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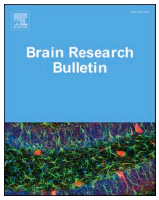

The disengagement deficit after right-hemisphere damage: Distinct roles of lateral frontal and parietal damage

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ABSTRACT

An influential model of spatial attention postulates three main attention-orienting mechanisms: disengagement, shifting, and engagement. Early research linked disengagement deficits with superior parietal damage, regardless of hemisphere or presence of spatial neglect. Subsequent studies supported the involvement of more ventral parietal regions, especially in the right hemisphere, and linked spatial neglect to deficient disengagement from ipsilateral cues. However, previous lesion studies faced serious limitations, such as small sample sizes and the lack of brain-injured controls without neglect. Additionally, some studies employed symbolic cues or used long cue-target intervals, which may fail to reveal impaired disengagement. We here used a machine-learning approach to conduct lesion-symptom mapping (LSM) on 89 patients with focal cerebral lesions to the left (LH) or right (RH) cerebral hemisphere. A group of 54 healthy participants served as controls. The paradigm used to uncover disengagement deficits employed non-predictive cues presented in the visual periphery and at short cue-target intervals, targeting exogenous attention. The main factors of interest were group (healthy participants, LH, RH), target position (left, right hemifield) and cue validity (valid, invalid). LSM-analyses were performed on two indices: the validity effect, computed as the absolute difference between reaction times (RTs) following invalid compared to valid cues, and the disengagement deficit, determined by the difference between contralesional and ipsilesional validity effects. While LH patients showed general slowing of RTs to contralesional targets, only RH patients exhibited a disengagement deficit from ipsilesional cues. LSM associated the validity effect with a right lateral frontal cluster, which additionally affected subcortical white matter of the right arcuate fasciculus, the corticothalamic pathway, and the superior longitudinal fasciculus. In contrast, the disengagement deficit was related to damage involving the right temporoparietal junction. Thus, our results support the crucial role of right inferior parietal and posterior temporal regions for attentional disengagement, but also emphasize the importance of lateral frontal regions, for the reorienting of attention.

1. Introduction

Disorders of spatial cognition are among the most frequent consequences of focal damage to the right cerebral hemisphere (Lunven and Bartolomeo, 2017). Posner's spotlight analogy (Posner and Cohen, 1984) stands out among cognitive models that intend to explain spatial attention deficits following brain injury. This model proposes that three mechanisms control the orienting of attention: disengagement, shifting, and engagement. This appealing and subjectively relatable analogy became very influential, particularly because impairment in one of the three operations results in specific effects that can be examined with a spatial cueing paradigm (Posner, 1980). The paradigm requires participants to react as quickly as possible to a visual target shown in the left or right visual field, preceded by a brief, lateralized cue which may appear at the same (valid cue) or the opposite side (invalid cue) of the target.

Several early studies involving patients with focal injury of the left or right hemisphere linked failures of the disengagement operation to damage affecting the parietal lobes (Losier and Klein, 2001; Morrow and Ratcliff, 1988; Posner et al., 1984). The first and most influential of these studies (Posner et al., 1984) reported that patients with parietal damage exhibit a strong difference between reaction times (RTs) across the hemifields when an invalid cue precedes the target. While RTs to ipsilesional targets were barely affected by cue validity, parietal patients

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exhibited noticeably increased RTs to contralesional targets following invalid cues. This *disengagement deficit* has been confirmed in several studies, and its association with parietal damage has been widely accepted in the scientific literature (Carter et al., 2017; Friedrich et al., 1998; Losier and Klein, 2001; Morrow and Ratcliff, 1988; Ptak and Bourgeois, 2024).

However, several methodological issues raise questions regarding the strength of the evidence supporting a crucial involvement of the parietal lobes in the disengagement operation. First, early studies selected patients based on the presence of parietal damage and consequently lacked a control group with damage outside this region (Friedrich et al., 1998; Petersen et al., 1989; Posner et al., 1984). This approach contrasts with modern lesion-symptom mapping (LSM), which attempts to apply hypothesis-free whole-brain analyses to identify crucial damage associated with a specific behavioral impairment. Some of the previous findings were also inconsistent regarding the importance of the left and right cerebral hemispheres for the disengagement of attention (Ptak and Bourgeois, 2024). Further, these studies generally tested small numbers of highly selected participants, casting doubt on the statistical power of the identified effects. While more recent studies included larger patient samples (Carter et al., 2017; Rengachary et al., 2011) they employed symbolic cues (leftward or rightward pointing arrows), which rely strongly on endogenous mechanisms of attention and are less likely to produce a disengagement deficit (Losier and Klein, 2001). Another limitation is the predictivity of the cue, as it mixes exogenous and endogenous effects and might strongly modulate performance (Bonato et al., 2018). In addition, recent studies have shown that the presence of a disengagement deficit depends on crucial characteristics of the cue such as task-relevance (Pedrazzini and Ptak, 2019; Ptak and Pedrazzini, 2021) or reinforcement value (Bourgeois et al., 2022).

We here used modern LSM methods to examine the neural correlates of the disengagement deficit in unselected patients with or without neglect, suffering from focal cerebral lesions located in the right and left hemispheres. To increase the likelihood that patients exhibit a disengagement deficit and to favor reflexive (exogenous) mechanisms of attention, the task employed peripheral non-predictive cues presented very briefly prior to target appearance.

