Tract-specific effects of sex and age on human white matter demonstrated with quantitative MR diffusion tractography.

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INTRODUCTION

There is a large body of literature that documents global and regional relationships between brain structure, sex and aging. With the advent of MR diffusion tractography, however, it has become possible to examine these relationships in finer detail. The effects of sex and age on white matter tracts can be evaluated with quantitative tractography, which produces an index of the probability that a voxel lies on the diffusion pathway connecting two regions in the brain (connection probability index).[1] In this study, we present quantitative tractography data supporting tract-specific differences between the white matter of human males and females, as well as tract-specific changes in white matter with age.

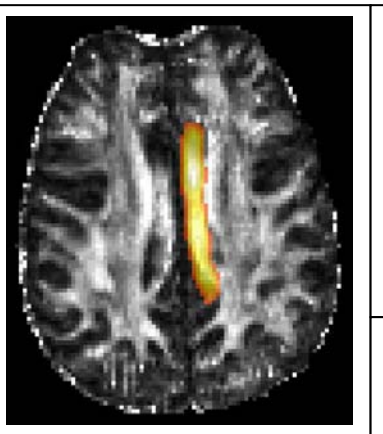

Figure 1: (Left) Cluster within left cingulate demonstrating correlation with sex. (Right) Streamline tractography of cingulate shown for reference.

METHODS

Diffusion tensor imaging (12-direction) was performed with a Siemens 3.0T scanner on 27 healthy right handed subjects (14 males and 13 females ranging in age from 21 to 52 years old). Datasets were registered using a combination of affine and nonlinear methods. Seed and target ROIs for individual white matter fiber tracts were defined using cortical and subcortical regions defined by the MNI atlas and coregistered across all subjects. Probabilistic tractography was performed for the major interlobar white matter tracts bilaterally. The probability maps generated for each tract were analyzed with cluster-level nonparametric testing using either age or sex as a covariate of interest, with the voxel size of the ROIs used as a confounding covariate. Both cerebral hemispheres were analyzed independently using this protocol.

RESULTS

Significant tract-specific correlations between connectivity, sex, and age were found in multiple white matter tracts. The majority of the left cingulate tract in females belonged to a cluster that demonstrated a significantly increased connection probability index compared to males, as depicted in Figure 1. In addition, a cluster consisting of the majority of the right inferior frontal-occipital fasciculus (IFO) demonstrated an inverse relationship between connection probability index and age, as depicted in Figure 2. In contrast, other tracts did not demonstrate significant correlations between connection probability index and either sex or age.

DISCUSSION

While broad decreases have been observed in the fractional anisotropy of the white matter of elderly subjects, a tract-specific decrease in the connection probability index within the right inferior frontal-occipital fasciculus suggests that this pathway may be particularly susceptible to the effects of aging. This may be due its greater length than most of the other tracts under study (increasing its likelihood of being affected by a diffuse process) or it may reflect the propensity of aging to affect frontal white matter.[2]

The volume of the orbitofrontal cortex has previously been demonstrated to be greater in females than males.[3] This study expands upon that finding, and suggests that increased orbitofrontal volumes may also be associated with greater white matter connectivity to other regions of the brain via the cingulate tract.

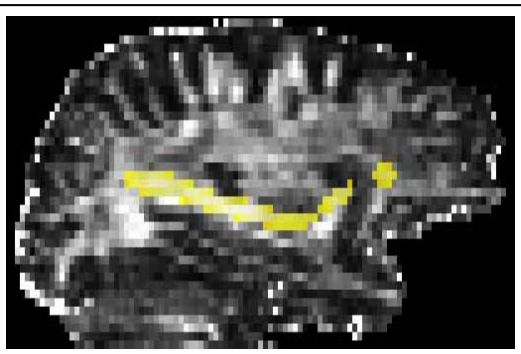

Figure 2: (Left) Cluster within right IFO demonstrating negative correlation with age. (Right) Streamline tractography of IFO shown for reference.

References

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