

Pathology of callosal damage in ALS: An ex-vivo, 7T diffusion tensor MRI study.

Cardena et al., *NeuroImage* (2017) 15, 200-208

In a collaborative study between the National Institute of Health, the University of Maryland and the University of Michigan, researchers used a 7 tesla (high intensity) MRI to image the donated brains from donors with ALS and compared the findings to those obtained from donors without ALS. Although the motor symptoms in ALS patients are caused by pathology in the motor regions of the brain and spinal cord, the nerve fibers connecting different regions in the two hemispheres of the brain (corpus callosum) is consistently abnormal in many ALS imaging studies. The strength of the MRI magnet used in this study was several times greater than what is typically used to image the brain in routine clinical practice. Also, each brain was imaged continuously for 23 hours to obtain the extensive data needed for analysis. The focus of this study were several fold: first, it was to establish that high resolution MRI on postmortem ALS brain is feasible; second, it confirmed the previously described changes in the corpus callosum using a high resolution MRI; and third, it allowed for an understanding of the microscopic abnormalities that underlie the alterations observed on the MRI.

The greater detail of the MRI analysis provided data confirming that the nerve fibers connecting the motor regions of the two hemispheres were more disorganized. When the tissue was analyzed microscopically, there was increased microglia-macrophages, which are signs of inflammation, and a loss of myelinated axons of neurons. The findings indicate that the MRI abnormalities are the result of complex changes on a microscopic level. Future research will address the exact sequence of the observed changes so that treatments can be developed to interact at the earliest point.

Dr. Justin Kwan who is a co-author of the paper discusses the importance of tissue donation with his patients. Several of his patients were included in this study. The spinal cord, brain and muscle samples are recovered by the University of Maryland Brain and Tissue Bank, which is supported by a grant from the Blazeman Foundation. Both the Blazeman Foundation and the Brain and Tissue Bank are acknowledged in the article.