2. Materials and methods

2.1. Participants

Eighty-nine patients (30 females; $Mean_{age} = 63.94 \pm 11.70$) with first-ever focal brain damage, including 69 with right-hemisphere damage (RH) and 20 with left-hemisphere damage (LH) participated in this study. The study was part of a larger project evaluating cognitive deficits associated with damage to frontoparietal networks (Doganci et al., 2024). Patients were enrolled upon admission to the Division of Neurorehabilitation at the University Hospitals of Geneva after discovery of a first-ever brain lesion resulting mainly from vascular disease (84 ischemic or hemorrhagic strokes; 5 tumors or other lesions). The exclusion criteria were the presence of prior vascular damage, severe cognitive impairment such as language comprehension deficits or confusion, and presence or antecedents of severe psychiatric disorders. Lesions of all patients are summarized in Fig. 4A. To compare patient performance with healthy controls, 54 participants (29 females; $Mean_{age} = 63.12 \pm 8.85$) without antecedents of neurological or psychological deficits were also recruited. Chi-square difference tests indicated no significant differences between the LH group, RH group and healthy controls in terms of sex [$\chi^2(2, N = 143) = 5.56$, $p = .062$] or handedness [$\chi^2(2, N = 143) = 3.29$, $p = .193$]. A one-way analysis of variance (ANOVA) revealed no significant age differences [$F(2, 140) = 0.19$, $p = .829$]. All participants provided informed consent, and the study was approved by the Ethical Commission of the Canton of Geneva on May 3, 2018 (reference number 2018–00135), in accordance with the Declaration of Helsinki. More information on the participants can be found in Table 1.

Before the task, all patients underwent a battery of neuropsychological tests to assess their spatial attention (see Table 1), including the Bells cancellation test (Gauthier et al., 1989), letter A cancellation (Mesulam, 1985), inverted T cancellation (Ptak et al., 2007), line bisection (Ronchi et al., 2012), reading compound words (Ptak et al., 2012), and clock drawing (Azouvi et al., 2006). Visual field loss was assessed through confrontation testing with finger movement detection for each quadrant of the visual field.

2.2. Spatial attention task

The experimental task was designed with E-Prime 2.0 software (Psychology Software Tools, Pittsburgh, PA) and presented on a 13" laptop with a 1280×800 pixel resolution, placed at 50 cm from participants. The task was an adaptation of the original Posner cueing paradigm (Posner, 1980; see Fig. 1 for stimuli and timings) where participants fixated on a central cross on the screen before a bold square (the cue) signaled the presentation of a target on either the right or left side of the screen. The peripheral squares marking possible target position and the cue were 150×150 pixels large and located at 25 % on the left or right of the screen. The cue was shown for 100 ms and followed by the target (a large X) either after 50 ms or 650 ms, corresponding to stimulus-onset asynchronies (SOAs) of 150 ms or 750 ms. Three quarters of the trials had short SOAs and one quarter long SOAs. The latter were included to prevent anticipatory responses and were not considered for further analysis.

Participants' instruction was to press a response key of a Cedrus response box (Cedrus, San Pedro, CA) as quickly as possible upon target presentation, while their reaction times were recorded. They were asked to maintain gaze on the central fixation cross, which was controlled during 20 praxis trials before starting the experiment. The experiment consisted of three blocks of 64 trials, with an orthogonal mapping of cue direction (left or right) and target side (left or right). Therefore, the cue

Table 1
Demographic and clinical characteristics of the participants (mean±SD).

		Group		
		Control	LH	RH
Sex	Female/male	29/25	7/13	23/46
Age	Years	63.12 ±8.85	64.84 ±12.29	63.68 ±11.61
Handedness	Right/left	54/0	20/0	66/3
Time post stroke	Days	-	44.15 ±19.10	50.49 ±28.55
Time post imaging	Days	-	14.10 ±20.80	34.80 ±43.30
Visual field loss	Preserved/ impacted	-	15/5	55/14
Neglect	No/yes	-	20/0	45/24
Bells cancellation	Left omissions (max. 15)	-	1.20 ±1.54	5.04 ±4.98
	Right omissions (max. 15)	-	1.85 ±2.35	2.25 ±2.68
Letter A cancellation	Left omissions (max. 17)	-	0.75 ±1.62	4.74 ±5.82
	Right omissions (max. 17)	-	0.95 ±2.01	2.26 ±3.37
Inverted T cancellation	Left omissions (max. 27)	-	0.40 ±0.75	8.76 ±9.71
	Right omissions (max. 27)	-	0.50 ±0.89	4.06 ±5.01
Line bisection	Bias, %	-	-1.52 ±3.72	5.33 ±12.32
Reading	Omissions (max. 40)	-	2.05 ±4.05	5.37 ±7.93
Clock drawing	Points (max. 10)	-	8.53 ±2.09	7.66 ±2.21

