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The anatomy of fronto-occipital connections from early blunt dissections to contemporary tractography

Stephanie J. Forkel [a,b,*], *Michel Thiebaut de Schotten* [a,c], *Jamie M. Kawadler* [a], *Flavio Dell'Acqua* [b,d], *Adrian Danek* [e] and *Marco Catani* [a]

[a] *NATBRAINLAB, Department of Forensics and Neurodevelopmental Sciences, King's College London, Institute of Psychiatry, UK*
[b] *Department of Neuroimaging Sciences, King's College London, Institute of Psychiatry, UK*
[c] *Inserm – UPMC UMRS 975, Brain and Spine Institute, Groupe Hospitalier Pitié-Salpêtrière, Paris, France*
[d] *NIHR Biomedical Research Centre for Mental Health at South London and Maudsley NHS Foundation Trust and Institute of Psychiatry, King's College London, UK*
[e] *Neurology Department, Ludwig-Maximilians-Universität Munich, Germany*

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ABSTRACT

The occipital and frontal lobes are anatomically distant yet functionally highly integrated to generate some of the most complex behaviour. A series of long associative fibres, such as the fronto-occipital networks, mediate this integration via rapid feed-forward propagation of visual input to anterior frontal regions and direct top–down modulation of early visual processing.

Despite the vast number of anatomical investigations a general consensus on the anatomy of fronto-occipital connections is not forthcoming. For example, in the monkey the existence of a human equivalent of the 'inferior fronto-occipital fasciculus' (iFOF) has not been demonstrated. Conversely, a 'superior fronto-occipital fasciculus' (sFOF), also referred to as 'subcallosal bundle' by some authors, is reported in monkey axonal tracing studies but not in human dissections.

In this study our aim is twofold. First, we use diffusion tractography to delineate the in vivo anatomy of the sFOF and the iFOF in 30 healthy subjects and three acallosal brains. Second, we provide a comprehensive review of the post-mortem and neuroimaging studies of the fronto-occipital connections published over the last two centuries, together with the first integral translation of Onufrowicz's original description of a human fronto-occipital fasciculus (1887) and Muratoff's report of the 'subcallosal bundle' in animals (1893).

Our tractography dissections suggest that in the human brain (i) the iFOF is a bilateral association pathway connecting ventro-medial occipital cortex to orbital and polar frontal cortex, (ii) the sFOF overlaps with branches of the superior longitudinal fasciculus (SLF) and probably represents an 'occipital extension' of the SLF, (iii) the subcallosal bundle of Muratoff is probably a complex tract encompassing ascending thalamo-frontal and

* *Corresponding author*. NATBRAINLAB, Department of Forensics and Neurodevelopmental Sciences, King's College London, Institute of Psychiatry, London, UK.
E-mail addresses: stephanie.forkel@gmx.net, Stephanie.Forkel@kcl.ac.uk (S.J. Forkel).
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descending fronto-caudate connections and is therefore a projection rather than an associative tract.

In conclusion, our experimental findings and review of the literature suggest that a ventral pathway in humans, namely the iFOF, mediates a direct communication between occipital and frontal lobes. Whether the iFOF represents a unique human pathway awaits further ad hoc investigations in animals.

1. Introduction

The occipital lobes have been intensively investigated in the last two centuries and many aspects have been clarified with regard to their anatomy and function. Comparative anatomy and neurophysiology studies suggest that the occipital lobes have undergone a complex rearrangement along the phylogeny scale (Rapoport, 1990; Orban et al., 2004). Primary visual areas are relatively smaller in humans with the expansion or addition of associative areas specialised, for example, in face perception (i.e., 'fusiform face area') or word recognition (i.e., 'visual word form area') (Cohen et al., 2000; Epelbaum et al., 2008). It has been proposed that these relatively 'new areas of the human brain' cooperate with more distant regions through long association tracts, whereas evolutionary old areas communicate through short association fibres (Deacon, 1990).

