Profiling of gut microbiome metabolites reveals novel correlations with host amino acid metabolism in Parkinson’s disease

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Introduction:
Gastrointestinal dysfunction and microbiome alterations are emerging as key prodromal features of Parkinson’s disease (PD) pathology. However, functional implications of gut dysbiosis on PD pathology and progression are still being defined. We performed comparative analysis of urinary amino acid metabolites profiles in PD to altered metabolites associated with the gut microbiome.

Methods:
A total of 64 urine samples obtained from healthy control. Samples were analysed by reverse phase (RP)/UPLC-MS/MS methods with positive and negative ion mode electrospray ionization (ESI) and HILIC/UPLC-MS/MS with negative ion mode ESI. Welch’s two-sample t-test was performed on log transformed data and p<0.05 was considered significant.

Results:
A total of 18 amino acid metabolites were significantly altered in PD patients. Additionally, we found 11 metabolites associated with the gut microbiome were differentially abundant in PD. Crucially, some altered amino acid metabolites in PD but not matched healthy individuals correlated with specific gut microbiome metabolites.

Conclusion:
• Our results highlight potential new links between altered amino acid metabolism in PD and functional changes in the Parkinsonian gut microbiome.
• High resolution metabolomics and metagenomics analyses have potential clinical utility for biomarker and therapeutic development in PD.

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Study Design

Figure 1. Differential expression of amino acid metabolites in Parkinson’s patients and matched healthy controls.
A total of 16 amino acid metabolites including a) vanillactate, b) 3-methoxytyrosine, c) dopamine, d) 3-methoxytyramine, e) 3,4-dihydroxyphenylacetate, f) L-carboxyethyltyrosine, g) 3-methoxytyramine sulfate, h) homovanillic acid (HVA), i) 3,4-dihydroxyphenylacetate sulfate, j) homovanillic acid sulfate, k) 3-sulfo-L-alanine, l) dopamine-3-o-sulfate, m) phenyllactate, n) dopamine-4-sulfate, o) 2-oxoadipate and p) creatine were differently expressed in PD patient urine compared to healthy controls. Welch’s two-sample t-test was performed. Data expressed as mean± SEM. **p<0.005, ***p<0.0005, ****p<0.0001.

Figure 2. Altered gut microbiome metabolism in healthy controls and Parkinson’s patient urine samples.
A total of 11 amino acid metabolites including a) cathechol sulfate, b) guaiacol sulfate, c) p-cresol sulfate, d) p-cresol glucuronide, e) catheol glucuronide, f) 4-ethyl glucuronide, g) phenylactate, h) indolelactate, i) deoxycholate, j) glycodeoxycholate and k) glycodeoxycholate 3-sulfate were differently expressed in PD patients urine compared to healthy controls. Welch’s two-sample t-test was performed. Data expressed as mean± SEM. **p<0.005, ***p<0.0005.

Figure 3. Correlation between amino acid and gut microbiome metabolites.
a) Dopamine, b) 3-methoxytyrosine, c) dopamine-3-o-sulfate and d) HVA showed significant correlation with glycodeoxycholate 3-sulfate and e) 3,4-dihydroxyphenylacetate sulfate, f) HVA sulfate g) acetobutyrate and h) HVA showed significant correlation with PLA. Pearson correlation *p<0.05, **p<0.005, ***p<0.0005, ****p<0.0001.