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Unraveling gut microbiota in Parkinson's disease and atypical parkinsonism

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OBJECTIVES

Recent evidences support the hypothesis that dysfunction in the gut microbiota may play a critical role in the pathogenesis of Parkinson's disease (PD). However, findings are heterogeneous probably due to the presence of several confounders. We evaluated the differences in gut microbiota among PD, atypical parkinsonism (i.e. multiple system atrophy [MSA] and progressive supranuclear palsy [PSP]) and healthy controls (HC) and whether microbiota may act as modulator of disease progression and clinical phenotype.

METHODS

We recruited patients with idiopathic PD (n=193, of whom 39 were de-novo), PSP (n=22), MSA (n=22), and HC (n=113). Several confounders were taken into account, including pharmacological therapy, dietary habits and genetic status. Information on the type of lactation were also recorded. (Table 1)

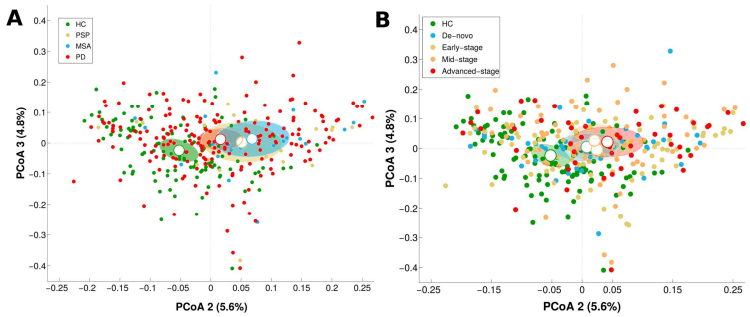

FIGURE 1: *Principal coordinates analysis of weighted UniFrac distances representing the differences in patients groups (A) and in disease duration stages (B).*

FEATURE	TAXONOMIC LEVEL			RELATIVE TAXA ABUNDANCE		EFFECT A		P-value
	PHYLUM	FAMILY	GENUS	BELOW THE MEDIAN (N=96)	ABOVE THE MEDIAN (N=97)	ADJ. DIFF. (SE)	OR [95%CI]	
NMSQUEST TOTAL SCORE, MEAN (SD)								
		Christensenellaceae		10.5 (5.4)	12.3 (5.4)	1.9 (0.8)	--	0.025
			Unclass. Christensenellaceae	10.5 (5.4)	12.3 (5.4)	1.7 (0.8)	--	0.038
INTELLECTUAL IMPAIRMENT, N (%)								
		Lactobacillaceae		9 (9.4)	30 (30.9)	--	3.86 [1.50-9.95]	0.005
			Lactobacillus	9 (9.4)	30 (30.9)	--	3.86 [1.50-9.95]	0.005
			Faecalibacterium	15 (15.6)	24 (24.7)	--	2.65 [1.10-6.41]	0.031
UPDRS-PART III TOTAL SCORE, MEAN (SD)								
		Lactobacillaceae		15.0 (10.6)	19.4 (11.9)	3.6 (1.8)	--	0.048
			Lactobacillus	15.0 (10.6)	19.4 (11.9)	3.6 (1.8)	--	0.049
UPDRS-PART III NONDOPAMINERGIC SCORE, MEAN (SD)								
			Unclass. Lachnospiraceae	4.4 (4.0)	3.0 (2.4)	-1.0 (0.5)	--	0.038
		Lactobacillaceae		2.7 (2.6)	4.6 (3.7)	1.1 (0.5)	--	0.022
			Lactobacillus	2.7 (2.6)	4.6 (3.7)	1.1 (0.5)	--	0.022
	Verrucomicrobia			3.2 (3.4)	4.2 (3.3)	1.0 (0.5)	--	0.040
GAIT DISTURBANCES, N (%)								
		Lachnospiraceae		30 (31.3)	11 (11.3)	--	0.25 [0.10-0.62]	0.003
POSTURAL INSTABILITY, N (%)								
			Unclass. Lachnospiraceae	21 (21.9)	7 (7.3)	--	0.17 [0.05-0.58]	0.005
		Lactobacillaceae		7 (7.3)	21 (21.6)	--	3.38 [1.03-11.12]	0.045
			Lactobacillus	7 (7.3)	21 (21.6)	--	3.38 [1.03-11.12]	0.045
HOEHN-YAHR STAGE, MEAN (SD)								
	Verrucomicrobia			1.9 (0.8)	2.1 (0.8)	0.2 (0.1)	--	0.048

TABLE 1. *Significant associations between relative taxa abundance and clinical features in Parkinson's disease patients.*

RESULTS

Despite simple non-parametric comparison of PD patients and HC showed several differences in relative taxa abundances, the number of significant comparisons was reduced after adjusting for multiple confounders. We observed a constant effect of age on almost all abundances. The use of COMT inhibitors appeared to influence the level of several taxa. Overall, PD patients had increased Verrucomicrobia, Christensenellaceae, Lactobacillaceae, and decreased Lachnospiraceae and Ruminococcaceae than HC. Reduced level of Lachnospiraceae was significant in all PD duration strata, while many of these differences were associated with disease progression. De-novo PD differed from HC only by lower abundance in Lachnospiraceae. Compared to PD, Lachnospiraceae and Ruminococcaceae were not significantly lower in MSA, while in PSP cases other genera of Ruminococcaceae and Lactobacillaceae were higher and comparable, respectively. Increased Lactobacillaceae, Christensenellaceae, Verrucomicrobia and decreased Lachnospiraceae were associated with worse disease severity, including intellectual impairment, axial features (gait disturbances and postural instability) and other non-motor symptoms. (Figure 1-2)

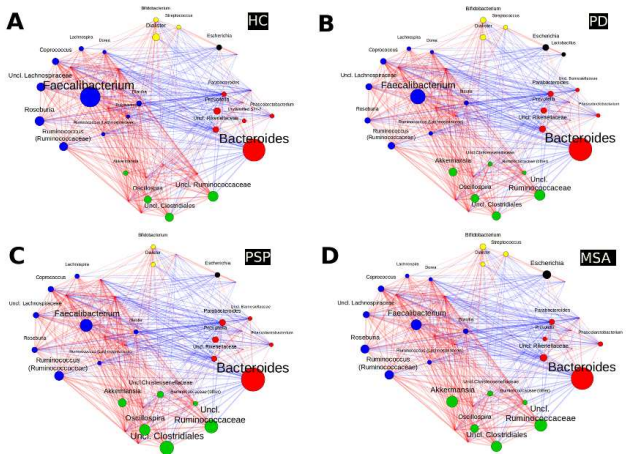

FIGURE 2. *Network plots describing co-abundance of bacterial genera in the gut microbiota.*

CONCLUSIONS

Gut microbiota may play a role in the pathogenesis of PD and act as modulator of individual differences in disease severity, especially non-dopaminergic features (cognition and axial symptoms).

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