MARKED DIFFERENCES IN BIOPTERIN METABOLISM BETWEEN PARK8 AND SPORADIC PARKINSON’S DISEASE

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Introduction: PARK8 is the most common form of familial Parkinson's disease (PD). PARK8 patients of the Japanese family, carrying I2020T mutation in leucine-rich repeat kinase 2, show diverse neuropathology, although their clinical pictures are similar to those in sporadic PD (sPD) patients [Hasegawa et al., Parkinsonism Relat. Disord. 15(4):300-6, 2009]. Since biopterin (BP) is a cofactor for tyrosine hydroxylase, which catalyzes the first step in the biosynthesis of dopamine, the measurement of BP and its related metabolites in biological fluids is significant for the investigation of various diseases.

Aim: To gain more insight into the PARK8 etiology, we measured the BP and monoamine metabolites levels in the cerebrospinal fluids (CSF) of 7 PARK8 (I2020T) patients, 2 asymptomatic mutation carriers, and 21 sPD patients.

Methods: The CSF levels of BP, neopterin, and monoamine metabolites were assayed by HPLC with fluorescence or electrochemical detection.

Results: The CSF levels of BP and 5-hydroxyindolacetic acid in PARK8 patients were significantly higher than those in sPD patients, although the symptoms were comparable in both groups. Because the decreased BP levels in sPD patients are thought to result from the degeneration of nigrostriatal dopaminergic neurons, these results suggest that PARK8 patients may exhibit parkinsonian symptoms without a concomitant reduction in BP levels likely because of less neurodegeneration than sPD patients.

Conclusion: Our first report of a distinctive biochemical difference between PARK8 and sPD provide new evidence supporting the involvement of dysfunction, rather than degeneration, of dopaminergic neurons in the onset of parkinsonian symptoms in PARK8.