In the human brain a large system of long range associative connections, encompassing the inferior longitudinal fasciculus (ILF), cingulum and inferior fronto-occipital fasciculus (iFOF), mediates fast feed-forward relay of visual input to anterior multimodal temporal, parietal and frontal regions and direct top–down modulation by these regions on early visual areas. The anatomy of the ILF and cingulum has been described in detail both in human and monkey brains, whereas the iFOF has been identified only in humans (Schmahmann et al., 2007; Catani, 2007; Umarova et al., 2010; Yeterian et al., 2012; Thiebaut de Schotten et al., 2012). The controversy further involves a dorsal fronto-occipital fasciculus, namely the superior fronto-occipital fasciculus (sFOF), which has been described in monkey but not in humans (Schmahmann et al., 2007; Thiebaut de Schotten et al., 2012). To further complicate the matter, a dorsal fronto-occipital fasciculus is found in human brains lacking the interhemispheric callosal connection (congenital agenesis), but not in healthy brains. This bundle is often referred to with the eponym 'Probst bundle'. These human–simian discrepancies may be attributed to: (i) methodological limitations of postmortem and in vivo dissections; (ii) inaccuracy of anatomical terms to indicate the same tracts in different species; (iii) influence of pathological processes on tract development and (iv) true interspecies differences.

In this study we intend to address the following questions: (i) do dorsal fronto-occipital connections described in the monkey and acallosal brains exist in healthy human subjects? (ii) are ventral fronto-occipital connections unique to humans?

To answer these questions we first review the experimental evidence for the existence of dorsal and ventral connections between occipital and frontal lobes in the normal brain, both in animals and humans. Second, we performed tractography dissections of the dorsal and ventral fronto-occipital fasciculus connections using a novel diffusion imaging approach based on spherical deconvolution (SD), which overcomes some of the limitations of the tensor model (Dell'Acqua et al., 2010; Thiebaut de Schotten et al., 2011a, 2011b, 2012; Dell'Acqua and Catani, 2012). Third, we provide dissections of the fronto-occipital connections in subjects with congenital agenesis of the corpus callosum and discuss them in the light of the literature. Finally, the first German–English translation of two seminal papers on the dorsal fronto-occipital connections is provided to clarify current nomenclature. The first of the two is the doctoral dissertation by Onufrowicz (1887) where the term fronto-occipital fasciculus is used to describe, for the first time, a dorsal connection in an acallosal patient. The second paper is Muratoff's (1893) experimental demonstration of a dorsal connection, the subcallosal bundle, in the animal brain.

Our hope is to clarify the anatomy and the history of the fronto-occipital connections and stimulate further functional and anatomical studies.

2. Methods

2.1. *Diffusion tractography of healthy subjects*

A High Angular Resolution Diffusion Imaging (HARDI) sequence optimised for SD was used to acquire 30 datasets from healthy volunteers (aged 23–37 years, 17 males) on a 3T GE Signa HDx (General Electric, Milwaukee, WI, USA). For each subject, a Spin Echo diffusion-weighted echo planar imaging (EPI) sequence was also acquired with the following parameters: voxel size $2.4 \times 2.4 \times 2.4$ mm, matrix 128×128, slices 60, NEX 1, TE 93 msec, b-value $= 3000$ sec/mm^2, 60 diffusion weighted directions and seven non-diffusion weighted volumes. Cardiac gating was applied with effective TR of 20/30 R–R intervals (Dell'Acqua et al., in press; Thiebaut de Schotten et al., 2011a, 2011b).

Data were corrected for head-motion and eddy current distortion using the FSL software package (FMRIB Software Library, Release 4.1, The University of Oxford). Fibre orientation distribution (FOD) was estimated using an SD approach based on the damped version of the Richardson–Lucy SD algorithm, which reduces partial volume effects and spurious fibre orientations (Dell'Acqua et al., 2010). Algorithm parameters were chosen as described in Dell'Acqua et al. (2010). Fibre orientation estimates were obtained selecting the orientation corresponding to the local maxima of the FOD profile. To