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Negative and positive volitional responses induced by stimulating the superior frontal gyrus: A case study

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Dear sir,

The processes behind human volition have always intrigued humankind, as is beautifully portrayed by Herman Melville [1] in his timeless novel, Moby Dick: "Is Ahab, Ahab? Is it God, I, or who, that lifts this arm?". Research in the past few decades has shown that voluntary movements are preceded by unconscious mental processes and that aware intentions arise slightly before the movement itself, and, therefore, are not likely to be the cause of it [2–5]. Later studies extended this finding, suggesting that human volition is based on activity of specific neural network located in the medial prefrontal regions [2,3,5,6], as well as in the parietal and frontopolar cortex [5–7]. Another aspect of intentional action is self-initiated inhibition, or the control of action. Studies have suggested that the neural network that is responsible for human volition contains a self-control mechanism [8]. However, the specific neural mechanisms behind the experience of conscious volition or its inhibition remain unclear.

Case study

The patient in this study was a right-handed, 56 years old male, who suffered from focal drug-resistant epilepsy since the age of 55, with daily simple partial seizures (right hand tremor) followed by occasional secondarily generalizations. His medications included Keppra, Tegretol, Frisium and Cipralex. Surface video-EEG monitoring showed left frontal seizure onset. In order to delineate the location of the epileptic focus, the patient was implanted with a 64-contact left fronto-parietal subdural grid and with 4-contact left parietal strip [AD-Tech, Racine, WI, USA], each with inter-contact distance of 10mm. The invasive video-EEG monitoring indicated onset of seizures in the left primary motor area (M1). Due to severe implications of resection in this area (paralysis or plegia of his right hand), the medical team decided to implant the patient with Responsive Neurostimulation (RNS), resulting in more than 90% decrease in his seizure frequency after one-year follow-up.

Electrical brain stimulation (EBS) was performed using Nicolet Cortical Stimulator [Natus, Middleton, WI, USA]. The stimulation was delivered using an alternating bi-polar current between all adjacent contacts with a bi-phasic wave, 300μsec wave width, 50Hz frequency and duration of 5 s. The induced current amplitude ranged between 1 and 10mA. EBS in this patient yielded motor, sensor and verbal responses. Electrical stimulation in the left superior frontal gyrus (SFG) provoked a set of emotional and behavioral changes that were not familiar to the patient as part of his habitual seizures. The patient described two distinct experiences. After stimulation of adjacent electrodes involving the lateral SFG [MNI: (−20, 6, 66); (−22, 14, 60)], the patient depicted a sensation of strong resistance to any kind of action: "I feel resistance to anything I am told to do […] the possibility of continuing in any action is blocked". Nonetheless, stimulation involving the more medial SFG [MNI: (−14, 14, 66); (−16, 4, 68); (−18, 14, 66)] caused the patient to report a sense of conscious resistance and, simultaneously, of urges for random goal-directed actions, such as throwing the pillow or leaving the room ("I feel strong resistance […] I feel it's enough, I want to get out of here … I want to throw the pillow" […] I want to switch languages from Hebrew to English"). Interestingly, the lateral and medial contacts were proximate to each other, separated by 10mm only.

We hypothesized that the subjective emotional experiences of our patient were a result of activation of a distributed neural network. Hence, we attempted to characterize the functional network that was activated in our patient's stimulation using resting state fMRI analysis. Functional connectivity was assessed using NiLearn toolbox's CanICA algorithm [9]. This Independent Component Analysis (ICA) detects functional networks of voxels with correlated BOLD activation in time. The 20 most dominant networks were produced and the network with the highest ICA component activation within the stimulated sites was chosen. Due to the proximity of the stimulation sites (merely 10mm distance), we did not compare their connectivity patterns. Nonetheless, as presented in Fig. 1, we found a well-defined functional network, comprising the left SFG (stimulation sites), the medial pre-frontal cortex and the left inferior parietal lobe.

Abbreviations: EBS, electrical brain stimulation; EPI, echo-planar imaging; fMRI, functional magnetic resonance imaging; ICA, Independent Component Analysis; RNS, Responsive Neurostimulation; SFG, superior frontal gyrus; SMA, supplementary motor area; SPGR, spoiled gradient.

