“Oral and Gut Microbiome in Multiple System Atrophy”

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Emerging evidence links perturbations in the gut microbiota to neurological disease. One recent publication involving six patients reported a possible role of intestinal dysbiosis in multiple system atrophy (MSA).

We investigated the fecal microbiome and metabolome in MSA by analyzing fecal samples from 17 patients and 17 age-matched spouses/siblings living in the same community. Clinical data, including dietary history (Food Frequency Questionnaire with 384 items) and constipation severity, were collected. Fecal DNA was extracted and amplicon sequencing targeting the V3-V4 region of the microbial *16SrRNA* gene was performed on Illumina MiSeq platform. Fecal metabolomics was performed using ^{1}H nuclear magnetic resonance spectroscopy (NMR).

There were no significant between-group differences in demographics, dietary intake, smoking history and diabetic status. Patients had worse constipation severity scores. At the operational taxonomic unit (OTU) level, patients had a five-fold reduction in *Paraprevotella* (OTU000073) abundance, predominantly *P. clara* ($P_{adjusted}$=0.021). At the genus level, patients had a five-fold reduction in *Paraprevotella* (OTU037) ($P_{adjusted}$<0.001) and a four-fold increase in *Bacteroides* (OTU034) ($P_{adjusted}$=0.003), predominantly *B. fragilis* (Figure1A). Multivariate analyses revealed no significant associations between the altered microbiome abundance with potential confounders such as gender, body mass index, dietary parameters, constipation severity or levodopa equivalent units; except for a relationship between *Bacteroides* with protein and fat intake. Fecal NMR data plot showed a clear separation in fecal metabolomics. Patients had significantly lower levels of short-chain fatty acids (SCFAs) (butyrate, acetate and propionate), and substrates of methylamine metabolism (choline and trimethylamine).

We found significantly altered fecal microbiome and metabolome in MSA. We have initiated a multicentre collaboration to expand this work in various ways including the oral microbiome.

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