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Traumatic brain injury: networks and neuropathology

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Although identification of pathological changes in mild traumatic brain injury (TBI) has posed challenges, 2012 has also been a year of advances and debate. Patients with mild TBI or concussion are generally thought to have a form of diffuse axonal injury, but this so-called stealth pathology is invisible to conventional imaging techniques.[1] However, diffusion tensor imaging shows promise in elucidation of disruption of white matter tracts consistent with diffuse axonal injury. Previous diffusion tensor imaging studies were often based on the premise that damage to white-matter tracts was spatially homogeneous, meaning that signal changes were uniform among basic imaging units (voxels) along individual tracts. However, analysis of individual voxels within a region of interest in 28 patients with mild TBI showed that only a cluster of voxels had abnormal fractional anisotropy compared with voxels in the area of interest in 28 healthy participants.[2] By adding the clusters of voxels from disparate regions of interest with abnormal fractional anisotropy, this research group calculated a white-matter injury load that differentiated patients with mild TBI imaged within 21 days after the injury from uninjured individuals. The cluster approach to diffusion tensor imaging analysis has also received support from a study of mild TBI due to blasts in military personnel.[3]

Resting state functional MRI after mild TBI has disclosed altered functional connectivity of neural networks that might compensate for the effects of diffuse axonal injury. Alteration of functional connectivity has been studied in the default mode network, which is active during task-independent introspective states, such as mind wandering. Although functional connectivity seemed to be normal in 14 asymptomatic athletes imaged about 10 days after a sports concussion, reimaging after a physical stress test revealed altered connectivity of the default mode network.[4] Repeated mild TBI might produce chronic changes in connectivity of networks contributing to pathological processes, such as apoptosis and degeneration, and exacerbate the effects of normal ageing.[5]

Although no consensus exists on the definition or mechanisms of chronic traumatic encephalopathy (CTE), it is thought to arise from repeated mild TBI. Studies of boxers, American football players, and participants in other contact sports have shown brain atrophy and cavum septum pellucidum along with amyloid β, tau, and TDP-43 pathologies.[6] Similar changes and chronic inflammation can occur after one moderate to severe TBI.[7,8] In a report, CTE-like changes were described after blast exposure, both in a few US military war veterans and in a mouse model of blast exposure.[9]

Many questions remain concerning early detection of CTE, its relation to other neurodegenerative disorders, genetic factors, interaction with comorbidities, and interventions to mitigate pathological changes. Prospective, longitudinal investigations of single and repeated mild TBI in relation to other severities of TBI are needed. To this end, portable accelerometers that measure head impacts during repeated exposures to contact sports can assess cumulative effects of mild TBI and subconcussive impacts.[10] We hope that these studies will collectively identify the relative risk to individuals and reveal potential therapeutic targets.

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