neural basis of endogenous and exogenous spatial orienting. A functional MRI study. *J. Cogn. Neurosci.* 11, 135–152.
- Rossetti, Y., Rode, G., Pisella, L., Farné, A., Li, L., Boisson, D., Perenin, M.T., 1998. Prism adaptation to a rightward optical deviation rehabilitates left hemispatial neglect. *Nature* 395, 166–169. doi:10.1038/25988
- Ruff, C.C., Bestmann, S., Blankenburg, F., Bjoertomt, O., Josephs, O., Weiskopf, N., Deichmann, R., Driver, J., 2008. Distinct causal influences of parietal versus frontal areas on human visual cortex: evidence from concurrent TMS-fMRI. *Cereb. Cortex N. Y. N 1991* 18, 817–827. doi:10.1093/cercor/bhm128
- 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, S89–100.
- 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. *J. Cogn. Neurosci.* 13, 698–710. doi:10.1162/089892901750363244
- Saevarsson, S., Kristjánsson, A., Hildebrandt, H., Halsband, U., 2009. Prism adaptation improves visual search in hemispatial neglect. *Neuropsychologia* 47, 717–725. doi:10.1016/j.neuropsychologia.2008.11.026
- Sala, J.B., Courtney, S.M., 2007. Binding of what and where during working memory maintenance. *Cortex J. Devoted Study Nerv. Syst. Behav.* 43, 5–21.
- Sarri, M., Greenwood, R., Kalra, L., Driver, J., 2011. Prism adaptation does not change the rightward spatial preference bias found with ambiguous stimuli in unilateral neglect. *Cortex J. Devoted Study Nerv. Syst. Behav.* 47, 353–366. doi:10.1016/j.cortex.2010.01.006
- Sarri, M., Kalra, L., Greenwood, R., Driver, J., 2006. Prism adaptation changes perceptual awareness for chimeric visual objects but not for chimeric faces in spatial neglect after right-hemisphere stroke. *Neurocase* 12, 127–135. doi:10.1080/13554790600598774
- Schindler, I., McIntosh, R.D., Cassidy, T.P., Birchall, D., Benson, V., Ietswaart, M., Milner, A.D., 2009. The disengage deficit in hemispatial neglect is restricted to between-object shifts and is abolished by prism adaptation. *Exp. Brain Res. Exp. Hirnforsch. Expérimentation Cérébrale* 192, 499–510. doi:10.1007/s00221-008-1585-4
- Serino, A., Angeli, V., Frassinetti, F., Làdavas, E., 2006. Mechanisms underlying neglect recovery after prism adaptation. *Neuropsychologia* 44, 1068–1078. doi:10.1016/j.neuropsychologia.2005.10.024

- Serino, A., Bonifazi, S., Pierfederici, L., Làdavas, E., 2007. Neglect treatment by prism adaptation: what recovers and for how long. *Neuropsychol. Rehabil.* 17, 657–687. doi:10.1080/09602010601052006
- Shinoura, N., Suzuki, Y., Yamada, R., Tabei, Y., Saito, K., Yagi, K., 2009. Damage to the right superior longitudinal fasciculus in the inferior parietal lobe plays a role in spatial neglect. *Neuropsychologia* 47, 2600–2603. doi:10.1016/j.neuropsychologia.2009.05.010
- 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. *J. Neurosci. Off. J. Soc. Neurosci.* 29, 4392–4407. doi:10.1523/JNEUROSCI.5609-08.2009
- Shulman, G.L., Pope, D.L.W., Astafiev, S.V., McAvoy, M.P., Snyder, A.Z., Corbetta, M., 2010. Right Hemisphere Dominance During Spatial Selective Attention and Target Detection Occurs Outside the Dorsal Frontoparietal Network. *J. Neurosci.* 30, 3640–3651. doi:10.1523/JNEUROSCI.4085-09.2010
- Siéoff, E., 2015. Acquired spatial dyslexia. *Ann. Phys. Rehabil. Med.* doi:10.1016/j.rehab.2015.07.004
- Silver, M.A., Kastner, S., 2009. Topographic maps in human frontal and parietal cortex. *Trends Cogn. Sci.* 13, 488–495. doi:10.1016/j.tics.2009.08.005
- Stone, S.P., Halligan, P.W., Greenwood, R.J., 1993. The incidence of neglect phenomena and related disorders in patients with an acute right or left hemisphere stroke. *Age Ageing* 22, 46–52.
- Stratton, G., 1896. Some preliminary experiments on vision without inversion of the retinal image. *Psychol Rev* 611–617.
- Striemer, C., Danckert, J., 2007. Prism adaptation reduces the disengage deficit in right brain damage patients. *Neuroreport* 18, 99–103. doi:10.1097/WNR.0b013e3280125670
- Striemer, C.L., Danckert, J., 2010. Dissociating perceptual and motor effects of prism adaptation in neglect. *Neuroreport* 21, 436–441. doi:10.1097/WNR.0b013e328338592f
- Striemer, C.L., Ferber, S., Danckert, J., 2013. Spatial working memory deficits represent a core challenge for rehabilitating neglect. *Front. Hum. Neurosci.* 7, 334. doi:10.3389/fnhum.2013.00334
- Striemer, C., Sablatnig, J., Danckert, J., 2006. Differential influences of prism adaptation on reflexive and voluntary covert attention. *J. Int. Neuropsychol. Soc. JINS* 12, 337–349.
- Sturm, W., de Simone, A., Krause, B.J., Specht, K., Hesselmann, V., Radermacher, I., Herzog, H., Tellmann, L., Müller-Gärtner, H.W., Willmes, K., 1999. Functional anatomy of intrinsic alertness: evidence for a fronto-parietal-thalamic-brainstem network in the right hemisphere. *Neuropsychologia* 37, 797–805.
- Sturm, W., Willmes, K., 2001. On the functional neuroanatomy of intrinsic and phasic alertness. *NeuroImage* 14, S76–84. doi:10.1006/nimg.2001.0839
- Thiebaut de Schotten, M., Urbanski, M., Duffau, H., Volle, E., Lévy, R., Dubois, B., Bartolomeo, P., 2005. Direct evidence for a parietal-frontal pathway subserving spatial awareness in humans. *Science* 309, 2226–2228. doi:10.1126/science.1116251
- Thiel, C.M., Zilles, K., Fink, G.R., 2004. Cerebral correlates of alerting, orienting and reorienting of visuospatial attention: an event-related fMRI study. *NeuroImage* 21, 318–328.
- Uddin, L.Q., Supekar, K., Amin, H., Rykhlevskaia, E., Nguyen, D.A., Greicius, M.D., Menon, V., 2010. Dissociable connectivity within human angular gyrus and intraparietal sulcus: evidence from functional and structural connectivity. *Cereb. Cortex N. Y. N 1991* 20, 2636–2646. doi:10.1093/cercor/bhq011
- Vallar, G., Perani, D., 1986. The anatomy of unilateral neglect after right-hemisphere stroke lesions. A clinical/CT-scan correlation study in man. *Neuropsychologia* 24, 609–622.
- Van Kessel, M.E., van Nes, I.J.W., Brouwer, W.H., Geurts, A.C.H., Fasotti, L., 2010. Visuospatial asymmetry and non-spatial attention in subacute stroke patients with and without neglect. *Cortex J. Devoted Study Nerv. Syst. Behav.* 46, 602–612. doi:10.1016/j.cortex.2009.06.004

