

# Disrupting posterior cingulate connectivity disconnects consciousness from the external environment



Guillaume Herbet<sup>a,b,c,\*</sup>, Gilles Lafargue<sup>d</sup>, Nicolas Menjot de Champfleury<sup>b,e</sup>,  
Sylvie Moritz-Gasser<sup>b,f</sup>, Emmanuelle le Bars<sup>b,e</sup>, François Bonnetblanc<sup>g,h</sup>, Hugues Duffau<sup>a,b</sup>

<sup>a</sup> Department of Neurosurgery, Montpellier University Medical Center, Montpellier 34295, France

<sup>b</sup> Institute for Neuroscience of Montpellier, INSERM U-1051, Hôpital Saint Eloi, Montpellier 34298, France

<sup>c</sup> University of Montpellier 1, Montpellier 34967, France

<sup>d</sup> Functional Neuroscience and Pathologies Lab, EA-4559, Université Lille Nord de France, Loos 59120, France

<sup>e</sup> Department of Neuroradiology, Montpellier University Medical Center, Montpellier 34295, France

<sup>f</sup> Department of Neurology, Montpellier University Medical Center, Montpellier 34295, France

<sup>g</sup> Cognition, Action and Sensorimotor Plasticity Lab, INSERM U-1093, UFR STAPS, Dijon 21078, France

<sup>h</sup> University of Montpellier 2, LIRMM, DEMAR Team, CNRS, INRIA, Montpellier 34095, France

## ARTICLE INFO

### Article history:

Received 21 November 2013

Received in revised form

5 January 2014

Accepted 27 January 2014

Available online 4 February 2014

### Keywords:

Posterior cingulate

Precuneus

External awareness

Consciousness disorders

Electrical stimulations

## 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.

© 2014 Elsevier Ltd. All rights reserved.

## 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; Horowitz et al., 2009; Picchioni, Duyn, & Horowitz, 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](mailto:guillaume.herbet@gmail.com) (G. Herbet).

2012), vegetative state (Cauda et al., 2009; Vanhaudenhuyse et al., 2010), 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 (Horowitz 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.

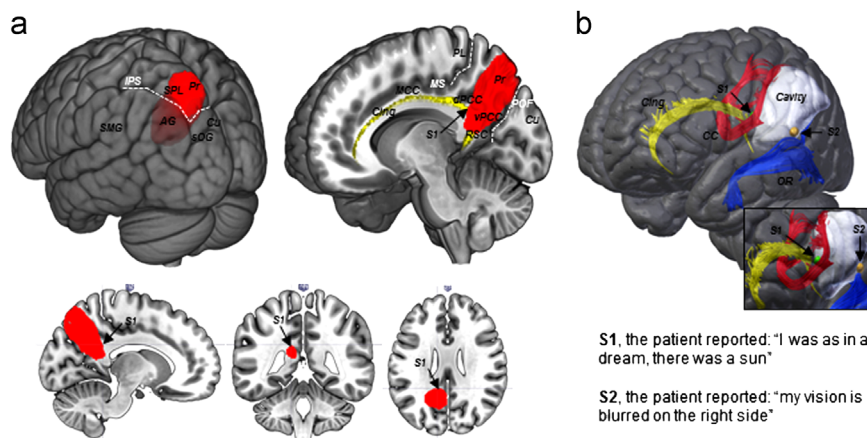
### 2.4. Ethical statement

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.

a sample of two control negative stimulations was obtained in the region surrounding the site of interest (distance > 5 mm; 6 no responsive control stimulations per functional sites).

Whereas no functional site was found on the cortical surface, at the level of the precuneus, two critical sites were spotted during a naming task in the depth of the resective cavity. First, transient visual blur was repetitively induced by stimulating the white matter fibers close to the internal parieto-occipital fissure. Second, beside this anatomical benchmark, more medially and superiorly, DESs were found to induce a dramatic alteration of conscious experience in a highly reproducible manner. The naming task was interrupted and the patient was unresponsive (verbal injunctions) during a time period of approximately 4 s, with a fixed regard. Quite surprisingly, he described himself retrospectively as in a dream, outside the operating room, and was able to fleetingly report his subjective experiences (stimulation 1: “I was as in a dream, there was a sun”; stimulation 2: I was as in a dream, I was on the beach”; stimulation 3: “I was as in a dream, I was surrounded by a white landscape”). No additional control sites were found to elicit the same acute manifestation in the surrounding anatomical space (6 control stimulations sum-total, Fig. 2). A more detailed characterization this subjective manifestation is proposed in the Supplementary material file.