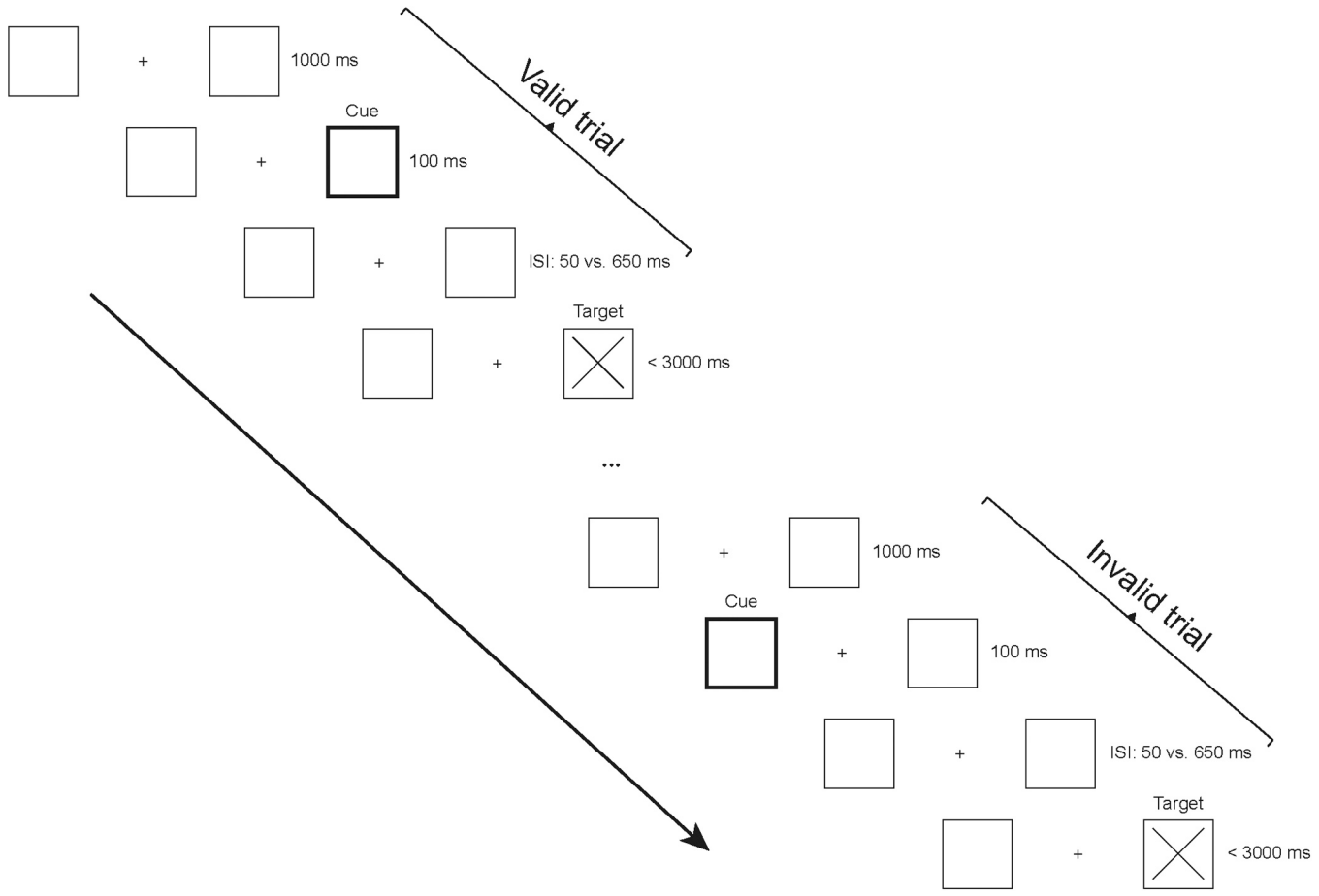

Fig. 1. Sequence and timing of events of the Spatial Attention Task. ISI = interstimulus interval.

was not predictive of target position.

2.3. Analysis

The RT analysis focused on responses for the short SOA (150 ms), which was more likely to yield a significant disengagement deficit (Losier and Klein, 2001). We first eliminated trials with RTs that deviated by more than two standard deviations from the individual mean of the participant. A mixed analysis of variance was then performed on the median RTs, including the between-subject factor of Group (RH vs. LH vs. Control) and the within-subject factors of Cue validity (Valid vs. Invalid) and Target side (Left vs. Right). To assess the relationship between neuropsychological scores and behavior in RH and LH patients, we calculated two indices. The *validity index* was calculated for each side by subtracting the RT in the valid condition from the RT of the invalid condition. The greater this value, the higher the cost associated with disengaging attention from misleading cues. The *disengagement index* was obtained by subtracting the left validity index from the right validity index. A positive value suggests a disengagement deficit, that is, effects of cue validity are greater for contralateral targets than ipsilateral targets. We further performed forward stepwise regression analyses focusing on the question whether clinical neglect tests are significant predictors of the validity index or the disengagement index. These analyses included the three cancellation tests and the line bisection test as predictors.

2.4. MRI acquisition and preprocessing

Lesion analyses were based on standard clinical T1- and T2-weighted MRI scans in 62 patients (TR: 6490 ms, TE: 90 ms, slice resolution: 4 mm) or high-resolution scans in 25 patients (TR: 3200 ms; TE: 407 ms, slice resolution: 1.1 mm), performed on a 3-T Trio scanner (Siemens Medical Solutions, Erlangen, Germany). Due to medical contraindications for two patients only CT scans were available.

The lesions of each patient were delineated manually using MRIcron software (Rorden et al., 2007), and exported as a volumetric mask (volume of interest; VOI). This VOI, as well as the scan in which the lesion was drawn (T2 or CT) were then coregistered with the T1-weighted image using Statistical Parametric Mapping software (SPM12; www.fil.ion.ucl.ac.uk/spm). All images were then normalized to the Montreal Neurological Institution (MNI) template space using the Clinical Toolbox (Rorden et al., 2012) implemented in SPM12. This toolbox uses an age-appropriate template for older participants. Image dimensions were reduced to 182×218×182 as required by the Lesion Quantification Toolkit (LQT; Griffis et al., 2021, see Section 2.5).

2.5. Lesion-behavior relationship

The primary objective of this study was to identify the anatomical predictors of spatial attention, as measured by the right validity, left validity, and disengagement indices in the spatial attention task. To achieve this, we first extracted grey and white matter from the patients' lesions using LQT, a MATLAB-based software designed to estimate grey matter damage and white matter disconnections in patients with focal lesions (Griffis et al., 2021).

Three dimensions of the relationship between performance in the spatial attention task and the lesions were investigated. (1) Grey Matter Parcel Lesion Load: Brain voxels associated with a lesion were mapped onto functionally or anatomically defined grey matter parcels or regions (Griffis et al., 2021), creating representations of the damage incurred by

individual parcels, referred to as lesion loads. (2) White Matter Disconnection Maps: The lesion segmentation was integrated into the complete collection of streamlines covering all 70 tracts of the HCP-842 streamline tractography atlas. This resulted in a subset of streamlines that intersected with the lesion, creating white matter disconnection maps. (3) White Matter Tract Disconnection Severities: The lesion was incorporated as a region-of-interest into the HCP-842 streamline tractography atlas, and the count of disconnected streamlines was converted into a percentage relative to the total number of streamlines assigned to that tract. This estimation provided the percentage severity of disconnection for each tract.