- Van Koningsbruggen, M.G., Gabay, S., Sapir, A., Henik, A., Rafal, R.D., 2010. Hemispheric asymmetry in the remapping and maintenance of visual saliency maps: a TMS study. *J. Cogn. Neurosci.* 22, 1730–1738. doi:10.1162/jocn.2009.21356
- 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 modeling. *J. Neurosci. Off. J. Soc. Neurosci.* 32, 10637–10648. doi:10.1523/JNEUROSCI.0414-12.2012
- Watanabe, S., Amimoto, K., 2010. Generalization of prism adaptation for wheelchair driving task in patients with unilateral spatial neglect. *Arch. Phys. Med. Rehabil.* 91, 443–447. doi:10.1016/j.apmr.2009.09.027

Figure legends

Figure 1. Activation studies in normal subjects and in patients with right hemispheric stroke. A. Brain activation in a group of 15 normal subjects during a visual target detection task before and after a session of rightward PA (adapted from Crottaz-Herbette et al., 2014). Top row: Surface renderings of the brain activation showing significant differences before (1: Pre-PA) vs. after PA (2: Post-PA). Graphs: Percent (mean $\pm$ SEM) BOLD signal changes in session 1 (light gray) and session 2 (dark gray) as function of the position of visual targets in the left angular gyrus (red circle) and in the right supramarginal gyrus (blue circle). Bottom row: Surface renderings of the brain activation showing significant changes in activity elicited by left, center and right targets: increased representation of the left, central and right visual field within the left IPL and decreased representation of the right and central visual field within the right IPL. B. Surface renderings and graphs of percent BOLD signal changes for a group of 15 patients with right hemispheric stroke (adapted from Crottaz-Herbette et al., Submitted), same comparisons as in A. Display of the lesions overlap across the 15 patients with a gray scale on the surface rendering.

Figure 2. Schematic representation of the dorsal and ventral attentional systems (DAS, VAS, outlined in blue and orange, respectively), the visual cortex and their interactions (based on Corbetta and Shulman, 2011; Koch et al., 2008). Situation in normal subjects is represented on the left (A, C) and in patients with neglect on the right (B, D). Changes induced by rightward PA (as reported by Crottaz-Herbette et al., 2014) are outlined in the bottom panel (C, D) and are highlighted in yellow. Arrows represent connectivity within the attentional systems (red and yellow) as well as between visual areas and VAS (black and gray). "-" marks inhibitory interconnections between DAS in either hemisphere. Black and gray denotes structural connections; gray are less effective in attentional tasks than black ones (Indovina and Macaluso, 2004). Dashed arrows highlight connections which are disrupted in neglect. The shift in hemispheric dominance within VAS, which is induced by rightward

PA, restores the VAS input to DAS via the left IPL and explains thus the positive effects of rightward PA in neglect. Following rightward PA, the left IPL receives visual information from both hemifields, but the afferents from right visual cortex are less effective, rendering most likely left visual stimuli less salient. This asymmetry in salience may account for several effects of rightward PA in normal subjects or their absence in neglect.

Detection task before PA versus after PA

A. Normal subjects

ANOVA: Main effect of Session (Pre vs Post PA)

B. Patients with right hemispheric stroke

ANOVA: Interaction Session X Stimulus position

Normal subjects

Patients with neglect

POST RIGHTWARD PRISMATIC ADAPTATION