Corticocortical Connectivity of Probst Bundle Fibers in Callosal Dysgenesis Revealed by Diffusion Tensor Imaging Fiber Tractography

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Introduction: Agenesis or hypogenesis of the corpus callosum (CC) is a relatively common congenital brain malformation that can arise as an isolated anomaly or coexist with a spectrum of other cerebral and/or extracerebral abnormalities [1]. In cases of complete or partial absence of the corpus callosum, commissural fibers that would ordinarily decussate across the midline in the normal brain instead course longitudinally along the medial aspect of each cerebral hemisphere. These bilaterally paired aberrant white matter tracts are known as the Probst bundles or, equivalently, the longitudinal callosal fasciculi (LCF). The only prior diffusion tensor imaging (DTI) fiber tractography study of callosal dysgenesis has been limited to two infants, and there was insufficient spatial resolution to parcellate the Probst bundle fibers [2]; hence the precise connectivity of the LCF has not previously been delineated. In this study, we perform 3T DTI at high spatial resolution and high angular resolution in 1 adolescent and 2 adult subjects with callosal dysgenesis to determine the corticocortical connectivity of the Probst bundle fibers in each cerebral hemisphere.

Methods: Three subjects ages 17-34 years, two with complete agenesis and the other with partial agenesis of the corpus callosum, as well as one normal young adult volunteer, were imaged on a 3T GE Signa EXCITE scanner with an 8-channel phased array head coil, using ASSET parallel imaging at an acceleration factor of two. Whole-brain DTI was performed with single-shot multislice axial spin-echo EPI (TR/TE = 14s/64ms) at 1.8-mm isotropic voxel resolution using 55 diffusion-encoding directions at b=1000 s/mm^2, as well as one b=10 s/mm^2 acquisition. Fiber tracking was performed using in-house software based on FACT [3]. Tracks were launched from every voxel in the brain, and only tracks passing through CC in the normal volunteer and LCF in the experimental subjects were selected. These tracks were further segmented based on connectivity to different Brodmann Areas (BAs) of the cerebral cortex. ROIs representing each BA were created by resampling the BA templates in Montreal Neurological Institute (MNI) space into each subject's brain using the affine transformation between the high-resolution structural 3D T1-weighted image in each subject and the averaged template in MNI space, using FLIRT (FSL package). Additional ROIs were applied in order to select corticocortical fiber tracks passing through CC in the normal volunteer and through LCF in the experimental subjects.

Results: In the normal volunteer, DTI fiber tracking of the corpus callosum showed the expected homotopic organization of commissural fibers, with orbitofrontal cortex (BAs 11, 47), medial prefrontal cortex (BAs 9, 10), somatosensory areas (BAs 1, 2), precuneus (BA 7), and visual cortex (BAs 18, 19) all connecting to the homologous contralateral BAs, in agreement with previous reports [4]. In the 3 subjects with callosal dysgenesis, LCF fibers in each hemisphere demonstrated selective connectivity between the medial frontal lobe (BAs 10, 11, 47) and the ipsilateral superior parietal area (BA 7 and parts of 1, 2, 3, 5). In one subject, fiber tracks connecting to BA 10 (*light blue*) are shown for the right hemisphere in Figure 1 and for the left hemisphere in Figure 2. The green fiber tracks project to BA 7 (*light green*) and the red tracks connect to somatosensory cortex (*red*). In this subject with agenesis of the corpus callosum, LCF fibers also showed connectivity between the medial prefrontal cortex (BA 10) and the anterior temporal lobe (BA 20) in the left hemisphere only (Figure 2, *blue tracks*). This specific pathway could not be adequately evaluated in the left hemispheres of the other two subjects with callosal dysgenesis due to the presence of extensive cortical malformations including polymicrogyria and gray matter heterotopia, but it was not present in the right hemisphere of any of the 3 experimental subjects. In all 3 of the subjects, we found that fibers within the superolateral aspect of the LCF had predominantly subcortical connectivity.

Discussion: This preliminary DTI fiber tracking study of callosal dysgenesis provides the first noninvasive mapping of the connectivity patterns of human Probst bundle fibers. The dominant corticocortical connectivity is between medial frontal lobe and the ipsilateral superior parietal area. In the only experimental subject without left hemispheric cortical malformations, connectivity between left medial prefrontal cortex and left anterior temporal lobe was also identified, and this tract was not present in the right hemisphere of any of the 3 subjects. It is presently unknown whether the LCF fibers represent functional axonal pathways. If they are active, one hypothesis regarding their function might be as part of the network that distinguishes "self" from "others", as such tasks are known to preferentially recruit medial prefrontal regions, superior parietal areas, and the left anterior temporal lobe [5]. Further investigation with diffusion tractography combined with fMRI and/or magnetoencephalography may elucidate the altered brain function and connectivity in callosal dysgenesis, and might also advance the understanding of hemispheric lateralization and interhemispheric communication in the normal human brain.

Figure 1

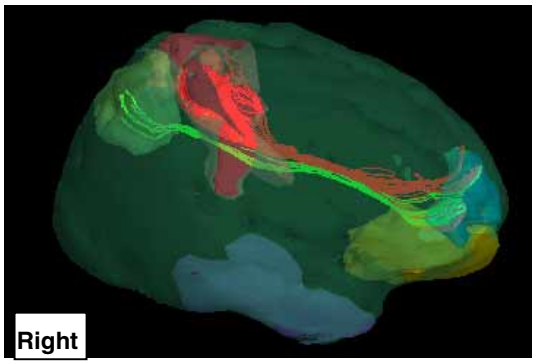
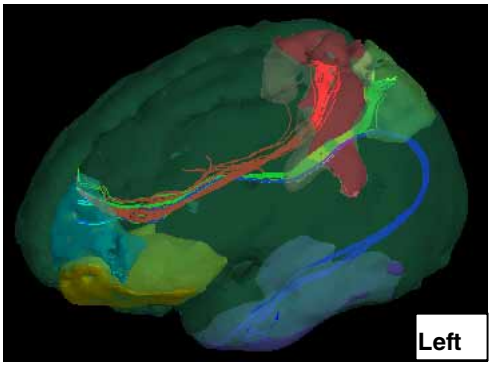


Figure 2



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