For (1) and (2), Support Vector Regression-Lesion Symptom Mapping (SVR-LSM) based on the MATLAB (R2022; The MathWorks, Inc.) toolbox by DeMarco and Turkeltaub (2018) was used to identify anatomical predictors of spatial attention. In order to mitigate the impact of rarely affected areas and to circumvent the spatial misalignment associated with LSM techniques (Sperber and Karnath, 2017), the analysis focused on voxels that exhibited damage in a minimum of 5 patients. β-values were thresholded voxel-wise at $p < .005$ based on 5000 permutations. To correct for multiple comparisons, a family-wise error rate of 0.05 was maintained using a cluster-extent threshold determined from the same 5000 permutations. The analysis was performed separately for the right validity, left validity and disengagement indices. For (3), further analysis was conducted on the top 20 % of tracts regarding the percentage of streamlines disconnected. The disconnection severities of these tracts were correlated with behavioral indices using Spearman-rank correlations, and p-values were adjusted within each index with an FDR correction.

3. Results

3.1. Spatial attention task

Fig. 2 shows the RT results in the spatial attention task. A mixed ANOVA revealed a significant main effect of Group [$F(1, 140) = 20.38$, $p < .001$, $\eta_p^2 = .23$], Validity of the cue [$F(1, 140) = 38.71$, $p < .001$, $\eta_p^2 = .22$] and Target side [$F(1, 140) = 9.15$, $p = .003$, $\eta_p^2 = .06$]. As shown by Bonferroni-corrected post-hoc tests, control participants were significantly faster at detecting the target than RH patients (Mean difference = 148.99, SE = 23.34, $p < .001$), but only marginally faster than LH patients (Mean difference = 80.23, SE = 33.63, $p = .055$). The two patient groups did not significantly differ from each other (Mean difference = 68.76, SE = 32.63, $p = .111$). The significant Validity effect reflected faster RTs in the valid condition than the invalid condition. The significant effect of Target side was due to faster RTs when targets were shown in the right visual field compared to the left visual field.

The ANOVA also revealed significant two-way interactions between Group*Target side [$F(2, 140) = 16.36$, $p < .001$, $\eta_p^2 = .19$], Group*Validity [$F(2, 140) = 12.67$, $p < .001$, $\eta_p^2 = .15$], and Target side*Validity [$F(1, 140) = 4.40$, $p = .038$, $\eta_p^2 = .03$]. More importantly, the interaction between all three factors was also significant [$F(2, 140) = 9.41$, $p < .001$, $\eta_p^2 = .12$]. Given the important qualitative and quantitative differences in performance between the three groups, we followed up this interaction with two-way repeated-measures ANOVAs across Validity and Target side for each group individually.

3.1.1. Within-group performance

An rANOVA on the data of control participants with Cue validity and Target side yielded a significant main effect of Cue validity [$F(1, 53) = 9.69$, $p = .003$, $\eta_p^2 = .15$], reflecting a significant advantage in the valid condition. The main effect of Target side [$F(1, 53) = 2.33$, $p = .133$, $\eta_p^2 = .04$], and the interaction [$F(1, 53) = 2.87$, $p = .096$, $\eta_p^2 = .05$] were not significant.

Similarly, LH-patients only showed a significant effect of Cue validity [$F(1,19) = 25.80$, $p < .001$, $\eta_p^2 = .56$], with faster RTs following valid cues. The effect of Target side [$F(1, 19) = 1.93$, $p = .181$, $\eta_p^2 = .09$] and the interaction [$F(1, 19) = 3.28$, $p = .086$, $\eta_p^2 = .15$] did not reach significance.

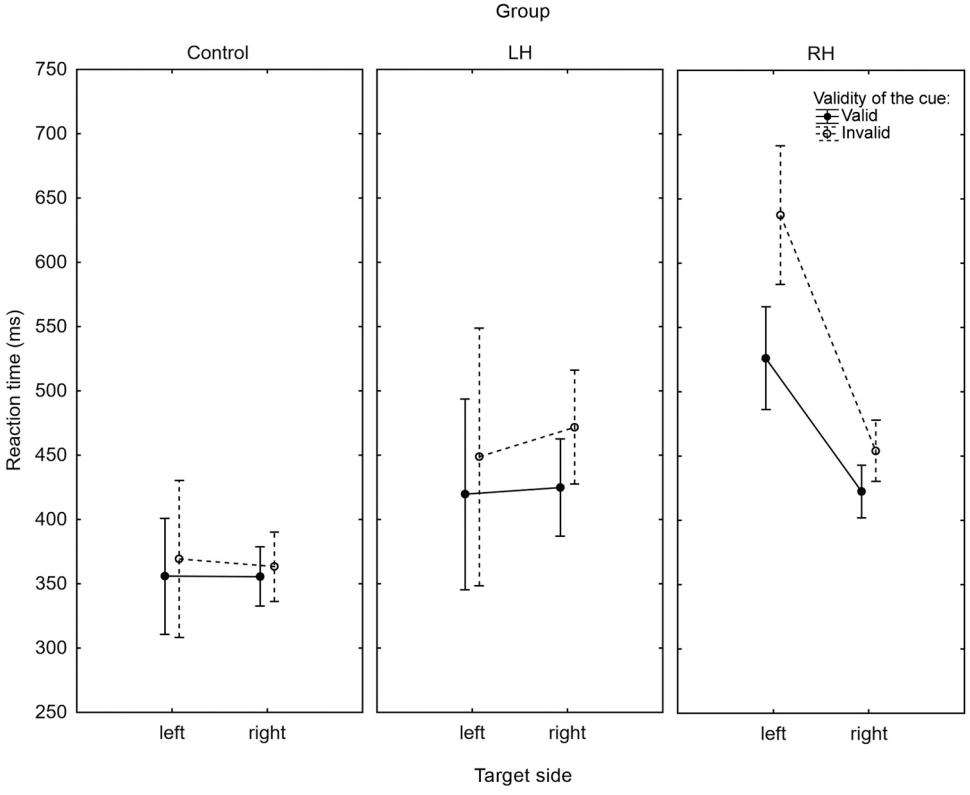

Fig. 2. Plot of the three-way interaction between Group (Control vs. RH vs. LH), Validity of the cue (Valid vs. Invalid) and Target side (Left vs. Right). Vertical bars denote 95 % confidence intervals.

