

Introduction

The interthalamic adhesion or massa intermedia (MI) is a midline bridge between the two thalami. The MI is reportedly absent in 2.3%-22.3% of human brains[1, 2]. Prior studies have demonstrated a higher prevalence and a bigger size of MI in female subjects[2-4]. More recently, behavioral studies have revealed MI may play a role in age-related attention[3].

Our group has recently demonstrated the passage of decussating stria medullaris fibers through the MI using probabilistic tractography based on diffusion tensor imaging, which further supports the notion of MI involvement in limbic and behavioral networks[5].

Given the variability in size and presence of MI, we further investigated the differences in fractional anisotropy (FA) measures in healthy brains between those with and without MI.

Methods

One hundred human brain MRI studies were obtained from the Human Connectome Project (HCP)[6]. Participants were healthy, unrelated volunteers ages 25-35 (54% female). All studies included preprocessed T1-weighted structural and diffusion-weighted sequences. Imaging was performed on a Connectome Skyra, which is a customized Siemens 3T Skyra platform (~42 mT/m and 100 mT/m gradients for structural and diffusion imaging respectively). The 3D structural T1 sequence had 0.7-mm isotropic resolution acquired in 7 minutes, 42 seconds (TR=2400ms, TE=2.14ms, TI=1000ms, flip angle=8°, FOV=224mm*224mm)[7].

Diffusion data were obtained using spin-echo EPI acquiring 1.25 mm isotropic voxels (TR=5520ms, TE=89.5ms, flip angle=78°, FOV=210mm*180mm, matrix size=168*144, echo spacing=0.78ms, partial Fourier=6/8, b-values=1000, 2000, 3000 s/mm², diffusion directions 90)[7].

T1-weighted structural MR sequences were manually inspected to identify MI presence by three experienced investigators and inter-rater agreement was calculated using the Fleiss kappa test (kappa=0.61, p-value<0.001). Ten brains were excluded due to inability to confirm MI presence or absence. Of the remaining 90 brains, 79 were found to have MI. Diffusion tensor images were reconstructed using the FSL dtifit command tool, and the FA images were then input to the TBSS pre-statistical processing pipeline[8]. Design matrix and contrast files were generated via built in scripts available on FSL. Subjects were grouped into those with MI and those without MI. A two-sample unmatched t-test was performed using FSL's randomise command[9]. To enhance robustness of results, we employed the threshold-free cluster enhancement option. A p-value of 0.05 was set to report significance. Results were projected onto MNI152 standard-space for visualization. Statistical analysis of non-MR data was performed using R.

Results

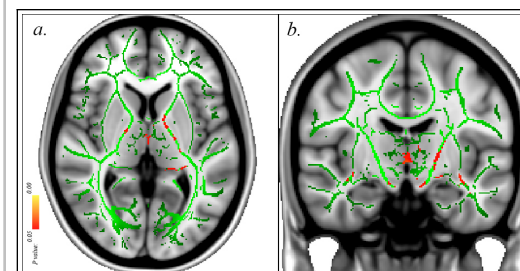
Out of 90 brains (53 female and 37 male), 11 individuals (5 female and 6 male) had no MI. FA values were significantly higher in subjects with MI over the anatomical location of MI (figure a and b, axial and coronal view respectively). The results further showed a significant difference in FA across the internal capsule (figure c), including anterior limb, genu, and posterior limb particularly in the left hemisphere where more extensive projections were noted. Further differences were seen in the FA across temporal stem (figure d)

Conclusions

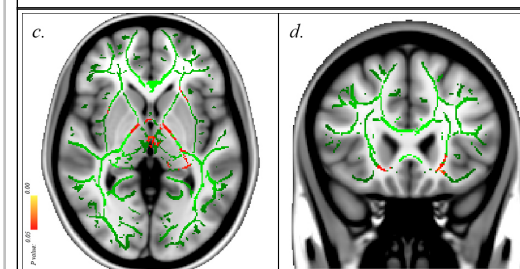
This is the first study using neuroimaging to demonstrate MI as a true conduit of fiber tracts in the human brain. MI presence did result in an increase of FA values with apparent lateralization. Further studies analyzing various fiber pathways can shed light on functional significance of this midline commissure.

Learning Objectives

Role of massa intermedia in structural connectivity of the human brain.



TBSS result showing area of significant higher FA value in healthy individual with MI (P value<0.05) projected onto MNI152 standard space, a. axial and b. coronal view of massa intermedia anatomic location.



TBSS result showing area of significant higher FA value in healthy individual with MI (P value<0.05) projected onto MNI152 standard space, c. internal capsule and d. temporal stem.

References

1. Takahashi, T., et al., Prevalence and length of the adhesion interthalamica in schizophrenia spectrum disorders. *Psychiatry Research: Neuroimaging*, 2008. 164(1): p. 90-94.
2. Nopoulos, P.C., et al., Sex differences in the absence of massa intermedia in patients with schizophrenia versus healthy controls. *Schizophr Res*, 2001. 48(2-3): p. 177-85.
3. Damle, N.R., et al., Relationship among interthalamic adhesion size, thalamic anatomy and neuropsychological functions in healthy volunteers. *Brain Struct Funct*, 2017. 222(5): p. 2183-2192.
4. Trzesniak, C., et al., Adhesion interthalamica and cavum septum pellucidum in mesial temporal lobe epilepsy. *Brain Imaging Behav*, 2016. 10(3): p. 849-56.
5. Kochanski, R.B., et al., Identification of Stria Medullaris Fibers in the Massa Intermedia Using Diffusion Tensor Imaging. *World Neurosurg*, 2018.
6. Van Essen, D.C., et al., The WU-Minn human connectome project: an overview. *Neuroimage*, 2013. 80: p. 62-79.
7. Van Essen, D.C., et al., The Human Connectome Project: a data acquisition perspective. *Neuroimage*, 2012. 62(4): p. 2222-31.
8. Smith, S.M., et al., Tract-based spatial statistics: voxelwise analysis of multi-subject diffusion data. *Neuroimage*, 2006. 31(4): p. 1487-505.
9. Winkler, A.M., et al., Permutation inference for the general linear model. *Neuroimage*, 2014. 92: p. 381-97.