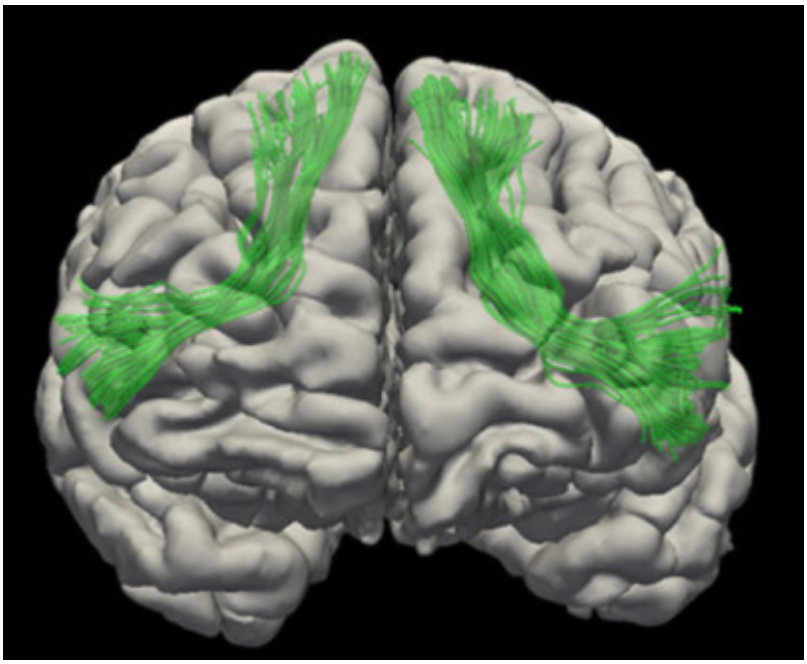
# Frontal aslant tract



The frontal aslant tract (FAT) is a major connection between the pre-supplementary motor area (pre-SMA) preSMA and Broca's area, whose functional role remains undefined.

It connects the posterior portion of the inferior frontal gyrus (IFG) to the supplementary motor area (SMA) and pre-SMA on the medial wall.

In this study we examined a patient presenting a morphological overregularization strategy in a verb generation task during awake surgery. This specific language deficit coincided with brain tumor resection at the level of the left FAT. During the task execution the patient formed the non-existent verbs by applying a morphological derivation rule to the given nouns, instead of retrieving the appropriate verbs. DTI results confirmed left FAT damage. Neuropsychological follow-up showed that this morphological derivation impairment partially persisted after surgery, whereas the results on a wide spectrum of other language-related tasks remained satisfactory [1)].

It's not every day that you hear about a newly described white matter pathway in the human brain. An interesting new study by a group of researchers in London and Chicago found a novel fiber tract implicated in verbal fluency impairments in patients with a lesser known neurodegenerative illness (Catani et al., 2013).

This short fiber tract connects two different regions in the frontal lobe. It was recently identified using a combination of diffusion imaging and post-mortem dissection (Lawes et al., 2008; Catani et al., 2012; Thiebaut de Schotten et al., 2012). Dubbed the frontal aslant tract (FAT) by Catani and colleagues, it connects the posterior portion of the inferior frontal gyrus (IFG) to the supplementary motor area (SMA) and pre-SMA on the medial wall.1

A number of experiments have already looked at the functional connectivity of these regions, during both resting state and task activation conditions. Statistically correlated fluctuations in the BOLD signal 2 are thought to reflect functional connectivity between two regions, but there is often no evidence that the two regions are directly connected anatomically. Therefore, in vivo structural MRI methods such as diffusion imaging can provide complementary data by visualizing white matter pathways to determine anatomical connections.

The diffusion tractography results were then compared to blunt dissection of tracts from post-mortem brains, which helped to validate a method that some view as prone to limitations and potential artifacts.3

Fig. 10 (modified from Catani et al., 2012). Coronal slices of the 'Digital Dejerine' maps 4 and post-mortem blunt dissections of the corresponding tracts. E) The frontal aslant tract (FAT) connecting inferior and superior frontal gyri.

A comparative study went further, showing that the results obtained from human tractography compared favorably to axonal tracing methods in monkeys (Thiebaut de Schotten et al., 2012).5

Fig. 6 (Thiebaut de Schotten et al., 2012). Reconstructions of the frontal aslant tract: comparison between post-mortem axonal tracing in monkey and human in vivo SD [Spherical Deconvolution] tractography shows simian-human similarities.

However, one difference between this tract in monkeys and humans is that the FAT is lateralized in humans, being larger in the left hemisphere than in the right (Catani et al., 2012). In the left hemisphere, posterior IFG is part of Broca's area. This brings us back to the clinical importance of this basic neuoanatomical work.

