Laterality of the Amygdalo-Fusiform Pathway in Humans Assessed by Diffusion Tensor Tracking

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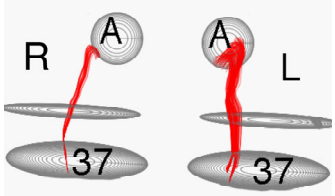
Introduction: MRI diffusion tensor tracking (DTT) of white matter pathways in animals and humans *(1-5)* produces line trajectories of neuronal fiber bundles in macroscopically ordered pathways with high accuracy and precision *(6-7)*. DTT has been used to identify a previously unknown amygdalo-fusiform pathway in four subjects *(8)*. This pathway interconnects cannonical Brodmann mid-fusiform area 37 with anteromedial temporal cortex (e.g., amygdala). A connection between mid-fusiform area 37 and anteromedial temporal lobe is expected to be involved in emotional modulation of higher-order visual functions (including face recognition). We used DTT in 12 normal living subjects to further investigate the laterality of this fiber pathway as a means to assess its role.

Methods: 12 healthy young adult volunteers were imaged under an IRB-approved protocol. Acquisition used a custom single-shot EPI sequence with tetrahedral-orthogonal diffusion encoding and 10 scan repeats, with 45 contiguous 2.5-mm slices. Acquisition and post-processing were as in *(1,6)*. Whole-brain track data were computed at an A_σ >0.14 threshold. Pathways were then selected from this whole-brain track set using spatial selection volumes (SSVs) as in *(1,6,8,9),* with the SSV location defined by atlas coordinates in atlas space. Pathway selection in each subject used a hierarchical selection procedure, first selecting all tracks that traversed a large coronal plane located between the amygdala and area 37. From these tracks, only those with origins or terminations adjacent to the mid-fusiform area 37 and anterior medial temporal lobe were selected. Large SSVs were used to select the pathway based on logical SSV combinations without limiting the number of tracks (Fig.). The number of pathway tracks in each hemisphere was counted to evaluate laterality. The DT-MRI data were inspected in all subjects to assure that artifacts did not distort the measured laterality.

Results: A pathway interconnecting mid-fusiform area 37 and the medial temporal lobe was identified bilaterally in all subjects (red in Fig.). The shape and anatomical details of the pathways were similar to *(8)* obtained in a smaller subject population. The number of tracks was, on average, greater on the left side by a factor or 3.1 (Table). The track counts were lateralized by -63%±7% (±1SEM), with laterality defined from 0 to ±100% for full left (-100) and right (+100) laterality. Furthermore, the left pathway appeared wider than the right (Fig.) in 11 of 12 cases.



A: Amygdala; **37:** Canonical mid-fusiform area37

Discussion: The finding of a bilateral amygdalo-fusiform pathway in humans was confirmed in a larger study of normal human subjects. The number of tracks is significantly higher on the left side. While differences in track counts could be due to a variety of factors (such as differences in anisotropy, pathway trajectory, etc.), the strong laterality of the track counts in conjunction with the consistently wider appearance on the left indicate left laterality of this pathway. This difference may be related to the known functional roles of the mid-fusiform region in humans; in particular the left has additional visual-lexical functions that the right does not have. While DTT in the temporal lobe can be limited by susceptibility artifacts, we ruled out such sources of false laterality by careful inspection of the DT-MRI data. We also evaluated the potential for crossing fibers *(10)* by evaluating tensor-derived parameters along the entire pathways, and no significant effects were found. Other factors such as inability to track the edge of the pathway *(9)* cannot account for the laterality. The observed direct connections between mid-fusiform area 37 and medial temporal lobe is consistent with the pathologic *(11)* and functional *(12)* abnormalities in area 37 in cohorts at high risk of Alzheimer's disease (AD), and with the co-activation of these regions in a variety of fMRI tasks. It is possible that the laterality of this pathway may be altered in different disorders such as AD.

Conclusion: The amygdalo-fusiform pathway was observed consistently in 12 subjects, and was found to be left-lateralized based on track counts and pathway width. The results also demonstrate the general use of DTT to assess pathway laterality in an objective manner using unconstraining atlas-defined selection regions.

Sub	left	right	Laterality
1	258	60	-77%
2	120	30	-75%
3	263	156	-41%
4	258	72	-72%
5	345	68	-80%
6	191	169	-12%
7	393	71	-82%
8	181	92	-49%
9	251	171	-32%
10	294	59	-80%
11	464	31	-93%
12	216	81	-63%
Ave	**270**	**88.3**	**-63%**
SD	**27.4**	**14.4**	**7%**

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