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Original article

A network-level approach of cognitive flexibility impairment after surgery of a right temporo-parietal glioma

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ABSTRACT

Objective. – The right "non-dominant" temporo-parietal junction is usually not considered as a highly eloquent area. This contrasts with its mirrored left "dominant" counterpart, which is known as highly eloquent regarding language function. The question arises about which functions should be monitored when operating lesions of the right temporo-parietal junction under awake conditions.
Methods. – We report the case of a patient who underwent a surgical resection of a glioma located in the right temporo-parietal junction. Cognitive evaluations were performed preoperatively and 4 months after surgery, as well as resting state fMRI and diffusion-based tractography.
Results. – Long-term postoperative cognitive examination revealed an important deterioration of cognitive control abilities, especially regarding set-shifting abilities as measured by Trail making test part B. Based on pre- and postoperative resting state fMRI and diffusion-based tractography, we demonstrate that surgical resection massively impacted structural and functional connectivity of the right fronto-parieto-temporal network, a network that is classically involved in cognitive control, reasoning and working memory.
Conclusion. – This case clearly illustrates how a white matter focal lesion can generate a neuropsychological deficit by remotely disconnecting distant cortical areas belonging to a functional network. Furthermore, our observation strongly supports the use of intraoperative cognitive control tests during surgery of the right temporo-parietal junction and promote the interest of pre and postoperative resting state functional connectivity to explore the potential mechanisms causing cognitive deficits.

1. Introduction

Set-shifting abilities belong to executive functions, which are classically associated with the frontal lobes. Among several others tasks, the Trail making test (TMT) is commonly used to assess executive functions clinically [1]. In particular, the part B of the test (TMT-B) emphasizes set-shifting abilities.

Task-related fMRI studies of the TMT-B have indicated increased activation in a large set of frontal, parietal and temporal areas in both hemispheres [2,3]. Lesion based analyses have revealed significant correlations between TMT-B error rate and damage to the dorsolateral prefrontal cortex [4]. However, this notion was recently challenged by other studies that showed inconsistent results [4–10] or that failed to supply supportive evidence of any difference in TMT-B performance between frontal and non-frontal lesions groups regarding error rate [11] and completion time [8]. Very few studies have investigated the link between lesions of white matter tracts and deficit in set-shifting abilities. One study in a population of healthy aging reported a correlation between decrease in TMT-B performance and decrease in fractional anisotropy of the corpus callosum, inferior fronto-occipital

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fasciculus (IFOF), superior longitudinal fasciculus (SLF) and uncinate fasciculus [12]. More recently, a lesional study in stroke patients supported a strong involvement of the left superior longitudinal fasciculus and the lateral cholinergic pathways in TMT-B performance [13]. On the whole, lesion studies have failed to produce concordant findings on the mechanisms supporting set-shifting abilities and to reconcile with fMRI reports in healthy controls.

From a hodotopic point of view [14], set-shifting abilities may depend on the interaction between frontal, parietal and temporal regions. Such a delocalized pattern would explain the discrepancy of the results of classical focal lesion studies [15]. In line with this hypothesis, we report the case of a patient who experienced a marked deterioration of performance on TMT-B after the removal of a glioma located in the right temporo-parietal junction. Based on pre and postoperative MRIs, we analyzed changes in structural and functional connectivity, with the aim to understand the mechanisms leading to cognitive flexibility loss in this patient.

2. Methods

2.1. Ethics statement

Patient gave full informed consent to participate to this study, which was approved by the ethics committee of Saint-Louis hospital (reference 2013/51).

2.2. Clinical case

A 40-year-old woman with no previous medical history was diagnosed on MRI with a right parietal diffuse low-grade glioma (see Fig. 1A), revealed by a generalized seizure. Seizures were controlled under anti-epileptic medication (Leviteracetam, 500 mg twice a day). After a short period of follow-up (3 months) confirming the slow evolution of the tumor (5 mm/year), the patient underwent a surgical resection in an awake condition, as described below. Resection was complete (see Fig. 1B) and there was no neurological complication (postoperative Karnofsky score unchanged, at 90/100). In particular, visual field test performed 3 months later was normal. She could resume her job as a cleaning lady 4 months after surgery.

