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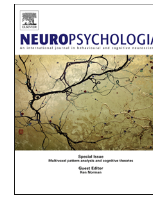

Disrupting posterior cingulate connectivity disconnects consciousness from the external environment

Guillaume Herbet [a,b,c,*], Gilles Lafargue [d], Nicolas Menjot de Champfleur [b,e], Sylvie Moritz-Gasser [b,f], Emmanuelle le Bars [b,e], François Bonnetblanc [g,h], Hugues Duffau [a,b]

[a] *Department of Neurosurgery, Montpellier University Medical Center, Montpellier 34295, France*
[b] *Institute for Neuroscience of Montpellier, INSERM U-1051, Hôpital Saint Eloi, Montpellier 34298, France*
[c] *University of Montpellier 1, Montpellier 34967, France*
[d] *Functional Neuroscience and Pathologies Lab, EA-4559, Université Lille Nord de France, Loos 59120, France*
[e] *Department of Neuroradiology, Montpellier University Medical Center, Montpellier 34295, France*
[f] *Department of Neurology, Montpellier University Medical Center, Montpellier 34295, France*
[g] *Cognition, Action and Sensorimotor Plasticity Lab, INSERM U-1093, UFR STAPS, Dijon 21078, France*
[h] *University of Montpellier 2, LIRMM, DEMAR Team, CNRS, INRIA, Montpellier 34095, France*

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ABSTRACT

Neurophysiological and neuroimaging studies including both patients with disorders of consciousness and healthy subjects with modified states of consciousness suggest a crucial role of the medial posteroparietal cortex in conscious information processing. However no direct neuropsychological evidence supports this hypothesis and studies including patients with restricted lesions of this brain region are almost non-existent. Using direct intraoperative electrostimulations, we showed in a rare patient that disrupting the subcortical connectivity of the left posterior cingulate cortex (PCC) reliably induced a breakdown in conscious experience. This acute phenomenon was mainly characterized by a transient behavioral unresponsiveness with loss of external connectedness. In all cases, when he regained consciousness, the patient described himself as in dream, outside the operating room. This finding suggests that functional integrity of the PPC connectivity is necessary for maintaining consciousness of external environment.

1. Introduction

Nowadays, in cognitive neuroscience and philosophy of mind, considerable attention is being paid to the posteromedial cortex (PMC), including the posterior cingulate, retrosplenial and ventral precuneal cortices. It belongs to the transmodal cerebral cortex (Mesulam, 1998) and harbors one of the most complex patterns of connectivity (Cocchi, Zalesky, Fornito, & Mattingley, 2013). The PMC have indeed excessive cortical connections across the entire brain, constitutes a major core of the human structural connectome (Hagmann et al., 2008; Gong et al. 2009; van den Heuvel & Sporns, 2011), and demonstrates a high level of intrinsic functional connectivity, reaching the rank of highly integrative neural hub (Buckner et al., 2009; Cauda et al., 2010). Together with the anterior cingulate/medial prefrontal cortex and the temporoparietal junctions, the PMC forms a broader whole of functionally and structurally interconnected areas that show a robust functional synchrony when the brain is resting, the so-called default mode network (DMN) (Gusnard, Akbudak, Shulman, & Raichle, 2001; Raichle et al., 2001; Greicius, Krasnow, Reiss, & Menon, 2003; Fransson & Marrelec, 2008).

Many hypotheses have been posed concerning the functional significance of this set of posterior midline structures. Among the more challenging are those arguing for a possible role of the PMC in conscious self-awareness (e.g. mindwandering, future episodic thought, and mental imagery) (Hassabis & Maguire, 2007; Schacter, Addis, & Buckner, 2007; Buckner, Andrews-Hanna, & Schacter, 2008; Andrews-Hanna, Reidler, Huang, & Buckner, 2010) and reflective social cognition (e.g. inferential mentalizing) (Schilbach, Eickhoff, Rotarska-Jagiela, Fink & Vogeley, 2008; Spreng, Mar, & Kim, 2009; Schilbach et al., 2012; Mars et al., 2012; Herbet et al., 2014). Other authors have suggested the PMC as pivotal in the neural network that may be concerned with maintaining consciousness (Vogt & Laureys, 2005; Horovitz et al., 2009; Picchioni, Duyn, & Horovitz, 2013). In the latter case, the evidence mainly comes from the study of neurological patients with disorders of consciousness such as coma (Norton et al.,

* Correspondence to; CHRU Montpellier, Hôpital Gui de Chauliac, Department of Neurosurgery, 80, avenue Augustin Fliche, 34295 Montpellier, France.
Tel.: +33 4 67 336 612; fax: +33 4 67 33 69 12.
E-mail address: guillaume.herbet@gmail.com (G. Herbet).

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2012), vegetative state (Cauda et al., 2009; Vanhaudenhuyse et al., 2010; Soddu et al., 2012), brain death (Boly et al., 2009), and epilepsy-induced loss of consciousness (Archer, Abbott, Waites, & Jackson, 2003; Danielson, Guo, & Blumenfeld, 2011). In all these pathological conditions, functional connectivity of the PMC is decreased or absent, and functional integration within the DMN is compromised. These observations are also true in healthy subjects with altered states of consciousness such as deep sleep (Horovitz et al., 2009) and sedation/anesthesia (Alkire, Hudetz, & Tononi, 2008; Greicius et al., 2008; Hudetz, 2012).

The assumption according to which the PMC may be a critical node in the neural network supporting conscious information processing remains to some extent elusive, mainly because uniquely derived from neurophysiological studies (e.g. functional MRI, EEG). The posterior midline structures of the brain are indeed relatively protected from brain injury as strokes (Cavanna & Trimble, 2006; Leech & Sharp, 2013). Consequently, neuropsychological studies including patients with well-defined, restricted lesions of these brain areas are almost non-existent, dramatically restricting the scope of our knowledge in this respect.

