Direct Interhemispheric Cortical Communication via Thalamic Commissures: A New White-Matter Pathway in the Rodent Brain

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Introduction: The corpus callosum (CC), the anterior (AC), and the posterior (PC) commissures are the principal axonal fiber bundle pathways that allow bidirectional communication between the brain hemispheres.

Methods: Here, we used the Allen mouse brain connectivity atlas and high-resolution diffusion-weighted MRI (DWI) to investigate interhemispheric fiber bundles in C57bl6/J mice, the most commonly used wild-type mouse model in biomedical research.

Results: We identified **1)** commissural projections from the primary motor area through the AC to the contralateral hemisphere; and **2)** intrathalamic interhemispheric fiber bundles from multiple regions in the frontal cortex to the contralateral thalamus. This is the first description of direct interhemispheric corticothalamic connectivity from the orbital cortex. **3-4)** We named these newly identified crossing points thalamic commissures. **5)** We also analyzed interhemispheric connectivity in the Balb/c mouse model of dysgenesis of the corpus callosum (CCD). **6)** Relative to C57bl6/J, Balb/c presented an atypical and smaller AC and weaker interhemispheric corticothalamic communication.

Conclusion: These results redefine our understanding of interhemispheric brain communication. Specifically, they establish the thalamus as a regular hub for interhemispheric connectivity and encourage us to reinterpret brain plasticity in CCD as an altered balance between axonal reinforcement and pruning.

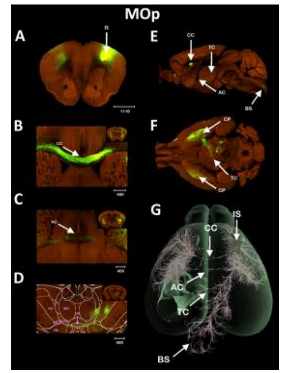

Figure 1. Anterior commissure connectivity. Tract-tracing of the Primary motor area (MOp. Injection site **(A)**, corpus callosum (CC) **(B)**, AC **(C)**, TC **(D)**, sagittal **(E)** and axial slice **(F)** slice and 3D reconstruction of the fibers **(G)**.

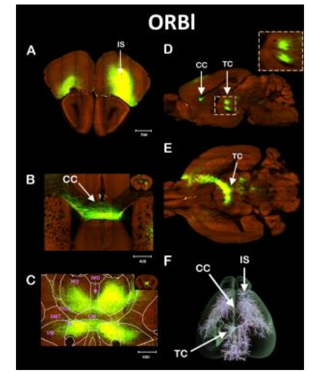

Figure 2. ORBI Interhemispheric thalamic connectivity. Injection site (IS) **(A)**, CC coronal view **(B)**, and of the thalamic commissure (TC) **(C)**. Sagittal **(D)** and axial **(E)** view of the Thalamic commissure, and the 3D reconstruction **(F)**.

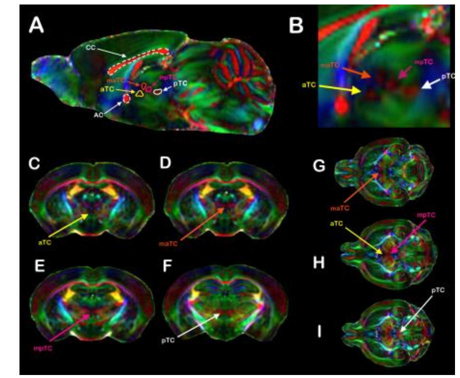

Figure 3. Thalamic commissures revealed by DWI. (A) DWI maps of a C57bl6/J mouse brain showing the Corpus Callosum (CC), anterior commissure (AC), and the thalamic commissures (TC). Anterior TC (aTC, yellow arrows), medial anterior TC (maTC, orange arrows), medial posterior TC (mpTC, magenta arrows), and posterior TC (pTC, white arrows). **(B)** TCs in greater detail. Coronal **(D-F)** and axial **(G-I)**.

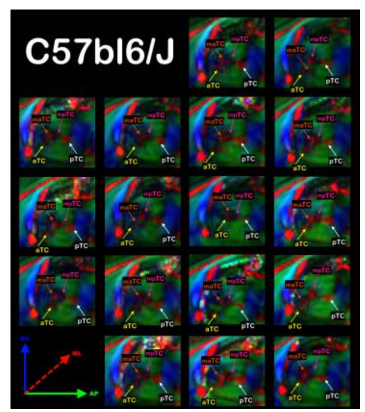

Figure 4. The Thalamic Commissures are a Common Feature in a Population of C57bl6/J mice. Mouse brain interhemispheric commissures, corpus callosum (CC), anterior commissure (AC), thalamic commissures (TC) and the fornix (FX) **A**. DWI maps show the thalamic commissures (TC) in a population of 17 C57bl6/J mice. Anterior TC (aTC, yellow arrows), the medial anterior TC (maTC, orange arrows), the medial posterior TC (mpTC, magenta arrows), and the posterior TC (pTC, white arrows).

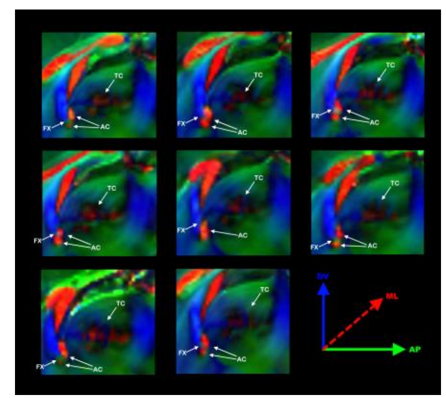

Figure 5. Commissural abnormalities in Balb/c. Corpus callosum (CC), anterior commissure (AC), thalamic commissures (TC) and the fornix (FX). DWI map of eight Balb/C mouse brains showing the anatomical variability of the anterior commissure (AC), fornix (FX), and thalamic commissures (TC).

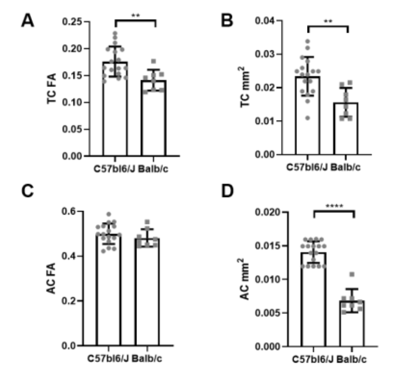

Figure 6. Commissural tissue properties. Comparative quantification of fractional anisotropy (FA) and cross-sectional areas of the thalamic (TC) and anterior (AC) commissures measured in C57bl6/J and Balb/c mice in the midsagittal MRI plane. ** $p < 0.01$. *** $p < 0.001$.