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Review

Contribution of tractography to neuroanatomical terminology - short association tracts of the frontal lobe

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Summary

Enormous development of neuroimaging technologies, and subsequently of research methods, opened new era of in vivo research of the white matter anatomy. This review analyzes recent connectomics and imaging data about short association fibers of the frontal lobe, and relates it to current status and to further development of anatomical terminology. In some recent terminologies, such as in Neuroanatomical Terminology, or in Terminology of German Anatomical Society, under the section *Fibrae associationis lobares Fasciculus frontalis obliquus, Fasciculus frontalis orbitopolaris* and *Fasciculus frontomarginalis* have been listed. Also, in this review anatomy of the potential candidates for adding into new terminologies is described, such as Fronto-parietal U-tracts, Fronto-insular tracts, and Frontal longitudinal fasciculus system. Suggestions considered in this review are related to our research of human brain morphology in order to overcome the lack of postmortem brain specimens, to contribute to the linking of different data, and to enable better morphological correlations.

Key words: frontal lobe, association fibers, tractography, terminology, white matter

Introduction

Hemispheric association fibers interconnect ipsilateral cortical areas and often are called fascicles (bundles or tracts), implicating bi- or multidirectional fibers forming related bundle. A *fasciculus (TNA Latin: Fasciculus)* is a bundle of nerve fibers within the CNS [1]. Anatomists divided association hemispheric fibers into long association fibers connecting cortical areas in different lobes (interlobar fibers), and short association fibers connecting areas within the same lobe (intralobar fibers). The short association fibers connecting primarily adjacent gyri or cortical areas, just below the deepest parts of the sulci forming U-shaped fibers around the sulci, follow the pattern of cortical folding [2, 3, 4, 5, 6, 7]. However, strict division into inter- or intralobar association fibers is vague and insufficient in the cases when short fibers connect different gyri of adjacent lobes, e.g. pre- and postcentral gyrus in relation to the central sulcus.

Despite their significance, the knowledge about short association fibers remains sparse and notably their functional role, and is highly underrepresented in current descriptions of the human brain connectome owing to the challenges in mapping using available post-mortem and in vivo methods [3, 6]. Not so long ago, among the short-range association fibers, several white matter areas were not classified in any of the tract families, notably in frontal and occipital lobes [7]. Even recently the short structural connectivity of central sulcus remained relatively unknown [8].

Conturo et al. [9] were among the first who, by magnetic resonance imaging (MRI), in vivo tracked the fiber bundles connecting nearby cortical regions (parietal lobe) and showed that tracks that connected adjacent gyri had tightly curved trajectories consistent with U-fibers, whereas tracks that traversed more distant gyri had a more complex trajectory. The continuously developing field of MRI has made a considerable contribution to the knowledge of brain architecture including human connectome and the delineation of short cortical association fibers is drastically improved, as well as the definition of their endings into the gray/white matter boundary [10, 11]. Recent success in discovering novel or forgotten association fibers has stoked interest in the less conspicuous short-range fiber connections, which can be more challenging to delineate. The in vivo techniques open an era of scalable data collection, reproducible computations, longitudinal measurements, and for the first time, the ability to test theories of human cognition [12, 13]. The MRI revolution in human neuroscience has opened the possibility of the widespread, repeated, in vivo study of human white matter, since we are now free from a reliance on the availability of post-mortem specimens [14]. The white matter fiber dissection technique combined with the sophisticated neuroimaging methods have led to a more profound understanding of the brain connectivity and anatomo-functional organization (including the short association fibers) [3, 13].

