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Progressive Oligodendrocytic Tauopathy and Chronic Tissue Atrophy After a Single TBI

Traumatic brain injury (TBI) has acute and chronic phases. To investigate tissue atrophy and phosphorylated tau increases in the chronic phase of TBI, mice received a sham impact or an impact above the parietal lobe. At 14 and 180 days after injury (DPI), the brains of these mice were imaged by T2 weighted and diffusion tensor (DT) MRI. The ipsilesional corpus callosum (CC) showed atrophy at 14 DPI on T2 MRI, which was unchanged at 180 DPI. At 14 DPI, CC decreased in fractional anisotropy, and increased in mean, radial, and axial diffusivity. These changes persisted to 180DPI. The CC was then assessed for phosphorylated tau positive (pTau+) cell density using QuPath software to detect cells stained with anti-tau antibodies (AT8, PHF1, S214) that recognize distinct tau phospho-epitopes. pTau+ cell density in the ipsilesional CC was assessed in 4 regions extending 2.4mm rostrally from the CC at the impact site. In region 1, most proximal to the injury site, only PHF1 showed an increase in pTau+ cell density, which was chronically high at both 14DPI and 180DPI. In region 2, S214 and AT8 pTau+ cell density was chronically high at 14DPI and 180DPI, while PHF1 pTau+ cell density increased progressively from 14DPI to 180DPI. In region 3 pTau+ cell density increased progressively from 14DPI to 180DPI with S214 and AT8. pTau+ oligodendendrocytes (OLs) have been previously described in injured brains. Sections were co-labeled using the OL marker olig2 and S214 to determine if OLs were the predominant pTau expressing cell type. In the CC, 95.7% ± 3.4 pTau+ cells were co-labelled with olig2 at 14DPI and 94.0% ± 1.7 at 180DPI suggesting that most pTau+ cells in CC are OLs. In summary, MRI of ipsilesional CC showed atrophy and microstructural damage that is chronic but not progressive. In contrast, detailed regional histological analysis of pTau+ OLs show localized and site-specific increases in pTau+ cell density, some of which are both chronic and progressive.