### 3.2. Postoperative neuropsychological observations

In addition to the standard neuropsychological investigation achieved in our center at the three months, the patient was asked to describe retrospectively his subjective experience. He reported experiencing no rumination and no negative thought for almost a month after the surgery. He described himself in a kind of contemplative state, with a subjective feeling of absolute happiness and timelessness.

He described also a persistent subjective feeling of “transparency” of his contralateral hand, accompanied by an impossibility to locate it spatially when this one was not under visual control (during approximately one month after the surgery).

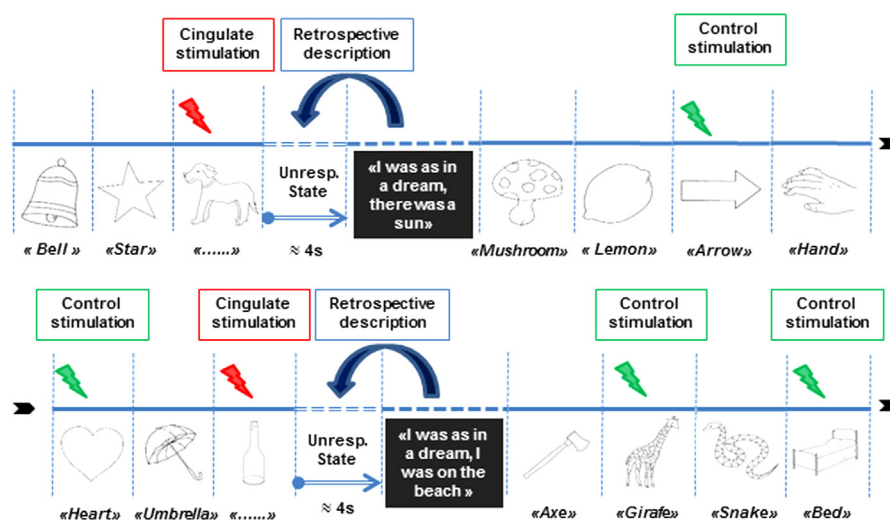
## 4. Discussion

Here we reported the case of an exceptional patient with a slow-growing lesion involving the left posteromedial cortex.

An awake surgery was performed, thus offering a unique opportunity to reach the posterior cingulate connectivity. We found that applying DESs on the white matter underlying the left posterior cingulate, close to the cingulum, induced in a reproducible manner a breakdown in conscious experience. No additional sites were demonstrated to elicit the same manifestation during electrical stimulations.

The posterior cingulate cortex (PCC) is currently posited to be essential in the neural network sustaining conscious information processing. This hypothesis is mainly derived from studies showing that complete loss of consciousness is systematically associated with functional deactivation of the PCC in a range of conditions such as coma (Norton et al., 2012), vegetative state (Vanhaudenhuyse et al., 2010), epilepsy (Blumenfeld et al. 2009; Danielson et al., 2011), deep sleep (Horowitz et al., 2009) and anesthesia (Alkire et al., 2008). In agreement with these observations, the finding reported here shows that functional disintegration of PCC connectivity gives rise to an altered state of consciousness characterized by a behavioral unresponsiveness and a loss of external connectedness. As our patient also reported dream-like states, it could be tempting to conclude that subjective consciousness was preserved. However, we cannot take its self-reports – by nature subjective but also retrospective in our study – for granted and rule out the possibility of confabulatory fabrications. The subjective descriptions of our patient have therefore to be taken with great caution. Nevertheless, it is worth noting, from a phenomenological standpoint, that this paradoxical situation (loss of connectedness, unresponsiveness, persistence of conscious experiences) is somewhat reminiscent of dream experiences occurring in rapid eye movement (RME) sleep (Sanders, Tononi, Laureys, & Sleigh, 2012) and that, at the physiological level, dreaming is known to be associated with decreasing neural activity in posterior cingulate as well as precuneus in imaging studies (Maquet et al., 1996; Desseilles, Dang-Vu, Sterpenich, & Schwartz, 2011). In the same line, subjective dreamlike feelings have been observed during anesthesia with intermediate dose of certain anesthetic agents that target specifically the posterior cingulate and its neighboring areas (for a review, see Alkire et al. (2008)).