Verbal Fluency and the Frontal Aslant Tract

Primary progressive aphasia (PPA) is a neurodegenerative disorder, the hallmark of which is the deterioration of specific speech and language functions. There are three variants, each with characteristic behavioral, neuroanatomical, and pathological features (Gorno-Tempini et al., 2011): Nonfluent/Agrammatic Variant PPA is characterized by halting, effortful speech with difficulties producing grammatical output and/or comprehending syntactically complex sentences. Word comprehension and object knowledge are intact. Atrophy in the left frontal cortex is apparent on MRI. Semantic Variant PPA is marked by impairments that include comprehending the meanings of words, naming objects and understanding their function. Motor speech production and grammatical output are spared. Atrophy is seen in the anterior temporal lobe. Logopenic Variant PPA involves word finding problems, phonological speech errors, and difficulties in repeating words and sentences. Word comprehension, object knowledge, and grammar are spared. Degeneration of left posterior temporal-parietal regions is observed.

In the latest study by Catani et al. (2013), 35 patients with PPA and 29 controls participated in behavioral testing and MRI scanning. The tests included standard evaluations of language abilities including the Western Aphasia Battery, the Boston Naming Test, and the Peabody Picture Vocabulary Test. Tractography identified the frontal aslant tract and the uncinate fasciculus, which connects anterior temporal lobe regions to the IFG pars orbitalis and the orbitofrontal cortex. Quantitative measures included the number of streamlines (tract volume), fractional anisotropy, and radial diffusivity (measures of white matter integrity and axonal/myelin damage, respectively).*

Results indicated that patients with Nonfluent/Agrammatic PPA were impaired in a speech production task that required telling the story of Cinderella from a picture book. Poor performance in verbal fluency was associated with the extent of damage in the FAT, but grammatical deficits were not. In contrast, patients with Semantic Variant PPA showed deficits in semantic processing which correlated with degeneration in the uncinate fasciculus.

What are the implications for the neuroanatomy of verbal fluency and speech output? …Patients with lesions of the pre-supplementary motor area present with various degrees of speech impairment from a total inability to initiate speech (i.e. mutism) to mild altered fluency. Our findings suggest that these

medial regions of the frontal lobe could facilitate speech initiation through direct connection to the pars opercularis of the inferior frontal gyrus. Indirect support of this interpretation comes from the frequent observation of impaired fluency in patients with deep lesions in the frontal periventricular white matter. In these cases, a disconnection of the frontal aslant could explain the emergence of symptoms usually associated with frontal cortical damage.

More broadly, characterizing the different patterns of degeneration in these PPA variants of frontotemporal lobar degeneration, their underlying neuropathologies (e.g., tau, ubiquitin/TDP43, or amyloid plaques) and genetic mutations are key areas of research (Gorno-Tempini et al., 2011). Why is the pathology in Semantic PPA preferentially located in anterior temporal regions, while the neuropathological processes in Nonfluent/Agrammatic PPA are drawn to the left frontal cortex? Identifying macro-level structural features such as FAT is extremely important, but the next step is to determine exactly why the frontal aslant tract is targeted.

* ADDENDUM (July 8 2013): as commenter Rob pointed out, “radial diffusivity is most often interpreted as a measure of myelination.” I amended the post to reflect what the authors actually said in their paper.

Footnotes

1 Also known as the frontal operculum, Brodmann area 44 is the posterior portion of the inferior frontal gyrus (i.e., the inferior frontal gyrus pars opercularis). In the left hemisphere, BA44 is part of Broca's area.

2 Studies of resting state functional connectivity studies have become an enormously popular way to characterize brain connectivity in health and disease states. We can issue technical caveats all around, including how closely the BOLD signal measures neural activity and how accurately diffusion tractography captures true white matter connections. More on that below.

3 Diffusion imaging is an MRI method that measures the diffusion of water molecules. After using complex mathmatical algorithms and tractography methods, it can be used to visualize white matter pathways. Some potential artifacts are discussed at PractiCal fMRI, and recent advances in advances in diffusion imaging and tractography methods are presented in Pushing the limits of in vivo diffusion MRI for the Human Connectome Project.

4 The authors describe how the ‘Digital Dejerine’ maps were constructed (Catani et al., 2012): Digital Dejerine Maps were obtained by constraining tractography in non-contiguous brain slices of 2 mm (Axial, Sagittal, Coronal). Tractography was started from 10 seed points randomly placed inside each brain voxel and for each fibre orientation. Streamlines were propagated as in the whole brain tractography following fibre orientations using Euler integration with a step size of .5 mm and an angular threshold of 45°. Tractography propagation was arbitrary stopped after 40 mm. This enhances visualization of the white matter bundles that propagate along the plane of the slice selected. Bundles that are oriented perpendicularly to the surface of the slice are visualized only as dots or very short streamlines. Tractography maps were finally visualized using a lookup table empirically tuned to simulate historical black-and-white anatomical drawings. 5 Here the authors discuss comparable results from the two methods (Thiebaut de Schotten et al., 2012): …axonal tracing allows for the identification of single axon trajectories (Schmahmann and Pandya, 2006) and detailed description of their cortical terminations, whereas SD tractography is based on the diffusion signal acquired from relatively large voxels containing multiple axonal bundles, and is limited in reconstructing tracts approaching cortical regions. This methodological difference may account for tracts that were identified in the monkey, but not in the human brain. Despite the above limitations, we show that the majority of frontal lobe connections described in the monkey brain through axonal

tracing, can be also visualised in the human brain using SD tractography.

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[1)]

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