Any advance rarely does come without its own challenges and limitations and the easy availability of data can come at the cost of increasing abstraction and the validity of the tractography model is hard to verify [14]. Therefore, it is necessary to acknowledge the inherent limitations of MRI based tractography and the specific shortcomings of the technique [11]. These limitations can lead to biases and errors in fiber mapping, even when based on high-quality diffusion MRI data [6]. It should be stressed that the terms origin and termination are arbitrary because dissection as well as tractography is blind to fiber direction, it cannot discriminate between afferent and efferent connections and also, the anatomical knowledge or atlas-based constraints may not apply to each single subject because of the intersubject variability [8, 14, 15, 16, 17]. An obvious source of error for tractography is in inference of MRI track orientation. This inference is fundamentally challenging, as the resolution of diffusion MRI is much coarser (millimeter range) than the neuronal architecture (micrometer range) [3]. Furthermore, both classical dissection techniques as well as modern MRI techniques are error prone and user-dependent [14]. To best visualize the short and highly curved fibers, the fiber length should be restricted between 3 and 10 mm (assuming a cortical thickness of 3 mm) [10].

Although there is still intense debate even about their existence, association fascicles are named in a confusing way in the current literature, especially with the emergence of tractography and the resultantly tremendous increase in white matter tract descriptions in the last decade [4]. In a field where descriptions and definition of structures are of paramount importance [14], the enormous increase of new obtained data requires detailed and precise anatomical definitions and terminologies of specific short hemispheric association tracts in humans. Anatomical terminology is increasingly important, not only in the study of anatomy (when students encounter concepts), but also for avoidance of different names for the same structures (standardization of professional language), and for entering data and specific terms correctly for further processing [18]. Related to this, the proposal toward the new classification of white matter tracts selects the origin as the primary criterion and the type of tract as the secondary criterion [19].

Comparing with previous Terminologia Anatomica - TA [20], in new Teminologia Neuroanatomica (NTA) [21], as well as in new Terminologia Anatomica [22] of the German Anatomical Society (Anatomische Gesellschaft) (TA2023AG), several new terms about short frontal lobe connections have been added (Table 1).

Table 1. Comparative list of anatomical terms for the frontal lobe short association tracts in previous (Terminologia Anatomica - TA) and in the current (Teminologia Neuroanatomica NTA and Terminologia Anatomica 2023 of the Anatomische Gesellschaft - TA2023AG) anatomical terminologies - empty fields indicate missing terms

Terminologia Anatomica TA 1998 [20]	Teminologia Neuroanatomica (NTA) (2017–2019) [21]	Terminologia Anatomica 2023 of the Anatomische Gesellschaft (TA-2023AG) [22]
Fibrae arcuatae breves	Fibrae associationis breves (Fibrae U- figuratae, Short associations fibers, Short associations fibres)	Fibrae associationis breves
		Fibrae associationis lobares
	Fasciculus frontalis obliquus (Frontal aslant tract, Frontal oblique tract)	Fasciculus frontalis obliquus
	Fasciculus frontalis orbitopolaris (Frontal orbitopolar fasciculus)	Fasciculus frontalis orbitopolaris
	Fasciculus frontomarginalis (Frontomarginal tract)	Fasciculus frontomarginalis

Additionally, in the current literature, but not in both of the recent anatomical terminologies (NTA) and (TA2023AG), Fronto-parietal U-tracts (FPUTs), Fronto-insular tracts, Frontal superior longitudinal fasciculus system and Frontal longitudinal fasciculus have been also described [23, 24].

In this text about the frontal lobe short association pathways, tractography and their terminologies the present controversies and emerging new anatomical terminology of frontal short association tracts are considered.

The frontal aslant tract - *FAT (Fasciculus frontalis obliquus; Frontal oblique tract)*

Connections, later named as FAT, were first described in 2008 by two independent groups [25, 26] studying human white matter [27]. One group, described a track connecting the superior frontal gyrus (SFG) to the pars triangularis of the inferior frontal gyrus (IFG), shown both on tractography and dissections [25]. Other group showed frontal short association fibers connecting the superior frontal „blade" and the inferior frontal "blade" [26]. These "blades" used for delineation of white matter bundles entering/exiting gyri, were identical to the „gyral window" defined by Prothero and Sundsten [28].

