Identification of an Amygdalo-Fusiform Pathway in Humans using Diffusion Tensor Tracking

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Introduction

Recently, MRI diffusion tensor tracking (DTT) of white matter pathways has become practical in animals and humans *(1-5)*. This approach can produce line trajectories of neuronal fiber bundles in macroscopically-ordered pathways with high accuracy and precision *(6-7)*. We used DTT in four normal living subjects to investigate fiber pathways interconnecting Brodmann mid-fusiform area 37 with anteromedial temporal cortex (e.g., amygdala). Area 37 is a complex high-order cortical region associated with visual object recognition, including special objects such as faces and, in the left hemisphere, visual-lexical functions. Area 37 and the medial temporal lobe are also involved in early pathologic stages of Alzheimer's disease (AD) *(8)*, and functional changes are observed in area 37 in asymptomatic subjects at high risk of AD *(9)*. We thus hypothesize the existence of a pathway interconnecting area 37 and anteromedial temporal lobe.

Methods

Four 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 whole-brain acquisition of 51 contiguous 2.5 mm slices. Acquisition and post-processing were as in *(1,6)*. Whole-brain track data were computed as in *(1,6)* at an A_σ threshold of 0.14. Pathways were selected using spatial selection volumes (SSVs) as in *(1,6,10)*. Boundaries for the definition of area 37 were based on recent atlases using Brodmann's work and current human anatomic data *(11)*. Pathway selection began in each subject by using SSVs to confine interest to tracks that resided in the temporal lobe and that traversed a plane representing the rostral (anterior) boundary of area 37 in Talairach coordinates. From these tracks, only those with origins or terminations adjacent to the central quarter of canonical area 37 were selected. Finally, from this remaining set, only tracks with origins or terminations adjacent to the anterior medial temporal lobe were selected. The same selection procedure was applied in all subjects.

Results

Tracks interconnecting Brodmann area 37 and the medial temporal lobe were identified bilaterally in all subjects (Fig. 1). The right and left pathways exhibited mirror symmetry. The tracks begin/end in mid-area 37 (mid fusiform gyrus) medial to the lateral occipito-temporal sulcus. The tracks then appear to curve slightly dorsally and laterally, pass into the medial temporal lobe, then hook inferiorly to end/begin in the region of the superolateral amygdala in each hemisphere. No interhemispheric connections were evident. Care should be observed in interpreting these data. DTT is limited by factors that affect the calculated tensor in a given voxel, e.g., susceptibility effects in the temporal lobe, and potential for crossing fibers *(12)*. Among other precautions, we evaluated tensor-derived parameters along the entire pathways to screen for possible effects from partial volume averaging or crossing fibers, and no significant effects were found.

Discussion

This work demonstrates specific direct connections between area 37 and medial temporal lobe in humans. A direct connection is consistent with functional abnormalities in area 37 in cohorts at high risk of AD *(9)*. Area 37 may thereby report dysfunction in the connected medial temporal lobe, where pathologic alterations first occur in AD. AD degeneration might also develop at an early neocortical stage in area 37 as a consequence of this direct connection. The identification of a human amygdalo-fusiform pathway thus has potential anatomical, functional, and pathologic significance.

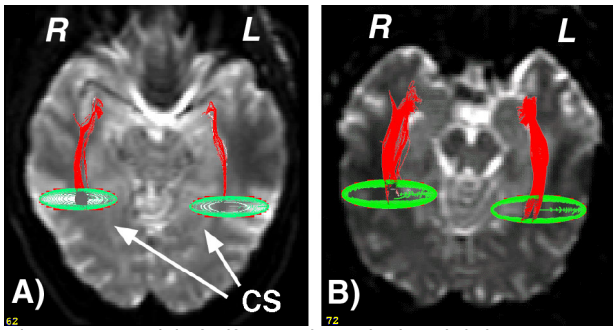

Figure 1. Amygdalo-fusiform pathway (red tracks) that connect Brodmann area 37 to the medial temporal lobe in two of the four subjects (A,B). Reference axial T2-weighted EPI images (b=0) are oriented parallel to the central long axis of the pathway. The area-37 SSV (green) and collateral sulcus (cs) are indicated.

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