A transitory functional dis-synchronization of the DMN might explain this highly restricted state of consciousness. There is indeed great evidence that functional connectivity between the frontal and posteromedial nodes of this neural system is anatomically mediated by the cingulum (van den Heuvel, Mandl,



**Fig. 2.** Schematic description of the intraoperative protocol. Each responsive stimulation (red lightning; three stimulations sum-total applied on the same anatomical location) was followed by two no responsive control stimulations (green lightning; six stimulations sum-total applied on the anatomical space surrounding the responsive site, with a minimal distance of 5 mm that corresponds to the spatial resolution of the bipolar electrode). Note that the same protocol was applied regarding the “visual blur” phenomenon. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Luigjes, & Hulshoff Pol, 2008; Greicius, Supekar, Menon, & Dougherty, 2009). However, even if we cannot thoroughly discredit this possibility, it seems unlikely because the cingulum was almost completely cut off and no behavioral disturbance was induced throughout its excision. Only few fibers were preserved, as shown in Fig. 1b. Moreover, there is no evidence in the few cases described in the literature that lesions damaging the cingulum induce severe disturbances of conscious experience (Valenstein et al., 1987; Rudge & Warrington, 1991). Lastly, the DMN is hypothesized to sustain what has referred to as “internal awareness”. However the mental state induced in our patient seems more related to a disturbance of “external awareness” (this does not mean, however, that internal subjective awareness has not been impacted), thought classically to be mediated by the lateral fronto-parietal network (Vanhaudenhuyse et al., 2011; Demertzi, Soddu, & Laureys, 2013). As a consequence, it is difficult to conceive that transient disruption of functional connectivity between the frontal and the posterior cortical node of the DMN may explain alone the behavioral counterpart of the electrical stimulations.

Recent data suggest that the posterior cingulate may be not a cortical node functionally homogeneous, but might play the role of a connector hub (i.e. involved not only in the DMN, but also in other large-scale networks). Specifically, several studies have provided evidence for a ventral to dorsal functional subdivisions of the PCC (Leech, Kamourieh, Beckmann, & Sharp, 2011; Leech, Braga, & Sharp, 2012; Leech & Sharp, 2013). Whereas the ventral part of the PCC seems to show functional integration within the DMN per se, the dorsal part of the PCC seems to show, for its part, functional integration within both the DMN and the lateral fronto-parietal network underlying cognitive control, attentional processes and more generally external awareness. This is consistent with the results of a recent work using connectivity analysis of fMRI data in order to investigate functional interaction patterns between the internal and external awareness networks (Fornito, Harrison, Zalesky, & Simons, 2012). In this study, it is shown that the DMN maintains cooperative interactions with the frontoparietal network during a memory recollection task. More specifically, and perhaps most relevantly for our data, the findings suggest that the PCC may be involved in mediating information exchange between the DMN and the frontoparietal network (and other intrinsic networks) when the brain is engaged in a cognitive-demanding task (see also Cocchi et al. (2013)). In our study, it is possible that electrical stimulations (rather applied to the dorsal sector of the PCC) have impacted both the DMN and the connectivity between the PCC and the lateral fronto-parietal network, explaining the transient disengagement from the external environment.

It is now well established that the posterior cingulate cortex and some nuclei of the thalamus are anatomically and functionally linked (Parvizi, Van Hoesen, Buckwalter, & Damasio, 2006; Cauda et al., 2010). Decreases of functional connectivity in this posterior cingulothalamic system has been repetitively related to disorders of consciousness but also to modified states of consciousness. Abnormal structural connectivity in this system has been recently identified in patients with pathological states of consciousness (Fernandez-Espejo et al., 2012; Horowitz et al., 2009). Some authors have also suggested a possible functional regulation of the intrinsic activity of the DMN by the thalamus (Danielson et al., 2011; Blumenfeld et al., 2009). Consequently, a cingulothalamic disconnection syndrome might lead to disturbance of consciousness induced in our patient. In this respect, it is valuable to note that the patient lesion was revealed because of absence seizures. This kind of seizure is characterized by a transient disengagement from the external environment with, sometimes, the persistence of some elements of minimal conscious experiences (Bayne, 2011). This is the case of our patient who was able to report retrospectively

that, after the ictal period, he was “elsewhere but aware of its body”. In this context, the comparison between the DES-evoked phenomenon in our study and preoperative absence seizures remains interesting to the extent that the common denominator appears to be loss of external connectedness. Neurophysiological studies have shown decreased activity of the posterior cingulate after absence seizures in concert with an abnormal activity in the thalamic system, suggesting a key pathophysiological mechanism in transient loss of consciousness during absence epilepsy (Danielson et al., 2011; Archer et al., 2003).