In contrast to these two groups, performance of RH-patients was characterized by significant effects of Cue validity [$F(1, 68) = 41.86$, $p < .001$, $\eta_p^2 = .38$], Target side [$F(1, 68) = 30.36$, $p < .001$, $\eta_p^2 = .31$], as well as a significant interaction between both factors [$F(1, 68) = 17.57$, $p < .001$, $\eta_p^2 = .21$]. Bonferroni-corrected post-hoc tests showed that RH-patients were faster in the valid than the invalid condition, but only when the cue appeared in the left visual field (Mean difference = 111.39, SE = 13.44, $p < .001$).

3.1.2. Relationship between neuropsychological scores and behavior

To assess the relationship between cognitive test scores and behavioral indices derived from the cueing paradigm we performed forward stepwise regression analyses on the data of the RH group.

Regarding the validity index for targets in the left hemifield (Fig. 3A) the analysis revealed significant effects for line bisection [$t(63) = -3.84$, $p < .001$] and inverted T cancellation [$t(63) = -3.06$, $p = .003$]. Interestingly, a very similar finding was observed for right hemifield targets (Fig. 3B) and the disengagement index (Fig. 3C), again identifying line bisection [$t(63) = -3.71$, $p < .001$ and $t(63) = -3.23$, $p = .002$, respectively] and inverted T cancellation [$t(63) = 3.43$, $p = .001$ and $t(63) = 2.65$, $p = .010$, respectively] as only predictors of the validity and disengagement indices.

3.2. Lesion-behavior relationship

3.2.1. Analysis of parcel load

Fig. 4A shows the overlap map of all patient lesions. The SVR-LSM analysis for the relationship between the degree of grey matter damage and the validity index for left targets (Fig. 4B) identified one significant cluster (cluster size = 3797 voxels, $p = .021$). This cluster encompassed the right middle frontal gyrus, the frontal operculum and the insular cortex descending into the white matter of the temporal lobe. No significant findings were obtained with the right validity index. In contrast, the analysis of the disengagement index yielded one significant cluster (cluster size = 2691 voxels, $p = .039$) covering the posterior supramarginal gyrus, parts of the angular gyrus, the posterior superior and middle temporal gyri, as well as lateral occipital cortex.

3.2.2. Analysis of disconnection maps

The SVR-LSM analysis for the relationship between the degree of lesion and the left validity index (Fig. 5A) highlighted one significant cluster (cluster size = 6422 voxels, $p = .004$). This cluster involved mainly frontal white matter indicating involvement of cortical and subcortical projections. No significant voxels were identified in the analysis of the right validity index. Analyzing the disengagement index yielded a significant cluster (cluster size = 6191 voxels, $p = .003$) involving the white matter underlying the middle frontal gyrus and the insula.

To further analyze which specific white matter tracts were significant predictors of behavior, we computed correlations between the white matter disconnection severities and the behavioral indices for the top 20 % tracts based on the percentage of streamlines disconnected (Fig. 5B). These correlations were significant for all tracts displayed in Figs. 5B and 5C (left panel). For the left validity index, the highest three correlations were found for the right arcuate fasciculus (AF; $r = 0.48$, $p < .001$), corticothalamic pathway (CT; $r = 0.42$, $p < .001$) and superior longitudinal fasciculus (SLF; $r = 0.38$, $p = .001$). The disengagement index correlated best with the right AF ($r = 0.48$, $p < .001$), CT ($r = 0.41$, $p < .001$) and inferior fronto-occipital fasciculus (IFOF; $r = 0.39$, $p < .001$). Results of these tract analyses are displayed in Figs. 5B and 5C.

4. Discussion

The current study was designed to overcome shortcomings of prior work examining the anatomical correlates of the disengagement deficit of attention following unilateral brain damage. The aim was to apply modern lesion-symptom mapping methods on a reasonably large sample of patients, and thus to avoid limitations of previous studies such as the selection of participants based on specific brain lesions or the lack of brain-injured controls. Behavioral results showed that the LH-patients, RH-patients and healthy control were largely comparable in terms of performance except when the target was in the left hemifield. Indeed, participants with damage to the RH were slower overall when reacting to targets in the left hemifield, yet particularly so in the invalid condition. Stepwise regression analyses further revealed that cue validity effects were associated with clinical measures indexing spatial neglect, such as contralesional omissions in cancellation tests, and line bisection bias. The fact that patients showed particularly significant contralateral slowing together with an increased validity effect after RH-damage agrees with previous observations (for a recent review, see Ptak and Bourgeois, 2024). The novel finding of our study concerns the neural correlates of the validity effect and the disengagement deficit. Our results highlighted a cluster localized at the level of the right middle frontal gyrus, frontal operculum, and insular cortex associated with the validity effect, and a posterior cluster located around the right temporoparietal junction predicting the disengagement deficit. The disconnection analysis emphasized the role of several fiber tracts, particularly the right AF, CT and SLF.

In view of these anatomical findings, it is important to show that our experimental setup is comparable to previous studies and leads to the expected results. Indeed, several behavioral outcomes of our study are in line with the literature on the Posner-type spatial attention task in healthy subjects and diverse clinical samples (e.g., Posner, 1980). First, a significant validity effect was present in all participant groups, confirming the strong impact of invalid cues on the deployment of spatial attention. Second, in accordance with studies on spatial neglect (e.g., Corbetta and Shulman, 2011; Li and Malhotra, 2015; Mort et al., 2003), RH patients overall, and a subgroup of RH patients exhibiting spatial neglect in particular, showed increased RTs to targets presented in the left visual field. Though the interaction between N- and N+ patients failed to reach significance, the latter exhibited an RT pattern consistent with a disengagement deficit (Morrow and Ratcliff, 1988; Posner et al., 1984; Ptak and Pedrazzini, 2021). As suggested by Losier and Klein (2001) two experimental factors are essential when measuring the disengagement deficit in patients with neglect: the utilization of peripheral cues and short cue-target intervals. Indeed, some previous studies using central, symbolic cues (arrows) and exceedingly long cue-target intervals failed to observe disengagement effects in patients with neglect (Carter et al., 2017; Rengachary et al., 2011). Short peripheral cues favor automatic (i.e., exogenous) attentional mechanisms (Olk et al., 2010), which appear to be essential for the observation of a disengagement deficit (Bartolomeo and Chokron, 2002; Olk et al., 2010). Our behavioral results are compatible with a deficit of patients with RH-damage in deploying attention reflexively following a brief peripheral cue.

