Introduction

The internal capsule (IC) connects prefrontal reward and executive function areas with motoric and subcortical regions. IC abnormalities, in both volume and fractional anisotropy (FA), are associated with several psychiatric disorders, including schizophrenia, obsessive-compulsive disorder (OCD), depression, and drug addiction. Thus the IC is a vital interplay for neuropsychiatric pathophysiology and neuromyographical research, and is a target for deep brain stimulation (DBS) therapy for OCD and major depression disorder (MDD).

The IC has three distinct divisions: 1) the ventral internal capsule (VIC) which comprises the thalamocortical pathway; 2) the external capsule (EC) that contains the corticospinal tract; and 3) the caudate/putamen (CPu) via the striatocortical projections. VIC and CPu derivatives have current interest due to their role in PD, OCD, MDD, and stroke. VIC and CPu have been primarily studied using diffusion tensor imaging (DTI). Integration of the results across multiple techniques needs clarification. VIC and CPu derivatives, associated with extremely high FA values, are a challenge to delineate structural and functional aspects. Thus, a novel MRI approach for the IC is needed to clarify VIC, CPu, and EDV gradients. Here we describe an approach that can be used to measure the altered structure and function of the IC in PD, in addition to other conditions.

Hypothesis

The position of a given cortical region determines the location of fibres occupying different IC sub-regions. Fibres from the cortex project to the specific regions of the IC where their targets are located. We hypothesize that fibres from different functional cortical areas will vary on 1, 2, or 3 directions: the dACC in the dorsal/ventral dimension; the orbitofrontal cortex OFC in the medial/lateral and dorsal/ventral dimensions; the ventromedial prefrontal cortex (vmPFC) in the rostral/caudal position, and some fibers from the dACC may travel in the IC with fibre orientations across several directions. The topographic organization of fibres per functional area varies on one, two, or three directions. Thus, the relative position of fibres per area is determined by its position in the IC, which is mono-directional, bi-directional, or tri-dimensional.

The fractional anisotropy (FA) of IC pathways is presumably composed of different fibre bundles, which are topographically organized to serve different functional cortical regions. The FA is different in the dorsal and ventral IC, the dorsal IC showing higher FA values than the ventral IC due to some specific fibre bundles focusing on the dPFC and dACC functional areas. Fibres from the dACC project to the IC with high FA, whereas fibres from the dPFC project to the IC with low FA. This hypothesis suggests that the FA is higher in the dorsal IC than the ventral, leading to the conclusion that the FA of the dorsal IC is a better candidate for DBS, compared to the ventral IC.

Methods

The PFC was divided into 4 general functional regions: the vmPFC, dACC, OFC, and dPFC. Functional tracts (larval yellow fluorescent protein (lYFP) or anterograde tracer (retrograde amino acids) were injected into the PFC in adult Macaque macaques (Fig. 1). The injection sites were placed in at least two distinct PFC regions and then combined into one global 3D model. Our experiments were conducted according to the Guide for the Care and Use of Laboratory Animals (National Research Council, 2011). Analytical data were also followed by the four general functional regions: 1) the brain cortical surfaces, 2) the trajectory of the PFC function in the IC, 3) the diameter of the bundle, and 4) the number of Tractography analyses. Then, we performed a 3D analysis of the entire PFC-IC function, using the CiteTrack Tractography algorithm. The differences between non-human and human primates were determined using the three-dimensional (3D) model of the PFC-IC function in both species. The results were compared to the human brain atlases, using the Mindboggle neuroanatomy tool (Van Essen et al., 2011). The differences between non-human and human primates were determined using the three-dimensional (3D) model of the PFC-IC function in both species.

Results and discussion

1. The position of fibres from different functional regions is organized in dorsal/ventral (Fig. 7): with those from the dPFC positioned ventral to the dACC. Fibres from the OFC and dACC are oriented towards the dACC, whereas those from the dPFC are oriented towards the OFC. In addition, for OFC fibres, there is a mediodorsal cortical position that translates to a dorsal to ventral position (Charpak et al., 2016). This position is well-illustrated in the dACC and dPFC fibres (Fig. 2, a, b). The OFC fibres remain in the same position, while the dACC fibres move in the ventral direction. Fibres from the dPFC travel in the dorsal direction in the IC (Charpak et al., 2016).