It could be argued that the manifestation described here is entirely based on the subjective reports of the patient. However this kind of subjective description has been previously shown to be very useful in grasping the nature and neurocognitive mechanisms of complex mental phenomena, especially in stimulation studies (e.g. intention to move or also out-of-body experience, Desmurget et al., 2009; Blanke, Ortigue, Landis, & Seeck, 2002). Another possible criticism is that three occurrences of the same phenomenon are not enough to draw inferences. Although we certainly acknowledge that more responsive stimulations would help to more definitive conclusions, this classical method in neurosurgical practice has been proved in the past to be reliable (Desmurget, Song, Mottolese, & Sirigu, 2013). In addition, we have to deal with the clinical context for obvious ethical reasons.

It should be reiterated here that the patient harbors a diffuse low-grade glioma. This type of lesion is known to induce important functional compensation phenomena, mainly because of its slow-growing progression (Desmurget et al., 2007). Consequently, it could be argued that the connectivity surrounding the PCC gets already re-organized at the time of the stimulation and that, maybe, the stimulation-evoked dream like experience is an artificial phenomenon. However, it has been recently demonstrated in the context of this neuropathological condition that, contrary to most of cortical areas involving in high-level processes, functional compensation of direct long-range associative pathways is poor, despite important lesion infiltration (Ius et al., 2011).

Postoperative neuropsychological disturbances were especially interesting regarding current thinking about the functional role of the posteromedial cortex. Based on findings from several activation fMRI and resting-state fMRI studies, it might be expected that the surgical excision of the precuneus and its adjacent cingulate and retrosplenial areas could induce a decrease of reflective self-awareness (Gusnard et al., 2001; Cavanna & Trimble, 2006). This is exactly what has been happened after the surgery in our patient. Retrospectively, he reported experiencing no rumination for almost a month after the surgery and to be in a contemplative state with a subjective feeling of absolute happiness and timelessness. Note that these subjective experiences characterize some meditative states and that fMRI studies with meditator subjects have shown an important decrease of the activity of the precuneus during mindfulness meditation (Ives-Deliperi, Solms, & Meintjes, 2011).

The patient's internal feeling of “transparency” of his right hand suggests a disturbance of self-body internal representations, resulting in a disorder of body scheme. This persistent phenomenon was accompanied for a month by impossibility of locating this hand in space except when looking at it. It is reminiscent of the case of a patient, described by the team of Husain, who presented a left superior parietal lesion (cyst) and was characterized by the same neuropsychological manifestation (Wolpert, Goodbody, & Husain, 1998). This “fading limb” was interpreted as a failure to maintain an internal representation of the body's state. Our data give additional support to the view that the precuneus cortex is essential in this type of high-level sensory-motor processes. In the same vein, it is interesting to mention that the precuneus has been also involved in other rare neuropsychological syndromes like alien hand (Schaefer, Heinze, & Galazky, 2010).

## 5. Conclusion

To conclude, interfering with the neural activity of the left posterior cingulate connectivity causes a breakdown in conscious experience. Although it remains difficult to provide a clear-cut neurophysiological account for this manifestation, this striking result is in agreement with current theories that hold that this brain region might be a “hot spot” in the neural network sustaining consciousness of external world (Vogt & Laureys, 2005; Horowitz et al., 2009; Picchioni et al., 2013). More broadly, this finding provides support to the view that the posterior cingulate is a pivotal hub within the brain's functional architecture (Hagmann et al., 2008; Gong et al., 2009; van den Heuvel & Sporns, 2011; Fornito et al., 2012; Cocchi et al., 2013).

## Acknowledgments

G.H. is funded by the Association pour la Recherche sur le Cancer (aides individuelles n° = DOC20120605069). We thank Jeremy Deverdun for preparing Fig. 1b.

## Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.neuropsychologia.2014.01.020>.