Our anatomical findings extend the conclusions of older studies. Our LSM analysis of the validity effect identified an anterior cluster overlapping with the right middle frontal gyrus, the frontal operculum, and the insular cortex. In contrast, the disengagement deficit was associated with damage at the temporoparietal junction, which is coherent with several previous studies Posner et al. (1984)(Carter et al., 2017; Friedrich et al., 1998; Losier and Klein, 2001; Morrow and Ratcliff, 1988). However, except for the study by Carter et al. (2017) these findings emanated from small samples ($N < 20$) that had been selected based on the presence of parietal damage and/or the presence of neglect. Such a proceeding is not hypothesis-free and may lead to severely biased outcomes. We here adopted a hypothesis-free approach that does not *a-priori* favor a specific brain region and hence examined an unselected sample. Interestingly, the only previous study that applied this logic by examining 70 patients with RH-damage, reported an association between the validity effect and subcortical white matter underlying the parietal lobe and the lateral frontal cortex (Carter et al., 2017).

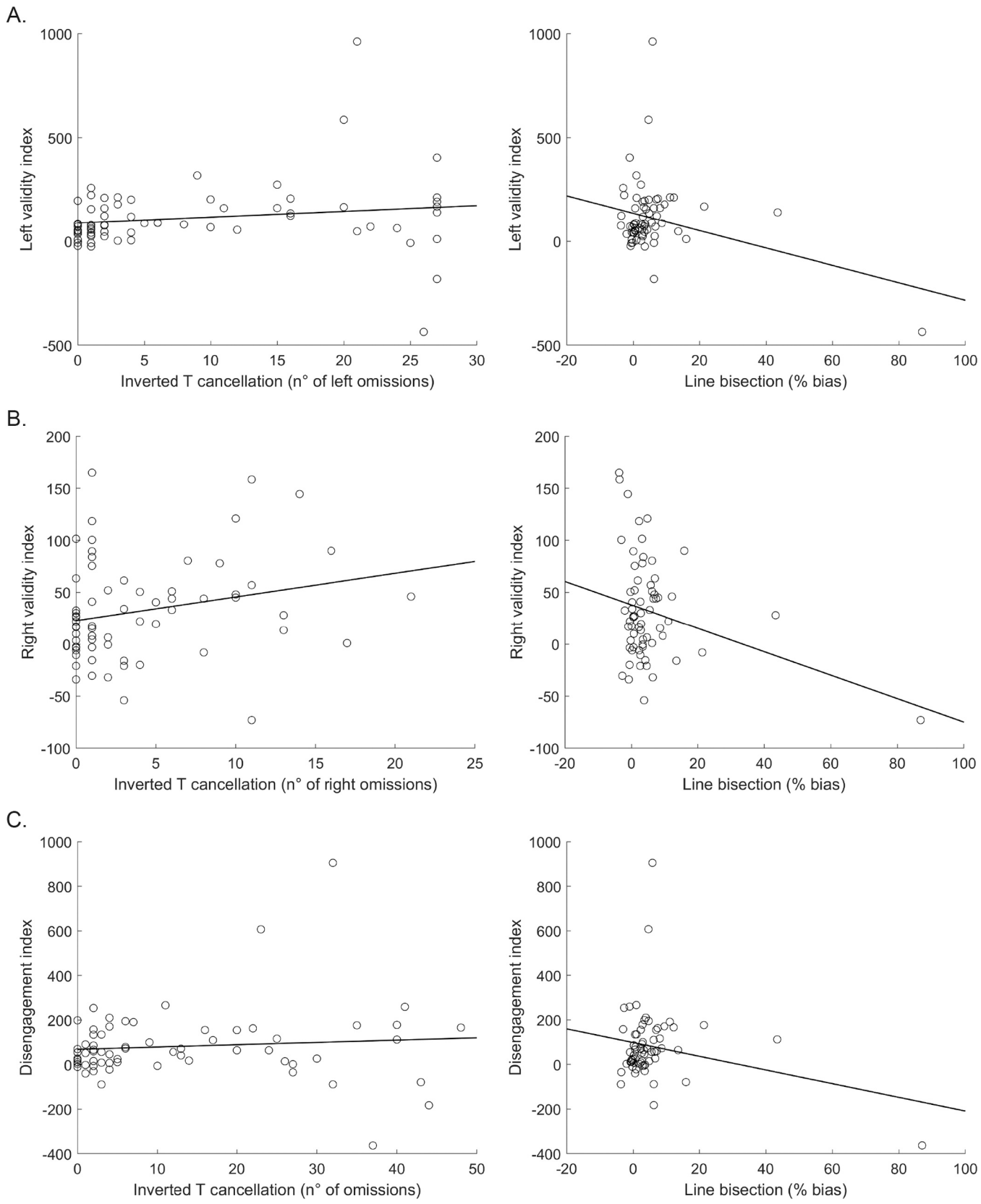

Fig. 3. Results of the stepwise regression analysis for the relationship between neuropsychological scores and behavior in RH patients. A. Relationship between the left validity index and the results at the inverted T cancellation (left panel) and line bisection (right panel) tests. B. Relationship between the right validity index and the results at the inverted T cancellation (left panel) and line bisection (right panel) tests. C. Relationship between the disengagement index and the results at the inverted T cancellation (left panel) and line bisection (right panel) tests. The regression line is shown in black.

