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Short frontal lobe connections of the human brain

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ABSTRACT

Advances in our understanding of sensory-motor integration suggest a unique role of the frontal lobe circuits in cognition and behaviour. Long-range afferent connections convey higher order sensory information to the frontal cortex, which in turn responds to internal and external stimuli with flexible and adaptive behaviour. Long-range connections from and to frontal lobes have been described in detail in monkeys but little is known about short intralobar frontal connections mediating local connectivity in humans. Here we used spherical deconvolution diffusion tractography and post-mortem dissections to visualize the short frontal lobe connections of the human brain. We identified three intralobar tracts connecting: i) posterior Broca's region with supplementary motor area (SMA) and pre-supplementary motor area (pre-SMA) (i.e., the frontal 'aslant' tract – FAT); ii) posterior orbitofrontal cortex with anterior polar region (i.e., fronto-orbitopolar tract – FOP); iii) posterior pre-central cortex with anterior prefrontal cortex (i.e., the frontal superior longitudinal – FSL faciculus system). In addition more complex systems of short U-shaped fibres were identified in the regions of the central, pre-central, perinsular and fronto-marginal sulcus (FMS). The connections between Broca and medial frontal areas (i.e. FAT) and those between the hand-knob motor region and post-central gyrus (PoCG) were found left lateralized in a group of twelve healthy right-handed subjects. The existence of these short frontal connections was confirmed using post-mortem blunt dissections. The functional role of these tracts in motor learning, verbal fluency, prospective behaviour, episodic and working memory is discussed. Our study provides a general model for the local connectivity of the frontal lobes that could be used as an anatomical framework for studies on lateralization and future clinical research in neurological and psychiatric disorders.

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1. Introduction

In the last two centuries the role attributed to the frontal lobes has progressively expanded from pure motor execution (Fritsch and Hitzig, 1870; Ferrier, 1875) to more complex functions such as attention and memory (Stuss et al., 1999; Fuster, 2009; Reilly et al., 2011), executive cognition (Fuster, 2009; Krause et al., 2012, Zappala' et al., 2012; Cubillo et al., 2012; Tsermentseli et al., 2012), social behaviour (Shamay-Tsoory et al., 2010; Sundram et al., 2012; Langen et al., 2012) and consciousness (Crick and Koch, 1990; Dehaene et al., 1998). This wide range of abilities relies on multiple networks of fibres composing the intricate anatomy of the frontal white matter (Yeterian et al., 2012; Thiebaut de Schotten et al., 2012). Through long-range projection and association fibres the frontal lobes receive sensory information from subcortical nuclei (e.g., thalamus) and sensory cortices (i.e., visual, auditory, somatosensory, gustatory and olfactory) and respond to environmental stimuli. These connections are also used to exert top–down control over sensory areas (Fuster, 2009). Shorter fibres that mediate the local connectivity of frontal lobes include U-shaped connections between adjacent gyri and longer intralobar fibres connecting distant areas within the same lobe (Yeterian et al., 2012). The anatomy and the functional correlates of these short frontal fibres are largely unknown in man. Therefore, our study aims at using tractography and post-mortem dissections to visualise these short connections of the human frontal lobes.

The short connections of the human brain were described in some detail by Theodor Meynert in the second half of the 19th Century. He attributed to the short U-shaped connections a central role in human cognition and correctly identified them as cortico-cortical short association connections of different lengths:

'The cortex exhibits on the convexity of each convolution the shape of an inverted U, which is changed in the next adjoining fissure to an upright U (top and bottom of the cortical wave)… The depressed surface of a cortical wave can be easily dissected out as from a smooth medullary groove, which on closer inspection is seen to consist of U-shaped medullary fibres…The U-shaped bundles of the cortex do not necessarily extend simply from one convolution to the one next adjoining, but they may skip one, two, three, or an entire series of convolutions…The shortest *fibrae propriae* lie nearest to the cortex.' (Meynert, 1885).

Meynert did not specify a pattern of distribution of these fibres and his anatomical observations led him to conclude that such U-shaped connections are ubiquitous in the brain. A decade later Heinrich Sachs produced a detailed atlas of the U-shaped fibres of the occipital lobe where he was able to identify and name prominent short connections organised in larger bundles visible on post-mortem dissections. Among these the U-shaped connections between the upper and lower banks of the calacarine sulcus (i.e., stratum calcarinum) and the dorsal to the ventrolateral occipital cortex (i.e., stratum profundum convexitatis) (Sachs, 1892). Unfortunately, Sachs limited his anatomical investigations to the occipital lobe leaving the mapping of the U-shaped connections of the entire human brain incomplete.

At the turn of the 19th Century, experimental studies in animals (Fritsch and Hitzig, 1870; Ferrier, 1875; Broca, 1861; Bianchi, 1895) and clinical observation in patients with aphasia (Broca, 1861) and epilepsy (Jackson, 1915) attracted the interest of anatomists to the frontal lobe (Catani and Stuss, 2012). In 1906 Cristfield Jakob described a system of longitudinal U-shaped fibres connecting adjacent frontal gyri (Jakob, 1906). He also described a 'brachial center' and a 'facio-lingual center' in the pre-central gyrus (PrCG) connected to parietal post-central cortex through direct U-shaped connections. It is unfortunate that Jakob's work on the frontal U-shaped fibres was published in Spanish and had scarce diffusion in the English literature (Theodoridou and Triarhou, 2012).

An original approach to short fibre mapping was made by Rosett who produced an atlas of short connections of the human brain (Rosett, 1933). His method consisted in the immersion of a previously fixed brain in a gas-compressed tank containing liquid carbon dioxide (CO_2). After quickly opening the valve of the tank the sudden reduction of pressure transforms the liquid CO_2 into a gas. The micro-explosions of the cerebral tissues cause a mechanical separation of the fibres along natural lines of cleavage. With this method Rosett described the main orientation of the short fibres of most the gyri and sulci of the human brain, but he was not able to visualize their entire course and terminal projections.

In more recent years the study of U-shaped connections continued in animals by means of axonal tracing studies. Yeterian et al. (2012) give a comprehensive account of the short frontal lobe connections in monkey. However, the significant differences between species in the anatomy and function of the frontal lobes suggest that probably translating *tout court* findings from axonal tracing to humans can be not as straightforward as previously thought (Thiebaut de Schotten et al., 2012).

Preliminary diffusion imaging tractography studies have reported U-shaped connections of the frontal lobes in the living human brain (Conturo et al., 1999; Oishi et al., 2008; Lawes et al., 2008; Guevara et al., 2011; Catani et al., 2002). These studies represent an important advancement in our understanding of human connectional anatomy but they need validation.

The present study aims at mapping the architecture of short frontal lobe tracts in the human brain by combining post-mortem blunt dissections (Klingler, 1935) and diffusion tractography based on spherical deconvolution (Dell'acqua et al., 2010; Thiebaut de Schotten et al., 2011a). This combined approach and in particular the use of spherical deconvolution models offers advantages that partially overcome the limitations of classical tractography (Catani, 2007; Thiebaut de Schotten et al., 2011b). The visualization of the tracts as Digital Dejerine maps (see methods section) facilitates the anatomical description of the short U-tracts.

2. Methods

2.1. MRI acquisition and preprocessing

Diffusion weighted MR data was acquired using a High Angular Resolution Diffusion Imaging (HARDI) acquisition optimized for