## References

- Alkire, M. T., Hudetz, A. G., & Tononi, G. (2008). Consciousness and anesthesia. *Science*, *322*, 876–880.
- Andrews-Hanna, J. R., Reidler, J. S., Huang, C., & Buckner, R. L. (2010). Evidence for the default network's role in spontaneous cognition. *Journal of Neurophysiology*, *104*, 322–335.
- Archer, J. S., Abbott, D. F., Waites, A. B., & Jackson, G. D. (2003). fMRI “deactivation” of the posterior cingulate during generalized spike and wave. *NeuroImage*, *20*, 1915–1922.
- Bayne, T. (2011). The presence of consciousness in absence seizures. *Behavioural Neurology*, *24*, 47–53.
- Blanke, O., Ortigue, S., Landis, T., & Seeck, M. (2002). Stimulating illusory own-body perceptions. *Nature*, *419*, 269–270.
- Blumenfeld, H., Varghese, G. I., Purcaro, M. J., Motelow, J. E., Enev, M., McNally, K. A., et al. (2009). Cortical and subcortical networks in human secondarily generalized tonic-clonic seizures. *Brain*, *132*, 999–1012.
- Buckner, R. L., Andrews-Hanna, J. R., & Schacter, D. L. (2008). The brain's default network: Anatomy, function, and relevance to disease. *Annals of the New York Academy of Sciences*, *1156*, 1–38.
- Buckner, R. L., Sepulcre, J., Talukdar, T., Krienen, F. M., Liu, H., Hedden, T., et al. (2009). Cortical hubs revealed by intrinsic functional connectivity: Mapping, assessment of stability, and relation to Alzheimer's disease. *Journal of Neuroscience*, *29*, 1860–1873.
- Boly, M., Tshibanda, L., Vanhaudenhuyse, A., Noirhomme, Q., Schnakers, C., Ledoux, D., Boveroux, P., Garweg, C., Lambermont, B., & Phillips, C. (2009). Functional connectivity in the default network during resting state is preserved in a vegetative but not in a brain dead patient. *Human Brain Mapping*, *30*, 2393–2400.
- Cauda, F., Geminiani, G., D'Agata, F., Sacco, K., Duca, S., Bagshaw, A. P., et al. (2010). Functional connectivity of the posteromedial cortex. *PLoS One*, *5*, e11811.
- Cauda, F., Micon, B. M., Sacco, K., Duca, S., D'Agata, F., Geminiani, G., et al. (2009). Disrupted intrinsic functional connectivity in the vegetative state. *Journal of Neurology, Neurosurgery, and Psychiatry*, *80*, 429–431.
- Cavanna, A. E., & Trimble, M. R. (2006). The precuneus: A review of its functional anatomy and behavioural correlates. *Brain*, *129*, 564–583.
- Cocchi, L., Zalesky, A., Fornito, A., & Mattingley, J. B. (2013). Dynamic cooperation and competition between brain systems during cognitive control. *Trends in Cognitive Sciences*, *17*, 493–501.
- Danielson, N. B., Guo, J. N., & Blumenfeld, H. (2011). The default mode network and altered consciousness in epilepsy. *Behavioural Neurology*, *24*, 55–65.
- Demertzi, A., Soddu, A., & Laureys, S. (2013). Consciousness supporting networks. *Current Opinion in Neurobiology*, *23*, 239–244.
- Desmurget, M., Bonnetblanc, F., & Duffau, H. (2007). Contrasting acute and slow-growing lesions: a new door to brain plasticity. *Brain*, *130*, 898–914.
- Desmurget, M., Reilly, K. T., Richard, N., Szathmari, A., Mottolese, C., & Sirigu, A. (2009). Movement intention after parietal cortex stimulation in humans. *Science*, *324*, 811–813.
- Desmurget, M., Song, Z., Mottolese, C., & Sirigu, A. (2013). Re-establishing the merits of electrical brain stimulation. *Trends in Cognitive Sciences*, *17*, 442–449.
- Desseilles, M., Dang-Vu, T. T., Sterpenich, V., & Schwartz, S. (2011). Cognitive and emotional processes during dreaming: A neuroimaging view. *Consciousness and Cognition*, *20*, 998–1008.
- Duffau, H., Capelle, L., Sichez, N., Denvil, D., Lopes, M., Sichez, J. P., et al. (2002). Intraoperative mapping of the subcortical language pathways using direct stimulations. An anatomo-functional study. *Brain*, *125*, 199–214.
- Fernandez-Espejo, D., Soddu, A., Cruse, D., Palacios, E. M., Junque, C., Vanhaudenhuyse, A., et al. (2012). A role for the default mode network in the bases of disorders of consciousness. *Annals of Neurology*, *72*, 335–343.
- Fornito, A., Harrison, B. J., Zalesky, A., & Simons, J. S. (2012). Competitive and cooperative dynamics of large-scale brain functional networks supporting recollection. *Proceedings of the National Academy of Sciences of the United States of America*, *109*, 12788–12793.
- Fransson, P., & Marrelec, G. (2008). The precuneus/posterior cingulate cortex plays a pivotal role in the default mode network: Evidence from a partial correlation network analysis. *NeuroImage*, *42*, 1178–1184.