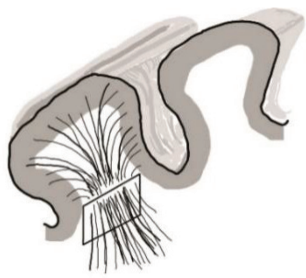

Figure 1. Gyral window according to Prothero and Sundsten [28]

However, it was suggested [29] that Aron et al. [30] first described the white-matter pathway connecting the inferior frontal cortex with the medial superior frontal cortex, as a part of the circuit pathway between the IFG, presupplementary motor area and subthalamic nucleus. Later, this pathway was named the frontal aslant tract (FAT) by Catani et al. [23], due to its oblique direction within the frontal lobe. Recently, the term Anterior Transverse System has been proposed for the FAT [4]. This newly described oblique bundle connects by a direct system of fibers the most posterior part of Broca's territory, (i.e., pre-central cortex and pars opercularis) in the IFG with medial frontal areas (including supplementary motor area - SMA, the preSMA and anterior cingulate cortex) in the ipsilateral SFG [5, 23, 25, 27]. As the third major fiber tract contributed to the speech network, FAT has become a research hotspot [24]. Four parcellations (by Human Connectome Project) of the SFG showed structural connectivity in the distribution of the FAT: 6ma, and SFL (as a parts of the SMA), 8BL, S6-8, and SFL. The relevant cortical regions that integrate to form the tract showed variable connections to the IFG (regions 44, 6r, FOP1, FOP3, and FOP4) and frontal operculum, as well as regions of the middle or anterior insula [27]. To "dissect" FAT, the first region of interest is located in the white matter of the IFG and the second region of interest in the white matter of the SFG [23, 25, 26]. Skilled fiber dissection, professional neuroanatomy knowledge, and fresh specimens are essential to obtain well-dissected FAT and informative fiber structure and to avoid the failure of separating the FAT from the superior longitudinal fasciculus (SLF-II) and from the arcuate fasciculus [24]. The presence of a bidirectional connection between the SFG to the Broca area has also been demonstrated through corticocortical evoked potentials [31].

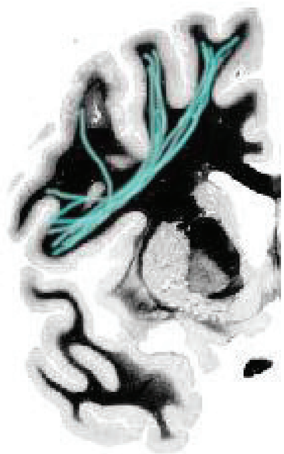

Figure 2. FAT - coronal view (diagram)

According to the extensive literature review of the FAT tractography [32] it was suggested that FAT is involved in speech and language functions, as well as in executive functions, visual–motor activities, orofacial movements, inhibitory control, working memory, social community tasks, attention, and music processing [30, 31, 32]. Some findings indicate that degeneration of the FAT underlies verbal fluency deficits in primary progressive aphasia [16]. In other review of the literature about the FAT in the non-dominant hemisphere (usually the right) [29], it has been found that despite the structural symmetry between the right and left FAT, these two tracts seem to display functional asymmetry. These facts about structural symmetry of FAT are actually expected according to our findings of smaller anatomical asymmetry of frontal operculum [33] or of frontal lobe [34] using the "essential gyral line".

However, conflicting evidence about volumetric lateralization of FAT could also be found in the current literature [30]. The FAT, although left-lateralized in most people, shows a more bilateral pattern compared with the arcuate fasciculus, which could explain the prompt recovery of speech functions in those patients with unilateral damage of this tract [23].

Fasciculus frontalis orbitopolaris *(Frontal orbitopolar fasciculus)*

Fasciculus frontalis orbitopolaris (Frontal orbitopolar fasciculus) or the fronto-orbitopolar tract connects posterior orbitofrontal cortex with anterior polar region. It runs on the ventral aspect of the frontal lobe and connects the posterior orbital gyrus to the anterior orbital gyrus and ventromedial region of the frontal pole [23].

Fasciculus frontomarginalis *(Frontomarginal tract)*

Fasciculus frontomarginalis (Frontomarginal tract) runs beneath the frontomarginal sulcus and connects medial and lateral regions of the frontopolar cortex [23].