In this study, we report the extremely rare case of a patient harboring a slow-growing lesion in the left posteromedial cortex (Fig. 1a). A surgery under local anesthesia ("awake" surgery) was performed to functionally map the cortical surface overhanging the tumour, but also the adjacent subcortical structure as the surgical resection progressed (Duffau et al. 2002; Ojemann & Mateer, 1979), thus offering a unique opportunity to reach the posterior cingulate connectivity and identify its functional significance. On the basis of the evidence reviewed above, the most straightforward hypothesis is that if the posterior cingulate is really crucial in conscious awareness, interfering with its neural activity should lead to a profound disturbance in the patient's conscious experience. As detailed below, we found that electrically stimulating the white matter underlying the left posterior cingulate cortex transiently disconnects consciousness from the external environment.

2. Material and methods

2.1. Case description

The patient is a 45-year-old man with high educational level. Following absence seizures, MRI scans were performed. A diffuse low-grade glioma – subsequently confirmed by postoperative neuropathological analyses – was discovered in the left posteromedial cortex. In accordance with our surgical approach, an "awake" surgery was performed.

The posterior and ventral part of the left precuneus was totally resected. Part of the left cingulate cortex and retrosplenial areas was also resected. The whole lesion was removed with however some degree of margin ("supracomplete resection") (Fig. 1a; see Fig. 1a–c and Table 1 in the Supplementary material file).

2.2. Cortical and subcortical functional mapping

To functionally map cortical and subcortical structures, direct electrical stimulations were applied with a bipolar electrode (biphasic current, pulse of 60 Hz, single pulse phase duration of 1 ms and intensity from 1.5 to 2 mA). This surgical procedure has been extensively been described in the past. The intraoperative protocol is further detailed in the Supplementary material file.

2.3. Imaging method for tractography reconstruction

MRI data were acquired using echo-planar imaging on 3 T magnet (Siemens, Skyra) with a standard head coil. High resolution T1-weighted anatomical images were acquired as well as diffusion MR images. Raw diffusion data were corrected for distortion secondary to eddy currents using FSL (FMRIB, http://www.fmrib.ox.ac.uk/fsl), and then tractography was realized using TrackVis software (streamline method). Tractographic seeds location was placed according to intraoperative stimulations (dream-like state stimulation, MNI co-ordinates: [−12 −44 27], visual blur stimulation, MNI co-ordinates: [−27 −56 21]) and tractography was initiated from these seeds (the size of both seeds was 10 mm diameter). A more detailed description of the method is provided in the Supplementary material file.

2.4. Ethical statement

Results presented in this article have not been obtained in an experimental, but in a classic clinical context. DESs were initially used to map language or visual processes and avoid long-term postoperative language or visual hemifield disturbances (i.e. contralateral hemianopia). This is a classical surgical procedure used in our center. A statement of informed consent to publish personal medical data was obtained from the patient.

3. Results

3.1. Cortical and subcortical functional mapping

Cortical and subcortical brain mapping was performed by applying direct electrical stimulations (DESs). In accordance with a well-established methodological procedure, an anatomical site was considered as functional if the response (i.e. stimulating the left arcuate fasciculus elicit phonemic paraphasia) was induced three times period (Ojemann & Mateer, 1979). Functional sites were not stimulated consecutively. After each positive stimulation,

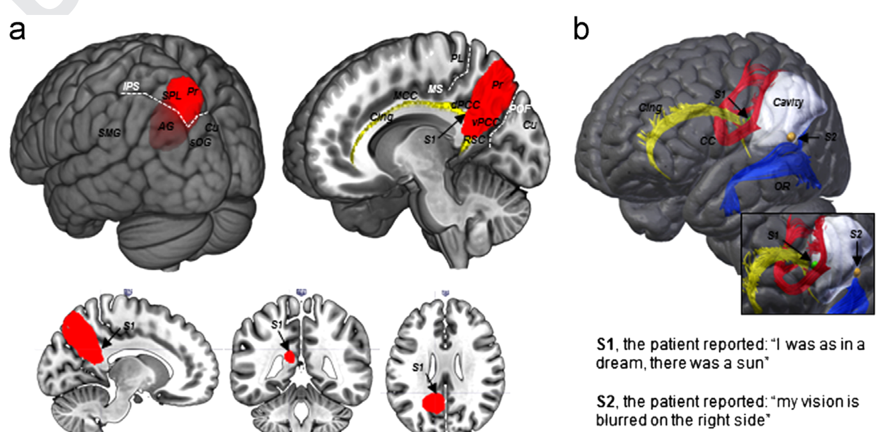

Fig. 1. Anatomical location of the "dream-like state" stimulation. (a) Location of the stimulation relative to the resective cavity. The "dream-like state" stimulation (S1) was applied on the white matter underlying the left posterior cingulate (black arrow, MNI coordinates: −12, −44, 27). (b) Tractography reconstruction. Whereas the "dream-like state" stimulation (S1) was identified close to the cingulum, the "visual blur" stimulation was identified close to optic radiations (S2). Pr=precuneus, PL=paracentral lobule, vPCC=ventral posterior cingulate cortex, dPCC=dorsal posterior cingulate cortex, MCC=middle cingulate cortex, RSC=retrosplenial cortex, SPL=Superior parietal lobule, Cu=cuneus, AG=angular gyrus, SMG=supramarginal gyrus, IPS=intraparietal sulcus, SOG=superior occipital gyrus, MS=marginal sulcus, POF=parieto-occipital fissure, Cing=cingulum, CC=corpus callosum, OR=optic radiations.

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