

**Young-onset Parkinson's disease: role of head trauma and sport practice**

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*Introduction:* Head Trauma (HT) may be responsible for the earlier onset of neurodegenerative diseases such as Amyotrophic Lateral Sclerosis and dementia. However, no studies examined the potential contribution of HT in young onset cases (YOPD, age at onset <50) of Parkinson's disease (PD), a condition whose environmental risk factors have not been identified yet.

*Objectives:* To assess HT history in a cohort of PD patients to estimate the associated risk, the impact on age of onset, and the effect on both clinical and biochemical features of the disease.

*Methods:* 94 PD patients (31 with YOPD, monogenic forms excluded) and 70 healthy controls, were screened for HT history using the Brain Injury Screening Questionnaire (BISQ), which investigates number, severity, and circumstances of HT across lifespan, calculating the associations with different clinical groups (case vs controls, YOPD vs late-onset PD). In all PD patients, HT history features were correlated with motor and non-motor scores, and to CSF levels of  $\alpha$ -synuclein, amyloid- $\beta$ 42, total and phosphoriled-181 tau, lactate, CSF/serum albumin into a subgroup.

*Results:* Positive HT history increased the risk for PD overall and for YOPD specifically. Sport-related HTs resulted a specific risk factor for YOPD, although the prolonged sporting life delayed PD onset. The individual number of HTs ("trauma score", TS) was higher in PD patients than controls, proportionally increasing the risk for PD. TS directly correlated with CSF t-tau in PD group, but not in the YOPD subgroup.

*Conclusions:* This study confirms HT as "dose-dependent" risk factor for PD overall, but specifically indicates its role in favoring YOPD. Sport-related HT is the most risky for YOPD, although the longer sporting life delays PD onset, protecting from YOPD. Contribution of HT in PD pathogenesis may involve tau-mediated mechanisms, which have greater relevance in those cases with later onset but not in YOPD.