Identification of parallel hippocampo-fusiform and amygdalo-fusiform pathways in living humans

C. D. Smith[1], E. Gultepe[2], E. Akbudak[2], N. Lori[2], T. E. Conturo[2]

[1]Neurology, University of Kentucky, Lexington, Kentucky, United States, [2]Radiology, Washington University, St. Louis, Missouri, United States

Introduction: MRI diffusion tensor tracking (DTT) of white matter pathways in animal and human brain *(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 *(8)* that interconnects canonical Brodmann mid-fusiform area 37 with anteromedial temporal cortex (e.g., amygdala). Such connections are expected to be involved in emotional modulation of higher-order visual functions (including face recognition). We further analyzed the DTT results in 12 normal living subjects to probe whether this pathway contains specific anatomical components. Using pathway features alone, we identified two distinct components with characteristic shapes, trajectories, and anatomical locations: the amygdalo-fusiform pathway proper, and a newly identified hippocampo-fusiform pathway.

Methods: 12 healthy young adult volunteers were imaged (IRB-approved) using a custom single-shot EPI sequence with tetrahedral-orthogonal diffusion encoding, 10 scan repeats, and 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. The composite pathway connecting area 37 and medial temporal lobe was 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 coordinates in atlas space. First, all tracks were selected that traversed a large coronal plane located between 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 selected pathways primarily based on logical SSV combinations. Initial pathway results were viewed in vector-graphic 3D projection display, which suggested a separation between superior and inferior parts of the pathway (pronounced in a few cases, but subtle in most). Another SSV was placed at the midpoint of the pathway length to separate the pathway into superior (red) and inferior (blue) parts, using a heuristic approach to divide the pathway at a "cleft" (when visible on lateral view), and/or at an apparent transition in the anterior-medial part (inspected on both views).

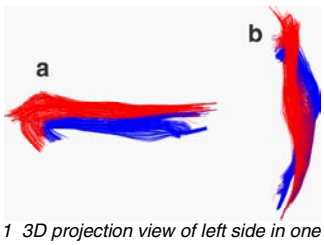

*Fig. 1 3D projection view of left side in one subject, viewed from the side (**a**) and above (**b**)*

Results: This superior-inferior (red-blue) separation (side view, Fig. 1a) revealed a medial-lateral separation (view from above, Fig. 1b). A separation in the anterior part was also highlighted, where the superior component took a sharp hook to terminate antero-laterally (red in Fig. 1b), while the inferior component took a gentle curve to terminate more posterior-medially (blue in Fig. 1b). This pattern was identified in all 12 of 12 subjects. 2D anatomical overlays showed that the superior (red) pathway terminated adjacent to the amygdala, while the inferior pathway terminated adjacent to the hippocampal head (Fig. 2), seen in all 12 subjects to varying degrees.

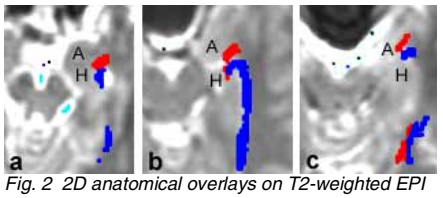

*Fig. 2 2D anatomical overlays on T2-weighted EPI for **a:** same subject and side as Fig. 1, and **b,c:** two other subjects.*

Discussion: A hippocampo-fusiform pathway has been found in living humans that is in close proximity to the amygdalo-fusiform pathway. The two pathways have a characteristic course and arrangement. The observation that the amygdala and hippocampus have parallel projections to area 37 may indicate the role of both of these medial temporal lobe structures in modulating visual-lexical functions and face processing (functions of area 37). The hippocampus and amygdala also have intimate roles in memory, with the amygdala modulating memory by emotional salience. These parallel pathways to/from area 37 suggest that such emotional modulation may occur by both medial temporal lobe structures receiving parallel information from remote sites such as area 37. In this study, technical factors, e.g., susceptibility artifacts and crossing fibers *(10)*, were found not to have a significant effect on the results. The observed direct connections between mid-fusiform area 37 and these two medial temporal lobe structures 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 known degeneration of both medial temporal lobe structures in AD.

Conclusion: Parallel hippocampo-fusiform and amygdalo-fusiform pathways were observed consistently in 12 subjects.

Acknowledgments: Funded by NIH R01 grants AG09862, NS36660, and NS39538; and NIH P20 MH71616.

References: **(1)** Mori S, et al, Ann Neurol 45 (1999) 265-9; **(2)** Conturo TE, et al, PNAS 96 (1999), 10422-7; **(3)** Poupon C, et al, NeuroImage 12 (2000), 184-95; **(4)** Basser PJ, et al, 44 (2000), 625-32; **(5)** Catini M, et al, NeuroImage 17 (2002), 77-94; **(6)** Lori NF, et al, NMR Biomed. 15 (2002), 494-515; **(7)** Lazar M, Alexander AL, NeuroImage, 20 (2003), 1140-53; **(8)** Smith CD et al., ISMRM (2004, Kyoto), 624; ISMRM (2005, Miami), 733; **(9)** Lori NF, et al *in* Diffusion in NMR and MRI (Y Cohen, ed), 26-30 Aug 2001, 57-72; **(10)** Tuch DS, et al, Mag Reson Med 48 (2002), 577-82; **(11)** Braak H, et al, J Neural Transm Suppl 98 (1998) 97-106; **(12)** Smith CD, et al, Neurology 53 (1999) 1391-6.