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A single head impact produces delayed atrophy of internal capsule and substantia nigra and parkinsonian-like motor deficits in mice

A single TBI increases the risk to develop Parkinson's disease (PD). Most rodent models of PD produce a unilateral lesion of substantia nigra (SN) resulting in increased turning behavior toward the lesioned hemisphere. Lesions of internal capsule (IC) that innervate SN are also associated with symptoms of PD. This behavior is rarely induced spontaneously. Rodent TBI models have shown some histological elements of PD pathology, yet the functional, motor aspects of the disorder are absent. In a study examining chronic effects of single closed head injury (CHI) or Sham-CHI in mice, clockwise rotations toward the impacted hemisphere and total rotations are assayed on open field at 7 or 180 days post injury (DPI). At 180, but not 7DPI, 28% of mice increased the percentage of clockwise over total rotations (N=7 at both 7 and 180DPI). These data suggest a single CHI can induce delayed turning bias toward the impacted hemisphere. IC and SN volume show significant chronic and progressive ipsilesional atrophy in injured mice at 180 but not 14 DPI, or in sham-injured mice at 14 or 180 DPI (IC, 180 DPI, 0.84 ± 0.02 mm3, 14DPI, 1.5 mm3 ± 0.05; Injury*Time, $F_{1,17}$ =15.3, p=0.001; SN, 180 DPI, 0.43 ± 0.05 mm3, 14DPI, 0.72 mm3 ± 0.02; Injury*Time, $F_{1,17}$ =6.4, p=0.02. 14 DPI, n=7, 180 DPI n=14). These data suggest a single CHI induces delayed atrophy of ipsilesional IC and SN. At 180DPI, injured mice with more than 60% ipsilesional SN volume loss also show atrophy in the contralesional SN (N=2, 41% ± 10%). Total SN atrophy significantly correlated with increased percentage of clockwise over total rotations (Sham-CHI vs CHI at 180DPI, N=13, p=0.02*). These data suggest delayed, chronic bilateral SN atrophy induces parkinsonian motor asymmetries following a single CHI in a subset of mice. These data suggest that a single CHI may produce late-onset parkinsonian behavior and pathophysiology and provides a model to study the onset and treatment of PD-like symptoms.