ABSTRACT
Accumulating evidence suggests that changes in microbiome and host metabolic changes occur in Parkinson's disease (PD). However, the functional implications of gut dysbiosis on PD pathology and progression are still being defined. Methods: We performed comparative analysis of urinary lipid metabolites profiles in PD to altered metabolites associated with the gut microbiome. Of the 64 urine samples, 31 samples were obtained from healthy control and 33 samples were collected from PD patients. Samples were deproteinsed and analyzed 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 14 lipid metabolites were significantly altered in PD patients. Among these, 5 were associated with bile acid metabolism, while 9 metabolites were involved in cholesterol metabolism. Changes in bile acid metabolites, particularly secondary bile acids are linked to alterations in bacterial diversity or the abundance of certain bacterial species in the PD population. Accordingly, we found 11 metabolites associated with the gut microbiome were differently abundant in PD. Crucially, some lipid metabolites in PD correlated with specific gut microbiome metabolites.

SUMMARY & CONCLUSIONS
• Altered lipid metabolism and microbiome dysbiosis are linked to PD pathology.
• Emerging evidence suggests altered microbiome metabolism can profoundly influence host pathophysiology.
• Our results demonstrate that elevated urine lipids in PD patients correlate with changes in microbiome pathways.
• Metabolomic profiling in conjunction with functional microbiome analyses could have potential clinical utility for diagnosis and stratification of PD patients.

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