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Clinical-biochemical profile of *de novo* Parkinson's disease with constipation

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Introduction: Prodromal constipation (PC) at Parkinson's disease (PD) onset suggests an early degeneration of the enteric nervous system. Presenting phenotype, biochemical signature, and clinical progression of PD patients with PC (PD+PC) may theoretically differ from those without (PDwoPC), as a consequence of distinct neurodegenerative trajectories [1–3].

Objective: We compared the clinical-biochemical profile of *de novo* PD patients with and without PC, and the respective mid-term progression, to establish the grouping effect of PC.

Methods: Baseline parameters, including Hoehn and Yhar stage (HY), MDS-UPDRS-pars III, Non-Motor Symptoms Scale (NMSS), MMSE, levodopa equivalent daily dose (LEDD), were assessed in n=57 *de novo* PD+PC patients and n=73 *de novo* PDwoPC. Baseline CSF biomarkers (α-synuclein, amyloid and tau peptides, lactate, CSF/serum albumin ratio or AR) were also examined into a smaller sample and in controls (n=46). Clinical progression was estimated by comparing HY and LEDD change 2.06±1.35 years from diagnosis.

Results: At onset, PD+PC patients had higher HY ($p<0.001$) and MDS-UPDRS-pars III scores ($p=0.004$), and higher CSF AR ($p=0.045$). PDwoPC had higher Non-Motor Symptoms Scale domain-2 score ($p=0.018$), and lower CSF α-synuclein level ($p=0.003$). At follow-up, PD+PC had greater LEDD ($p=0.004$).

Conclusions: PC identifies a group of *de novo* patients with more severe motor impairment at onset, biochemical signature suggestive of blood brain barrier disruption, and greater dopaminergic requirement at mid-term; conversely, PDwoPC *de novo* patients complain with major fatigue at onset and exhibit more pronounced synucleinopathy. PC may thus mark distinct patterns of clinic-pathological progression in PD.

References

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