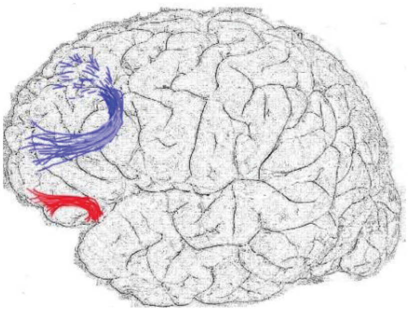

Figure 3. *Fasciculus frontalis orbitopolaris* - red and *Fasciculus frontomarginalis* - blue (broken lines indicate parts within the medial hemispheric surface) (diagram)

Fronto-parietal U-tracts

Fronto-parietal U-tracts is a chain of U connections, between the precentral (frontal cortex) and postcentral (parietal cortex) gyrus. These connections can be divided into three groups, superior group in the region of paracentral lobule, middle (complex) group in the hand knob region and the ventral group [23]. The middle of the three prominent connections between the middle parts of the pre- and postcentral gyri (marked as 2 on figure 4), named the "pli de passage fronto-pariétal moyen" by Broca, is localized in the hand region [3]. The hand region, recognized and described on axial imaging as an omega sign in the middle bend of the precentral gyrus [35], represents a landmark of the motor hand area [3]. The study of the short fiber bundles connecting the adjacent pre- and postcentral gyri showed significant asymmetry and increased density of MRI tracks in the middle part of the central sulcus (Rolandic region) in each hemisphere, consistent with the description by Broca of the "pli de passage moyen" [3].

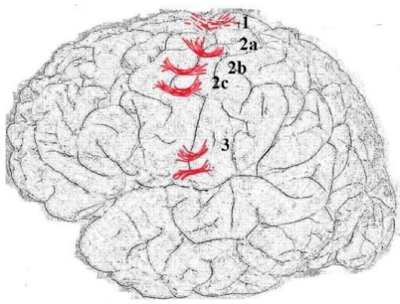

Figure 4. Frontoparietal U-tracts in Rolandic region. 1 - superior group (region of *lobulus paracentralis* - interrupted lines); 2 - complex middle group with three parts (2a, 2b, 2c); 3 - inferior group (diagram according to 3, 8, and 23)

Similarly, around the central sulcus there are three main high-density areas in the ventral, central and dorsal parts of the group connectivity space of both hemispheres (Figure 4), with five bundles identified bilaterally: one bundle in the functional area of the tongue (ventral end), three bundles in the functional area of the hand and one in the functional area of the foot (dorsal end) in all subjects [8]. Beside the description of U-shape short-range connectivity along the central sulcus at group level a significant relationship between the position of three hand related U-shape fibre bundles and the handedness score of subjects has been found [8]. Regarding the central sulcus, three local maxima of the streamline (i.e., U-shape fibres) are present in both left and right hemispheres [8]. However, the variability in morphology and the sex differences of human paracentral lobule [36] may affect the results for the superior group of these connections.

Fronto-insular tracts

Fronto-insular tracts are a system of U-shaped fibers organized around the peri-insular sulcus connecting the inferior frontal and precentral gyrus (frontal operculum) to the insula [23].

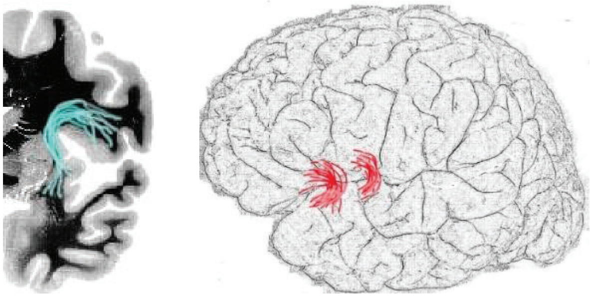

Figure 5. Fronto-insular tracts (diagram). Left - frontal section, diagrams; right - oblique view

The frontal longitudinal system

The frontal longitudinal system connects posterior with anterior prefrontal cortex. This parallel system composing the chain of U-shaped connections of different length, resembling a prolongation of the superior longitudinal fasciculus, connects the dorsolateral cortex of the premotor and prefrontal cortex and converges anteriorly to the same regions of the frontal pole [23]. This corresponds to the Dejerine's concept of chains even as a parts of long association tracts. Dejerine promoted views of the tract as a collection of fibers, from different sources and potentially carrying different information, which have been amalgamated together within the tract [14].