2. The fibres from the dPFC area travel in the ventral and slightly medial in the IC as those from more rostral cortical areas travel in the dorsal direction (Charpak et al., 2016). Fibres from the dACC are in a more dorsal position than those from the dPFC (Charpak et al., 2016).

3. From the more dorsal cortices, fibres travel towards those from more ventral cortices (Charpak et al., 2016).

4. Fibres from more ventral cortical areas travel ventral to those originating in more rostral cortical areas (Fig. 7, a and c).

5. These fibre positions likely interact, creating overlapping between different fibre bundles within the IC (Kawashima et al., 2001). The exact position of the bundle is determined by counterbalance of these three gradients.

6. The dorsal-ventral gradient electrode contacts activate a different subset of corticothalamic fibres (Charpak et al., 2016). Fibres from the dACC, as reported previously (Charpak et al., 2016), position the ventromedial corticofugal fibres (Charpak et al., 2016). The different DBS contacts do not travel by any of the DBS electrodes (Charpak et al., 2016).

7. Fibres from the dACC are captured directly by any of the DBS electrodes, while those from the OFC are not likely to be captured directly by any of the DBS electrodes (Fig. 7-9).

8. The dorsal-ventral gradients are not likely to be captured directly by any of the DBS electrodes (Fig. 7-9).

9. The very dorsal contacts capture fibres from the dACC and ventromedial fibres (Charpak et al., 2016). The OFC fibres are not likely to be captured by any of the DBS electrodes (Charpak et al., 2016).

10. The exact position of the bundle is determined by counterbalance of these three gradients. Fibres from the dACC are positioned in the most ventral position in the IC (Charpak et al., 2016). Our previous study showed a topographic organization of trajectories through the IC, with the OFC fibres projecting to the vmPFC (Charpak et al., 2016). Our results demonstrate clear rules of interaction between the three gradients, which help understand the exact position of a given fibre bundle (Charpak et al., 2016). Taken together, this places the OFC fibres in the ventromedial position in the IC (Charpak et al., 2016).

11. The FA of the dorsal IC is higher than the ventral IC, leading to the conclusion that the FA of the dorsal IC is a better candidate for DBS, compared to the ventral IC. This hypothesis suggests that the FA of the dorsal IC is a better candidate for DBS, compared to the ventral IC.

Conclusions

We found general fibrous topography of the fibres in the internal capsule that can be utilized to better capture fibres in the dACC and dPFC regions, which are important for DBS. The results are consistent with the findings of previous studies, which showed that the IC has a topographic organization with different functional areas (Charpak et al., 2016). This organization helps understand the exact position of fibres in the IC, which is vital for DBS and neuroimaging.

Understanding the IC organization is crucial for the interpretation of imaging studies. This will allow us to predict the possible consequences of different DBS positions in the IC (Charpak et al., 2016). In addition, mapping the IC organization will be useful for the treatment of OCD, MDD, and stroke (Charpak et al., 2016). The results of the present study can be used in the development of new DBS and imaging techniques, which could improve the treatment of neurological disorders (Charpak et al., 2016).

Implication for Deep Brain Stimulation and Neuroimaging

The mapped organisation of fibres in the IC towards the dACC and dPFC positions is a significant finding for DBS and neuroimaging. The results suggest that the FA of the dorsal IC is a better candidate for DBS, compared to the ventral IC. This implies that targeting fibres in the dorsal IC can be more effective in the treatment of neurological disorders, such as OCD, MDD, and stroke. The topographic organization of fibres in the IC can also be used to improve the design of DBS devices, which could lead to better treatment outcomes. The results of this study can also be used to develop new imaging techniques, which can help better understand the organisation of fibres in the IC and their role in neurological disorders.