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Deregulation of blood microRNAs in Parkinson's disease

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Background: MicroRNAs (miRNAs) are small, non-coding RNAs that are endogenously expressed to regulate the expression of many genes involved in disparate physiological functions and pathologies, including Parkinson's disease (PD).MiRNAs are strong and specific gene regulators and therefore promising candidates to be diagnostic markers and potential therapeutic targets. Suitable biomarkers from easy accessible sources, such as peripheral blood, plasma, and serum,which reflect system-wide biology, could be used to detect and monitor PD in early stages, even before symptoms appear. To date, only few studies have assessed the expression of blood miRs related to PD. Although miRshave been intensively investigated as potential diagnostic markers, currently there is no reliable and clinically validated biomarker for PD.

Objective: The aim of the study was to profile the expression of several candidate miRNAs in peripheral blood mononucleated cells (PBMCs) from Levodopa (L-dopa) treated and drug-naïve PD patients versus unaffected controls and to interpret the expression data in a biological context.

Methods: We analyzed RNAs from PBMCs of 36L-dopa-treated, 10 drug-naïve PD patients and unaffected controls matched by sex and age. We evaluated expression by RT-qPCRand we analyseddata using a two-tailed paired t-test. To detect miRNA targets, several miRNA resourceswere combined to generate an overall score for each candidate gene using weighted rank aggregation.

Results: Significant overexpression of miRNAs 103a-3p, 30b-5p, and miR-29a-3p in treated PD patients was observed and promising candidate target genes for these revealed by an integrated *in silico* analysis.

Conclusions: We revealed three candidate biomarkers for PD. MiRNAs 30b-5p and 29a-3p replicated a documented deregulation in PD albeit opposite to published data. For miR-103a-3p we demonstrated for the first time an upregulation in treated PD patients.Expression studies in patients before and following L-dopa administration are necessary to define the involvement of L-dopa treatment in the observed deregulation.Our *in silico* analysis to prioritize targetsof overexpressed miRNAs identified candidate target genes, including genes related to neurodegeneration and PD. Despite the preliminary character of our study, the results provide a rationale for further clarifying the role of the identified miRNAs in the pathogenesis of PD and for validating their diagnostic potential.

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