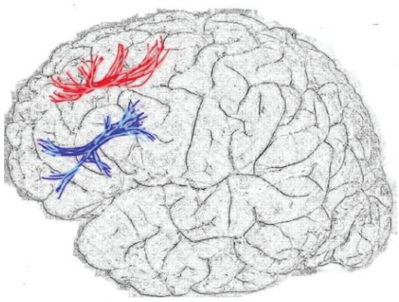

Figure 6. The frontal longitudinal system with two (superior and inferior) chains (diagram according 23)

Another novel identifying short frontal intralobar fiber tract has been named as the **frontal longitudinal fasciculus** (FLF or FLF fasciculus system) because of its longitudinal course [24]. Some of its fibers originated from the anterior part of the middle frontal gyrus (MFG) and from the pars triangularis of IFG. Then, the FLF is traced across the FAT inferior and medial to the MFG and ends in the caudal MFG, caudal SFG, and dorsal precentral gyrus [24]. In considering the above-mentioned results it is important to keep in mind the asymmetry and sex dimorphism of the medial frontal gyrus [37] or of the paracentral lobule [36]. Generally, controversies related to tractography results can be related to the gyral and sulcal pattern of brain, in this case of the frontal lobe. The very complex and variable structure and the sex differences in the hemispheric white matter, for example such as the corpus callosum [37, 38, 39], requires careful explanation of results of white matter studies.

The "blades" of white matter, used by Oishi et al., [26] correspond to the „gyral window" [28] (Figure 1), as the peripheral white matter which fills the space within the gyri. Its surface projection defined as the "essential gyral line", indicates the basic longitudinal directions of the gyri containing white matter. By its use, basic morphological symmetry of frontal operculum has been shown [33], and very variable morphology of gyri and sulci on the convexity of the frontal lobe has been significantly reduced [34]. We suggest that this line can be used in anatomical analysis of cortical connections in all cases with preserved gyral patterns of the brain, such as specimens, photographs, drawings or digital images and data.

Conclusions

Numerous new literature data about frontal lobe short association fibers obtained by various specific imaging methods, beside of limitations related to the methods or to morphological variability, generally complement the anatomical data, contribute to the development of neuroanatomical terminologies and are stimulatory for further studies of human frontal lobe short association fibers and its functionality.

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Doprinos traktografije neuroanatomskoj terminologiji - traktovi kratkih asocijacionih vlakana čeonog režnja

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Neslućen razvoj tehnologija neuroimidžinga i metoda istraživanja otvorili su novo doba u in vivo istraživanjima anatomije bele mase mozga čoveka. Prikazani su i analizirani novi podaci, (konektomike i imidžinga) o kratkim asocijacionim vlaknima čeonog režnja i povezani su sa stanjem i razvojem anatomske terminologije. U savremenim terminologijama, kao što su Neuroanatomska Terminologija ili Anatomska Terminologija Nemačkog Anatomskog Društva, pod odrednicom *Fibrae associationis lobares,* uključeni su *Fasciculus frontalis obliquus, Fasciculus frontalis orbitopolaris* i *Fasciculus frontomarginalis*. U radu su razmotreni i mogući kandidati za unošenje u nove terminologije, kao što su: *Fronto-parietal U-tracts, Fronto-insular tracts* i *Frontal longitudinal fasciculus system*. Date su i sugestije povezane sa našim ranijim istraživanjima morfologije čeonog režnja da bi se prevazišao nedostatak anatomskih preparata mozga, da se povežu brojni različiti podaci i da se omoguće njihove bolje morfološke korelacije. Sve ovo doprinosi, kako tačnijoj analizi rezultata, tako i razumevanju kontroverzi nastalih usled stalnih i dinamičnih promena u terminologiji bele mase mozga čoveka.

Ključne reči: čeoni režanj, asocijaciona vlakna, traktografija, terminologija, bela masa