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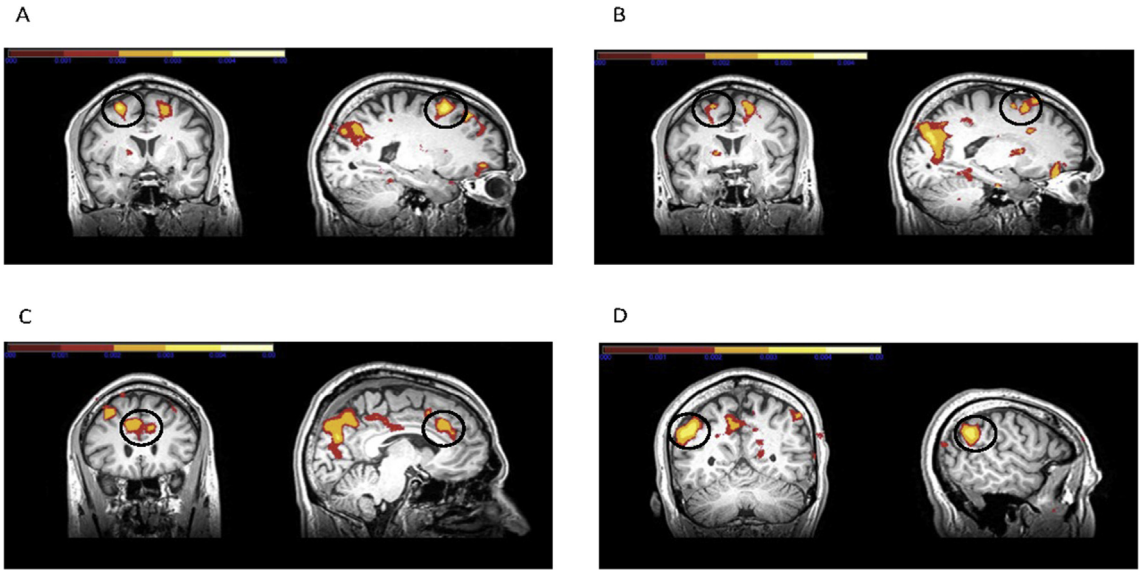

Fig. 1. fMRI connectivity analyses showing functional network that includes EBS stimulation site
Functional connectivity network derived from resting-state fMRI of our patient. Resting-state fMRI scans were acquired with a gradient echo-planar imaging (EPI) sequence of functional T2-weighted images (duration = 100sec, TR = 3000 ms, TE = 35 ms, flip angle 90°, FOV 20 × 20cm, matrix 64 × 64mm) divided into 39 axial slices (thickness 3mm, gap 0mm). Anatomical 3D spoiled gradient (SPGR) echo sequences were obtained with high-resolution 1mm slices. Analysis of functional connectivity of the stimulated electrodes, revealed a functional network including the superior frontal gyrus (stimulation sites) (A, B), the median frontal cortex including the anterior cingulate cortex (C), and the inferior parietal lobe (D). Those areas have previously characterized as involved in volition, motivation, perseveration and consciousness. Note that the left side of the picture represents the left side of the brain.

Discussion

Our study suggests that the SFG, along with the functional neural network connected to it (the medial prefrontal cortex and the inferior parietal lobe, see Fig. 1), is involved in the conscious experience of both volition and its inhibition, possibly mediating the conflict between them. Interestingly, volition for specific actions was observed after stimulation of the more medial aspect of the SFG, as opposed to stimulation in the lateral SFG that produced inhibitory responses only. Based on this finding, we conjecture that the SFG mediates a range of inhibitory and excitatory volitional responses. Furthermore, the closer the stimulation is to its medial part, the more excitatory responses are produced.

These results are in line with previous studies that shed light on the involvement of the medial prefrontal cortex [2,3,5,6,10] and the inferior parietal lobe [3,5,7,11] in volition and support the notion that the functional connectivity of the medial and lateral aspects of the prefrontal cortex is engaged in internally guided action planning. Moreover, other studies have suggested that the mechanism of volitional inhibition is intrinsic to the mechanism of volition, located in the medial prefrontal cortex [8,11,12]. Our study strengthens this hypothesis since both excitatory and inhibitory responses were elicited simultaneously, possibly involving the same functional network. Moreover, it suggests that intentional inhibition may be elicited not only in the fronto-medial cortex itself, but also in the lateral SFG. Our findings may have implications for neuropsychiatric disorders, such as abulia, that might be caused after a dorsolateral frontal damage. The opposite, obsessive-compulsive disorders and Tourette Syndrome, may also indicate loss of balance of the volitional and inhibitory components of action.

In summary, we describe a peculiar first-person experience of simultaneously induced intentional inhibition and desires for complex actions during SFG stimulation. The study thus sheds light on the complexity of the network generating human action, where volitional acts are a final product of processes that release and inhibit motor output.

Declarations of interest

None.

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