- Gong, G., He, Y., Concha, L., Lebel, C., Gross, D. W., Evans, A. C., et al. (2009). Mapping anatomical connectivity patterns of human cerebral cortex using in vivo diffusion tensor imaging tractography. *Cerebral Cortex*, *19*, 524–536.
- Greicius, M. D., Kiviniemi, V., Tervonen, O., Vainionpää, V., Alahuhta, S., Reiss, A. L., et al. (2008). Persistent default-mode network connectivity during light sedation. *Human Brain Mapping*, *29*, 839–847.
- Greicius, M. D., Krasnow, B., Reiss, A. L., & Menon, V. (2003). Functional connectivity in the resting brain: A network analysis of the default mode hypothesis. *Proceedings of the National Academy of Sciences of the United States of America*, *100*, 253–258.
- Greicius, M. D., Supekar, K., Menon, V., & Dougherty, R. F. (2009). Resting-state functional connectivity reflects structural connectivity in the default mode network. *Cerebral Cortex*, *19*, 72–78.
- Gusnard, D. A., Akbudak, E., Shulman, G. L., & Raichle, M. E. (2001). Medial prefrontal cortex and self-referential mental activity: Relation to a default mode of brain function. *Proceedings of the National Academy of Sciences of the United States of America*, *98*, 4259–4264.
- Hagmann, P., Cammoun, L., Gigandet, X., Meuli, R., Honey, C. J., Wedeen, V. J., et al. (2008). Mapping the structural core of human cerebral cortex. *PLoS Biology*, *6*, e159.
- Hassabis, D., & Maguire, E. A. (2007). Deconstructing episodic memory with construction. *Trends in Cognitive Sciences*, *11*, 299–306.
- Herbet, G., Lafargue, G., Bonnetblanc, F., Moritz-Gasser, S., Menjot de Champfleury, N., & Duffau, H. (2014). Inferring a dual-stream model from the white matter fibres disconnection. *Brain*.
- Horowitz, S. G., Braun, A. R., Carr, W. S., Picchioni, D., Balkin, T. J., Fukunaga, M., et al. (2009). Decoupling of the brain's default mode network during deep sleep. *Proceedings of the National Academy of Sciences of the United States of America*, *106*, 11376–11381.
- Hudetz, A. G. (2012). General anesthesia and human brain connectivity. *Brain Connectivity*, *2*, 291–302.
- Ius, T., Angelini, E., Thiebaut de Schotten, M., Mandonnet, E., & Duffau, H. (2011). Evidence for potentials and limitations of brain plasticity using an atlas of functional resectability of WHO grade II gliomas: towards a “minimal common brain”. *NeuroImage*, *56*, 992–1000.
- Ives-Deliperi, V. L., Solms, M., & Meintjes, E. M. (2011). The neural substrates of mindfulness: An fMRI investigation. *Society for Neuroscience*, *6*, 231–242.
- Leech, R., Braga, R., & Sharp, D. J. (2012). Echoes of the brain within the posterior cingulate cortex. *Journal of Neuroscience*, *32*, 215–222.
- Leech, R., Kamourieh, S., Beckmann, C. F., & Sharp, D. J. (2011). Fractionating the default mode network: Distinct contributions of the ventral and dorsal posterior cingulate cortex to cognitive control. *Journal of Neuroscience*, *31*, 3217–3224.
- Leech, R., & Sharp, D. J. (2013). The role of the posterior cingulate cortex in cognition and disease. *Brain*.
- Maquet, P., Peters, J., Aerts, J., Delfiore, G., Degueldre, C., Luxen, A., et al. (1996). Functional neuroanatomy of human rapid-eye-movement sleep and dreaming. *Nature*, *383*, 163–166.
- Mars, R. B., Neubert, F. X., Noonan, M. P., Sallet, J., Toni, I., & Rushworth, M. F. (2012). On the relationship between the “default mode network” and the “social brain”. *Frontiers in Human Neuroscience*, *6*, 00189.
- Mesulam, M. M. (1998). From sensation to cognition. *Brain*, *121*(6), 1013–1052.
- Norton, L., Hutchison, R. M., Young, G. B., Lee, D. H., Sharpe, M. D., & Mirsattari, S. M. (2012). Disruptions of functional connectivity in the default mode network of comatose patients. *Neurology*, *78*, 175–181.
- Ojemann, G., & Mateer, C. (1979). Human language cortex: Localization of memory, syntax, and sequential motor-phoneme identification systems. *Science*, *205*, 1401–1403.
- Parvizi, J., Van Hoesen, G. W., Buckwalter, J., & Damasio, A. (2006). Neural connections of the posteromedial cortex in the macaque. *Proceedings of the National Academy of Sciences of the United States of America*, *103*, 1563–1568.
- Picchioni, D., Duyn, J. H., & Horowitz, S. G. (2013). Sleep and the functional connectome. *NeuroImage*, *80*, 387–396.
- Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences of the United States of America*, *98*, 676–682.
- Rudge, P., & Warrington, E. K. (1991). Selective impairment of memory and visual perception in splenial tumours. *Brain*, *114*(1B), 349–360.

