CSF DOPAMINE METABOLITES ARE RELIABLE STAGE BIOMARKERS IN EARLY PARKINSON'S DISEASE PATIENTS

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Background: In Parkinson's disease (PD), stage disease biomarkers are elusive, albeit a recent study (Lunardi et al., 2009) indicated a reduced ratio between dopamine (DA) and its metabolites as biomarker of advanced stages.
Methods: In this pilot study, we collected cerebrospinal fluid (CSF) samples 120 min after a challenge dose (200 mg) of levodopa (LD) and utilized high performance liquid cromatography (HPLC-ALEXYS) to measure DA, 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanilic acid (HVA). The cohort was composed of non fluctuating early PD patients, stage 1-2, below 42 months disease duration.
Results: The DA title in response to LD challenge (5.48 nM/L), as expected, was not correlated to the UPDRS score (R = 0.4). However, it was significantly lower, in basal CSF samples, if compared to non-PD patients. In contrast, the intermediate product DOPAC (and, in part, the end product HVA) were tightly correlated with the degree of the motor impairment. The analysis post-hoc, assuming a motor cut-off of 20, depicts two subpopulations: group I, mean UPDRS 13.3 and group II, (mean UPDRS 24) showing a ratio DOPAC/DA respectively 5:1 vs 13:1.
Conclusion: These observations support the notion that DA metabolites titles reflect the neuro-degeneration of the nigro-striatal terminals with high sensitivity; the DOPAC/DA ratio seems in fact capable to monitor slight UPDRS changes. Reasonable explanations include compensatory processes among surviving dopaminergic neurons or altered endogenous turnover. Either way, it promises to be a useful and not costly biomarker to validate neuro-rescuing strategies.