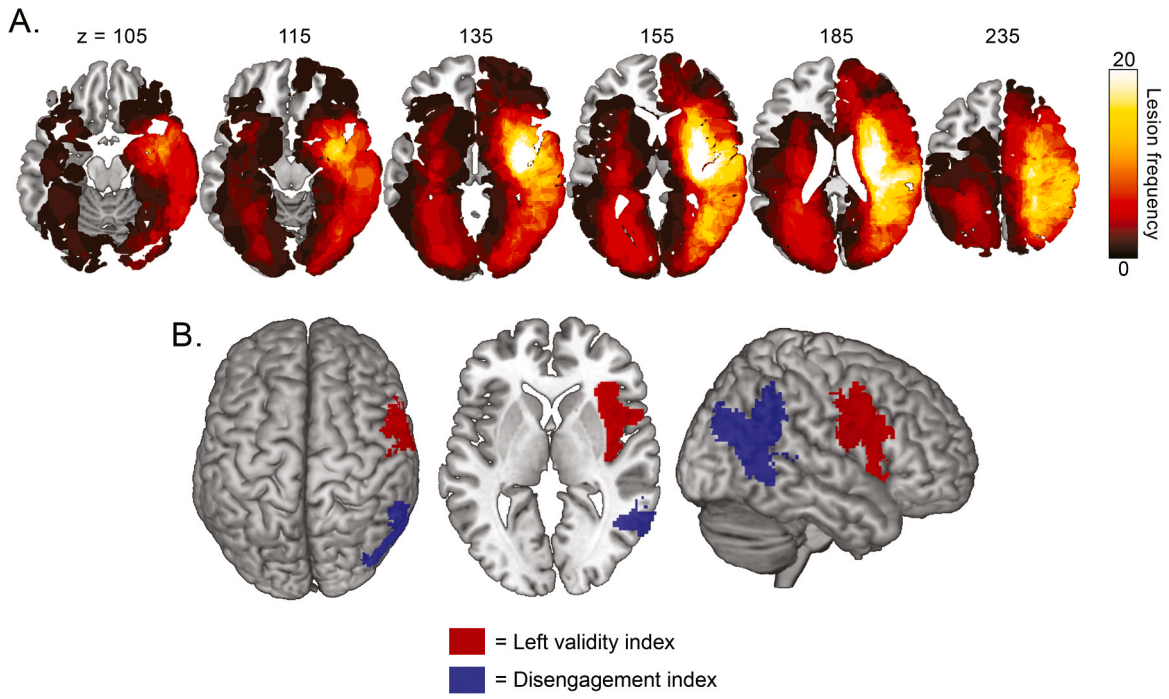

Fig. 4. Results of the Support Vector Regression-Lesion Symptom Mapping (SVR-LSM) analysis for the relationship between the degree of lesion and behavioral indices in grey matter. A. Lesion overlap plot of the patients showing color-coded frequencies of damage (N = 89). B. Overlapped FWE-corrected p <.05 clusters resulting from the grey matter parcel load analyses with the left validity (in red) and disengagement (in blue) indices.

Unfortunately, this study did not focus on the disengagement deficit, but only examined the validity effect.

The present anatomical findings suggest a direct role for frontoparietal cortex in reorienting attention following an ipsilateral distracter stimulus (invalid cue). To comprehend the respective contribution of frontal and parietal regions to the reorienting of attention it is important to consider the specifics of the validity effect and disengagement deficit. The validity effect reflects purely contralateral effects of inhibitory cues, irrespective of the extent of a similar deficit on the ipsilateral side. It fails to capture an imbalance of attention deployment between the hemifields, such as a purely unilateral difficulty of shifting attention following invalid cues. In contrast, the disengagement index indicates a lateralized impairment, and therefore is a purer measure of a specific difficulty with shifting attention contralesionally.

Several functional imaging studies have implicated the lateral frontal cortex, particularly the inferior frontal gyrus and insula, in the reorienting of spatial attention (Corbetta et al., 2000; Indovina and Macaluso, 2007; Kincade et al., 2005; Vossel et al., 2006). Indovina and Macaluso (2007) observed activations of a right-hemispheric network when participants' attention was captured by task-relevant stimuli presented in the unattended visual field. This functional network included the angular gyrus, the frontal eye fields (FEF), the inferior frontal gyrus and insula. Importantly, salient but not relevant distracters did not activate this network, suggesting that it is tuned to task-relevance. In a recent lesion study we observed that this sensitivity to task relevance is driven by functional interactions between the insula and the TPJ (Ptak and Pedrazzini, 2021). Corbetta and Shulman (2002) proposed an influential model distinguishing between a dorsal and ventral attention network, respectively implicated in goal-driven (dorsal) and stimulus-driven (ventral) reorienting. This proposal is based on the observation that dorsal regions are activated by attention-orienting cues, while ventral regions activate when observers reorient attention to an unexpected location. Interestingly, the authors ascribe to the lateral frontal cortex the role of an integrator between both networks. According to this idea this region relays top-down biases from the dorsal network to ventral regions, and transfers reorienting signals to the dorsal network when a salient stimulus occurs (Corbetta et al., 2008).

This is not necessarily in contradiction with the idea that this region integrates goal-driven (top-down) and stimulus-driven signals processed in the ventral attention network. Damage to lateral frontal cortex may isolate ventral regions from modulating influence, and thus exaggerate the effect of stimulus-driven saliency signals. This would lead to increased and prolonged capture of attention by the salient cue, and thus to a bias in exogenous orienting. As our current findings suggest, increased capture of attention reflects the action of more posterior regions of the attention network, in particular the TPJ (Ptak and Pedrazzini, 2021). In addition, our white matter analyses indicate that disconnection of the lateral frontal cortex from other regions of the attention network crucially contributes to the disengagement deficit. Indeed, we found that various fiber tracts are affected by the critical damage predicting the disengagement deficit. These can be roughly separated into anterior-posterior (SLF, IFOF, AF), ventro-dorsal (FAT) and cortico-subcortical (corticothalamic pathway). Interestingly, several of these white matter tracts connect regions of the right-hemispheric attention network and have been implicated in spatial neglect (Hattori et al., 2018; Pedrazzini and Ptak, 2020). This is particularly the case for the SLF, which connects the inferior parietal lobe with ventral premotor cortex (Bartolomeo et al., 2012; Shinoura et al., 2009; Thiebaut de Schotten et al., 2014), but also the IFOF (Urbanski et al., 2011) and the AF (Carter et al., 2017). The FAT provides a connection between ventral and dorsal premotor cortices (Catani et al., 2012), and might be important for the communication of signals that bias attention toward task-relevant information (Ptak, 2012). Thus, the involvement of several fiber tracts crucial for spatial attention suggests that the disengagement deficit cortex damage reflects fronto-parietal disconnections that may isolate stimulus-driven and goal-driven influences on attention.