- Sanders, R. D., Tononi, G., Laureys, S., & Sleigh, J. W. (2012). Unresponsiveness not equal unconsciousness. *Anesthesiology*, *116*, 946–959.
- Schacter, D. L., Addis, D. R., & Buckner, R. L. (2007). Remembering the past to imagine the future: The prospective brain. *Nature Reviews Neuroscience*, *8*, 657–661.
- Schaefer, M., Heinze, H. J., & Galazky, I. (2010). Alien hand syndrome: Neural correlates of movements without conscious will. *PLoS One*, *5*, 0015010.
- Schilbach, L., Bzdok, D., Timmermans, B., Fox, P. T., Laird, A. R., Vogeley, K., et al. (2012). Introspective minds: Using ALE meta-analyses to study commonalities in the neural correlates of emotional processing, social & unconstrained cognition. *PLoS One*, *7*, e30920.
- Schilbach, L., Eickhoff, S. B., Rotarska-Jagiela, A., Fink, G. R., & Vogeley, K. (2008). Minds at rest? Social cognition as the default mode of cognizing and its putative relationship to the “default system” of the brain. *Consciousness and Cognition*, *17*, 457–467.
- Spreng, R. N., Mar, R. A., & Kim, A. S. (2009). The common neural basis of autobiographical memory, prospection, navigation, theory of mind, and the default mode: A quantitative meta-analysis. *Journal of Cognitive Neuroscience*, *21*, 489–510.
- Valenstein, E., Bowers, D., Verfaellie, M., Heilman, K. M., Day, A., & Watson, R. T. (1987). Retrosplenial amnesia. *Brain*, *110*(6), 1631–1646.
- van den Heuvel, M., Mandl, R., Luigjes, J., & Hulshoff Pol, H. (2008). Microstructural organization of the cingulum tract and the level of default mode functional connectivity. *Journal of Neuroscience*, *28*, 10844–10851.
- van den Heuvel, M. P., & Sporns, O. (2011). Rich-club organization of the human connectome. *Journal of Neuroscience*, *31*, 15775–15786.
- Vanhoudenhuysse, A., Demertzi, A., Schabus, M., Noirhomme, Q., Bredart, S., Boly, M., et al. (2011). Two distinct neuronal networks mediate the awareness of environment and of self. *Journal of Cognitive Neuroscience*, *23*, 570–578.
- Vanhoudenhuysse, A., Noirhomme, Q., Tshibanda, L. J., Bruno, M. A., Boveroux, P., Schnakers, C., et al. (2010). Default network connectivity reflects the level of consciousness in non-communicative brain-damaged patients. *Brain*, *133*, 161–171.
- Vogt, B. A., & Laureys, S. (2005). Posterior cingulate, precuneal and retrosplenial cortices: Cytology and components of the neural network correlates of consciousness. *Progress in Brain Research*, *150*, 205–217.
- Wolpert, D. M., Goodbody, S. J., & Husain, M. (1998). Maintaining internal representations: The role of the human superior parietal lobe. *Nature Neuroscience*, *1*, 529–533.