Healthcare Innovations
How practice has changed

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Gut microbiome metabolites correlate with host lipid metabolism in Parkinson's disease

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Background

Converging lines of evidence indicate that dysfunctional host and gut microbial metabolism are dysregulated in the prodromal phase of Parkinson's disease (PD) prior to the onset of motor symptoms. There are currently no biomarkers for early detection of Parkinson's disease. This represents an urgent unmet medical need to enable the effectiveness of current and future therapeutic interventions for PD. The aim of this study was to understand changes in host and microbial metabolism in PD patient biofluids which could reflect a transition from the healthy to diseased state.

Methods

We performed a comprehensive untargeted metabolomics analysis of urinary lipid metabolites in PD together with altered metabolites associated with the gut microbiota. Age and sex-matched healthy controls recruited from the Royal Brisbane and Women's Hospital (RBWH) and the UQ Centre for Clinical Research (UQCCR) were used for comparison. A total of 64 urine samples consisting of 31 from healthy control and 33 from PD patients were used in this study. Samples were deproteinized and 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

After routine quality control cut-offs were implemented, we detected a total of 14 lipid metabolites that were significantly altered in PD patients. Five metabolites were associated with bile acid metabolism and nine form the cholesterol pathway. Changes in secondary bile acid metabolism, particularly secondary bile acids indicative of microbial metabolism changes were evident in PD patients with 11 altered metabolites associated with the gut microbiota being significantly altered in this cohort. Interestingly, several lipid metabolites that were altered in PD correlated with specific gut microbiome metabolites.

Conclusions

Our results provide new insights into altered lipid metabolism and gut dysbiosis in PD but confirmation in a larger or different cohort would be needed. Urine metabolomics profiling could have utility to identify disease-related metabolic signatures from microbial and host metabolites that are dysregulated in prodromal and clinical PD.

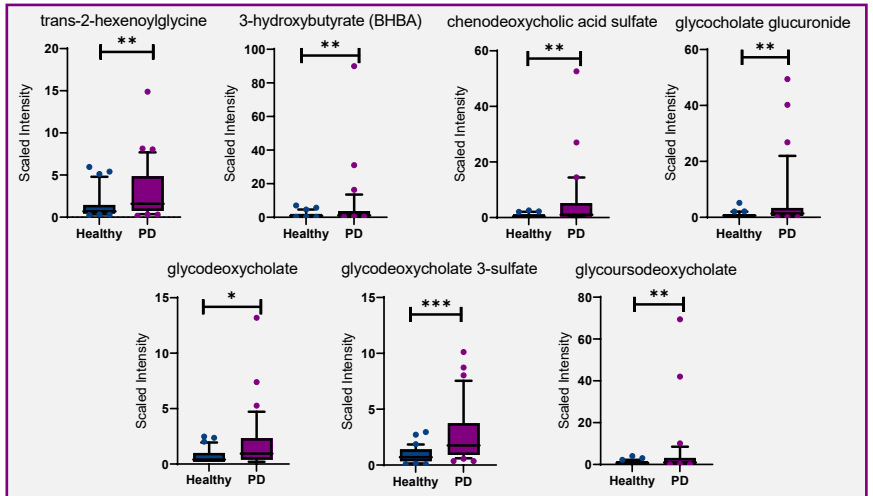

Figure 1. Significantly elevated lipid and bile acid metabolites in PD patient urine samples compared to healthy controls. Welch's two-sample t-test was performed. Data represented as median ± SEM (n=33 PD and 31 healthy controls; *p<0.005, **p<0.0005)

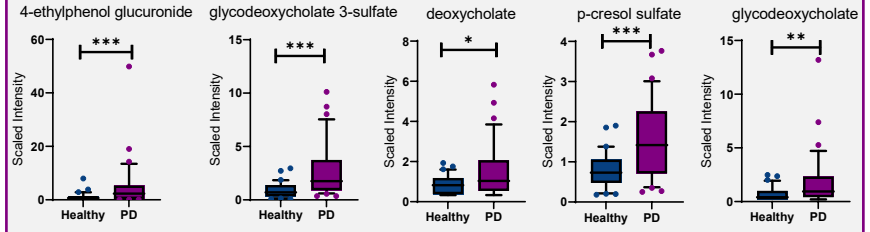

Figure 2. Altered gut microbiome metabolism in healthy controls and Parkinson's patient urine samples. Welch's two-sample t-test was performed. Data expressed as mean ± SEM (n=33 PD and 31 healthy controls; *p<0.005, **p<0.0005)

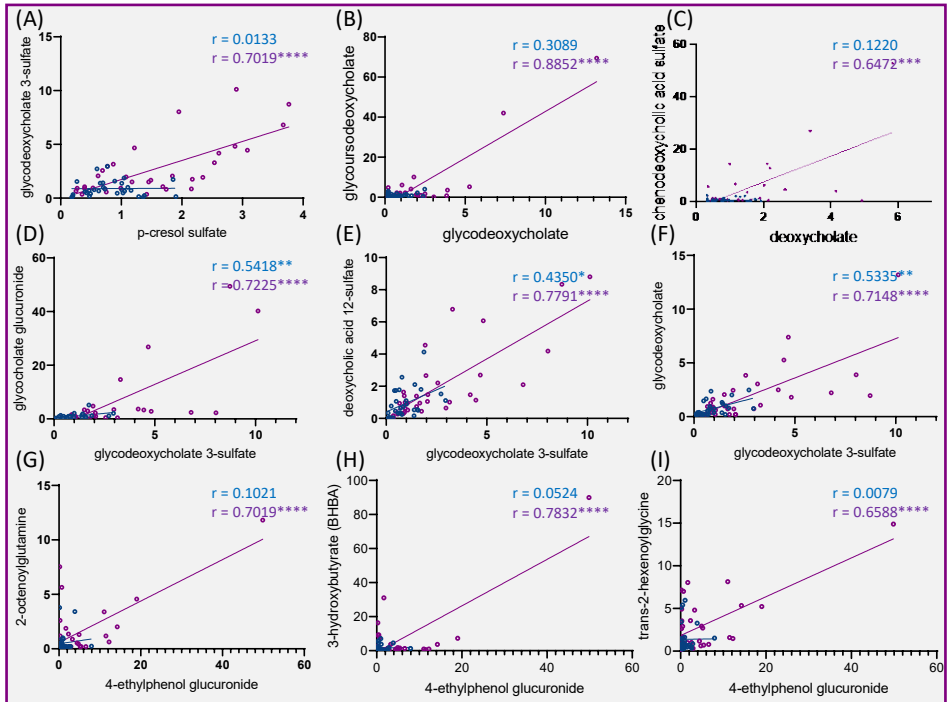

Figure 3. Scatterplot showing correlation of urine lipids with gut microbiome metabolites in PD (purple) and healthy controls (blue). Simple linear regression was used (n = 33 PD and 31 healthy controls). (A) glycodeoxycholate 3-sulfate showed significant correlations with p-cresol sulfate; (B) glycoursodeoxycholate showed significant correlations with glycodeoxycholate; (C) chenodeoxycholic acid sulfate showed significant correlation with deoxycholate; (D) glycocholate glucuronide, (E) deoxycholic acid 12-sulfate and (F) glycodeoxycholate showed significant correlation with glycodeoxycholate 3-sulfate; (G) 2-octenoylglutamine, (H) 3-hydoxybutyrate (BHBA) and (I) trans-2-hexenoylglycine showed significant correlations with 4-ethylphenol glucuronide. Pearson correlation was performed; *p<0.05, **p<0.005, ***p<0.0005, ****p<0.0001