

Decreased functional connectivity between the mediodorsal thalamus and default mode network in disorders of consciousness

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Introduction

Severe traumatic or non-traumatic brain injury can give rise to disorders of consciousness (DOC), such as vegetative state/unresponsive wakefulness syndrome (VS/UWS) and minimally conscious states (MCS). Behavioral assessment is the primary method for the clinical detection and measurement of consciousness. For neurologists, consciousness can be considered in relatively simple terms of arousal and awareness [1]. Recent studies suggest that the diagnosis (and treatment) of DOC patients may be improved by using functional neuroimaging, a novel and objective measure of brain activity that can quantify interactions between distant brain areas [2]. There is recent and consistent evidence that a collection of human brain regions, including the medial prefrontal cortex, posterior midbrain regions, medial temporal lobes and lateral parietal cortex, shows high levels of activity when no explicit task is being performed. Decreased connectivity in the right hemisphere in DMN was found for VS/UWS patients, suggesting DMN may play as a neural marker [3]. Also, both correlations and anticorrelations were significantly reduced in VS/UWS [4]. In addition, the importance of the thalamus in DOC has been demonstrated previously in both neuropathological and structural neuroimaging studies. Bilateral deep brain stimulation in the central thalamus improved behavioural responsiveness and awareness of DOC patients. A number of studies have investigated functional connectivity between the thalamus and DMN in DOC, but most have considered the thalamus as a homogenous structure. The purpose of the present study is to address this by investigating functional connectivity between individual thalamic nuclei and the DMN in DOC patients.

Material and method

The study participants initially included 17 DOC patients, clinically assessed using the Coma Recovery Scale-Revised (CRS-R), and 10 age-matched healthy controls. The controls had no history of neurological or systemic illness, head injury, or drug or alcohol abuse. Of the initial participants, we excluded those diagnosed with lock-in syndrome (1 patient), and those who failed registration because of severe structural deformations (4 patients) or had severe motion artifacts (3 patients and 1 control). Motion artifacts were identified using Statistical Parametric Mapping (SPM8, Wellcome Department of Cognitive Neurology, London, UK; <http://www.fil.ion.ucl.ac.uk/spm/software/spm8/>). Finally, 9 DOC patients (4 female, mean \pm SD age: 40 ± 17 years) and 9 age-matched healthy controls (3 female, mean \pm SD age: 41 ± 10 years) were included in this study.

MRI was carried out using a GE Signa HDi 3.0T scanner. Despite using wedge-shaped foam padding to try and reduce it, the head motion of DOC patients during scanning remained too large for good quality fMRI data to be obtained. Functional images were collected axially by using an echo-planar imaging sequence sensitive to blood oxygen level-dependent contrast. The acquisition parameters were as follows: 33 slices, repetition time/echo time = 2000/30 ms, thickness/gap = 4.0/0.6 mm, FOV = 220×220 mm, resolution within slice = 64×64, flip angle = 90°. The FOV covered the entire brain. These scans were obtained in the resting state, with participants instructed to keep their eyes closed, remain as motionless as possible, and not to think about anything in particular. Each fMRI scan lasted for 8 min, and 240 volumes were obtained.

Results and Discussion

There were no significant differences in age ($p = 0.88$) or sex ($p = 0.65$) between DOC patients and normal controls. In comparison to healthy controls, DOC patients had significantly decreased functional connectivity between the mediodorsal thalamus and brain areas within the DMN, including the medial prefrontal cortex and posterior cingulate cortex/precuneus. Patients and controls did not show differences in functional connectivity for any thalamic nucleus other than the mediodorsal thalamus (as shown in Fig. 1).

The present study utilized two analysis methods, ICA and a ROI-based approach, to investigate how functional connectivity between the thalamus and the DMN differed between DOC patients and healthy controls. Our results suggest that functional connections between mediodorsal thalamus and DMN may be important in impairments of consciousness in DOC patients.

References

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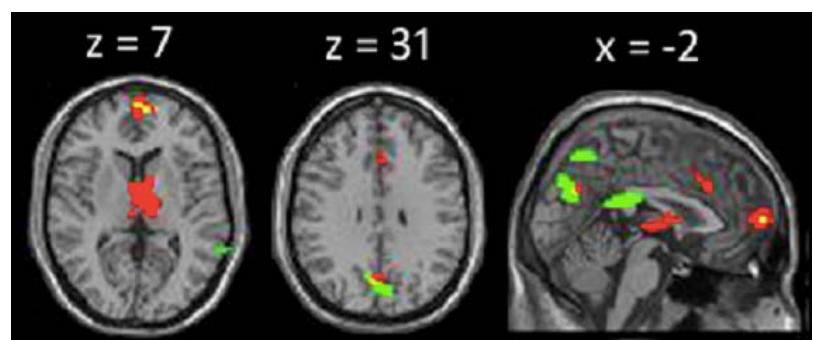


Fig.1 Brain areas with decreased functional connectivity in patients with disorders of consciousness. Green represents areas identified with ICA within the default mode network ($p < 0.05$, FDR correction). Red represents areas identified with region of interest-based functional connectivity analysis ($p < 0.05$, AlphaSim correction, the left mediodorsal area identified in ICA was the seed region). Yellow represents overlapping areas (i.e., those identified by both types of analysis), including the bilateral superior medial frontal gyri and left precuneus/cuneus.