2.3. Diffusion-weighted imaging (DWI)

Diffusion imaging was acquired 4 months after the surgery. A 3T Siemens Skyra system (Siemens, Erlangen, Germany) with a 64-channel phased-array head coil, was employed to acquire DWI of the entire head with an anterior-posterior phase of acquisition. DWI parameters consisted of a matrix of acquisition of $108 \times 108 \times 120$ voxels of 2.3 mm^3 with a total field of view of $250 \times 250 \times 120$ mm. DWI was acquired along 64 directions with a weighting $b = 2000\ s/mm^2$. Additionally non-weighted ($b = 0$) volumes were also acquired. Echo Time (TE) was set at 95 ms and Repetition Time (TR) at 7700 ms. The whole sequence lasted 9 min 45 s.

2.4. Tractography

At each slice, diffusion-weighted data were simultaneously registered and corrected for subject motion and geometrical distortion adjusting the gradient accordingly (http://www.exploredti.com; see [16]). A damped Richardson Lucy Spherical Deconvolution [17] was computed to estimate multiple orientations in voxels containing different populations of crossing fibers [18–20]. Algorithm parameters were chosen as previously described [21]. A fixed-fiber response corresponding to a shape factor of $\alpha = 2 \times 10^{-3}\ mm^2/s$ was chosen [21]. Whole brain tractography was performed selecting every brain voxel with at least one fiber orientation as a seed voxel. From these voxels, and for each fiber orientation, streamlines were propagated using Euler integration with a step size of 1 mm (as described in Dell'Acqua et al., 2013). When entering a region with crossing white matter bundles, the algorithm followed the orientation vector of least curvature [22]. Streamlines were halted when a voxel without fiber orientation was reached or when the curvature between two steps exceeded a threshold of 45°. Spherical deconvolution, fiber orientation vector estimations and tractography were performed using in Startrack (http://www.natbrainlab.co.uk).

2.5. Resting state functional magnetic resonance imaging (rs-fMRI)

rs-fMRI was acquired pre, post and 4 months after the surgery. During this sequence the participant was instructed to rest but not sleep with her eyes closed. Images sensitive to bold contrast were acquired using a gradient echo planar imaging (EPI) sequence along 130 time points with a total matrix of $94 \times 94 \times 36$ voxels of $2.1 \times 2.1 \times 3$ mm and a field of view of $200 \times 200 \times 108$ mm. Additionally TR was set at 3200 ms and TE at 30 ms. The total resting state acquisition lasted seven minutes.

2.6. Resting state analysis

To determine the location of resting state networks (RSN), we used a data-driven method based on Independent Component Analysis (ICA). It has been shown that this method is able to extract networks which resemble those recruited during the actual

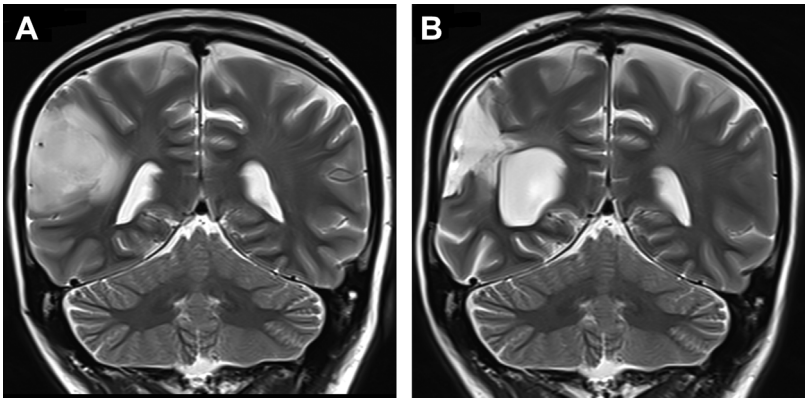

Fig. 1. A. Coronal slice of T2-weighted preoperative MRI. B. Coronal slice of T2-weighted postoperative MRI.

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