In conclusion, our study provides evidence that the right lateral frontal cortex is associated with purely contralateral effects of inhibitory cues, while damage to the temporoparietal junction predicts a specific difficulty with shifting attention contralesionally. The failure to reorient attention also entails extended disconnections affecting core regions of

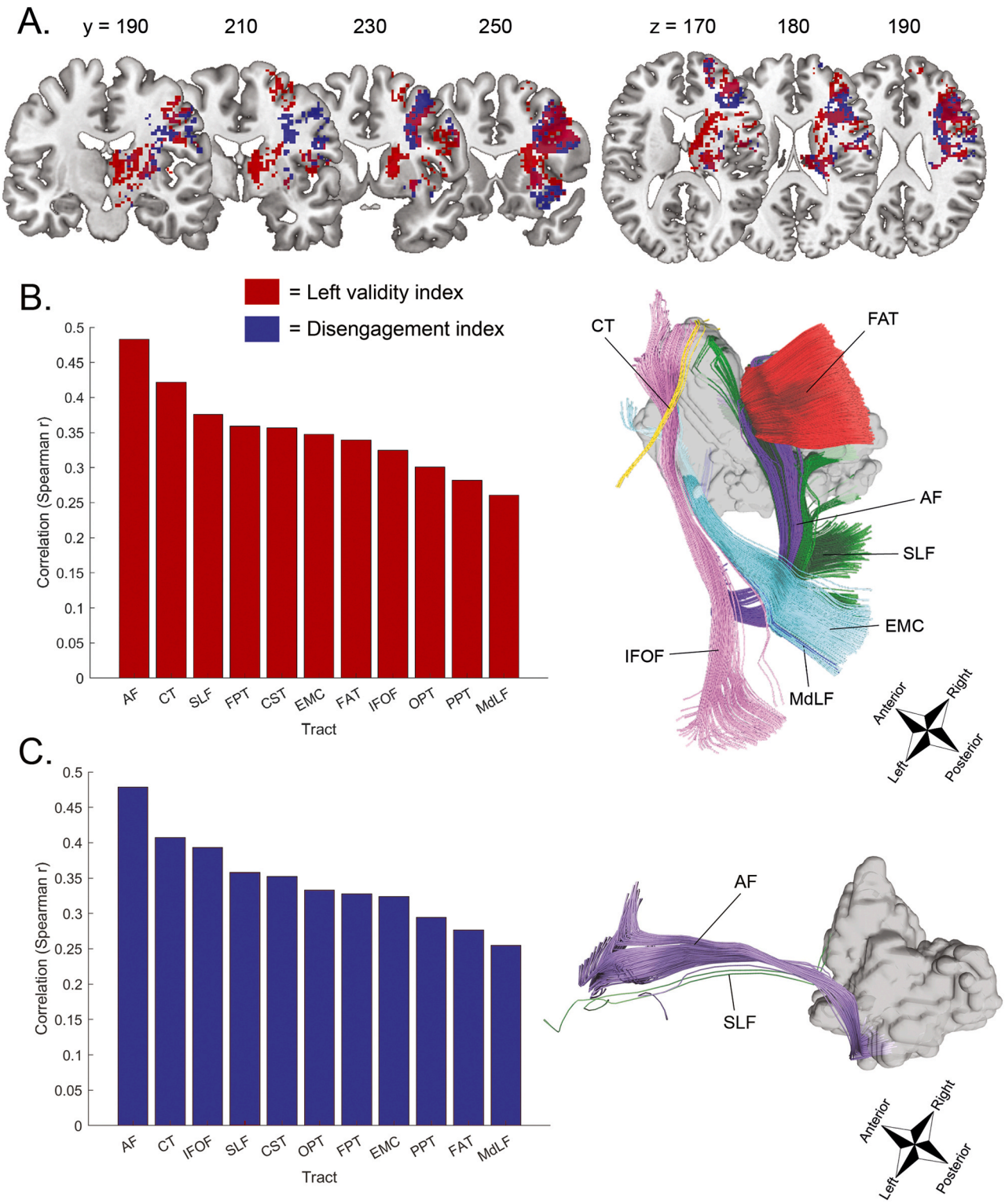

Fig. 5. Results of the analyses at the white matter level. A. Overlapped Support Vector Regression-Lesion Symptom Mapping (SVR-LSM) results for the relationship between the White Matter Disconnection Maps and the left validity and disengagement indices. Color renderings represent FWE-corrected $p < .05$ cluster for the left validity (in red) and disengagement (in blue) indices. B. Significant Spearman-rank correlations between the disconnection severities of the top 20 % tracts regarding the percentage of streamlines disconnected and the left validity index (left panel), as well as their 3D representation (right panel) with the lesion highlighted in the Grey Matter Parcel Lesion Load analysis (in grey). C. Significant Spearman-rank correlations between the disconnection severities of the top 20 % tracts regarding the percentage of streamlines disconnected and the disengagement index (left panel), as well as their 3D representation (right panel) with the lesion highlighted in the Grey Matter Parcel Lesion Load analysis (in grey). AF = arcuate fasciculus; CT = corticothalamic pathway; SLF = superior longitudinal fasciculus; FPT = fronto-pontine tract; CST = corticospinal tract; EMC = extreme capsule; FAT = frontal aslant tract; IFOF = inferior fronto-occipital fasciculus; OPT = occipitopontine tract; PPT = parietopontine tract; MdLF = middle longitudinal fasciculus.

the right-hemispheric attention network.

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CRediT authorship contribution statement

Sélim Coll: Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation. **Emilie Marti:** Writing – review & editing, Methodology, Investigation, Data curation. **Naz Doganci:** Writing – review & editing, Methodology, Investigation, Data curation. **Radek Ptak:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data Availability

Data will be made available on request.

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