

Gut microbial taxa-associations with cognitive functional measures in Patients with Alzheimer's Disease

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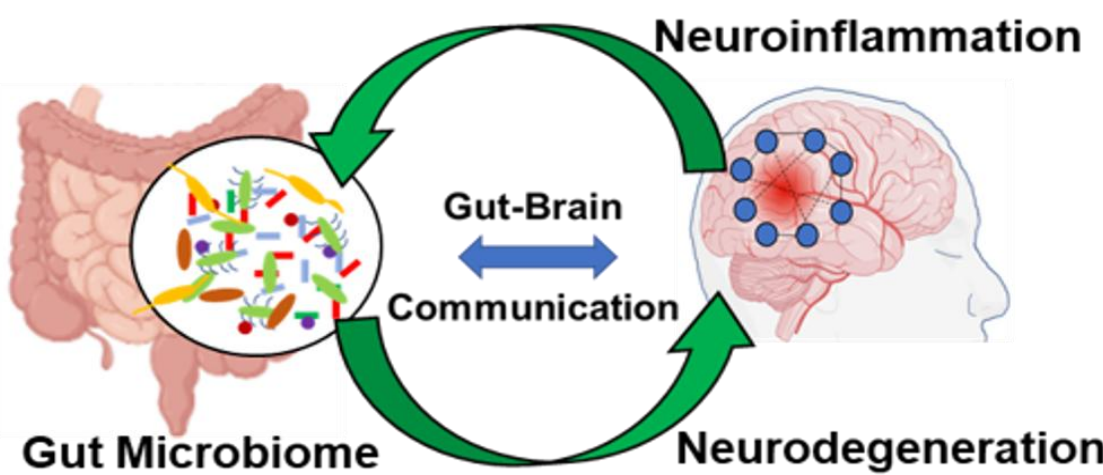
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BACKGROUND

- ❖ Alzheimer's disease (AD) is associated with alterations in gut microbial diversity and composition.
- ❖ Changes in specific gut microbial taxa have been linked to neuroinflammation and cognitive dysfunction.
- ❖ Emerging evidence suggests that the gut microbiome may play a mechanistic role in AD progression through the gut-brain axis.
- ❖ Characterizing microbiome-cognition relationships may provide insights into disease pathogenesis.
- ❖ The gut microbiome represents a promising target for therapeutic interventions aimed at preserving cognitive function.

Study Objective



- Characterize the gut microbial composition and diversity in Alzheimer's disease and identify disease-associated microbial signatures.
- Examine associations between gut microbiome profiles and cognitive performance measures and understand gut-brain axis contributions to AD pathogenesis.

METHODS

Study Design:

A pilot study was conducted on participants in the Norton Neuroscience Memory Center cohort of Alzheimer's disease (AD, n=18) compared to age-matched controls with no cognitive impairment (NCI; n=11)

Biospecimen Collection and Analyses:

- Metataxonomic profiling of fecal samples was performed by 16S rRNA gene sequencing.
- Assessment of plasma markers of gut permeability and inflammation was performed using the Meso Scale Discovery platform
- Neurocognitive assessments were performed by the Montreal Cognitive Assessment (MoCA) and Tablet-based Cognitive Assessment Tool Brain Health Assessment (TabCAT-BHA).

Statistical Analysis:

Pairwise two-sample t-tests and non-parametric Mann-Whitney tests were used to assess continuous outcomes. Non-parametric unadjusted Spearman correlation models were used to evaluate the association between gut microbiome and cognitive/memory measures

RESULTS

Cognitive Performance is Impaired in Alzheimer's Disease Patients

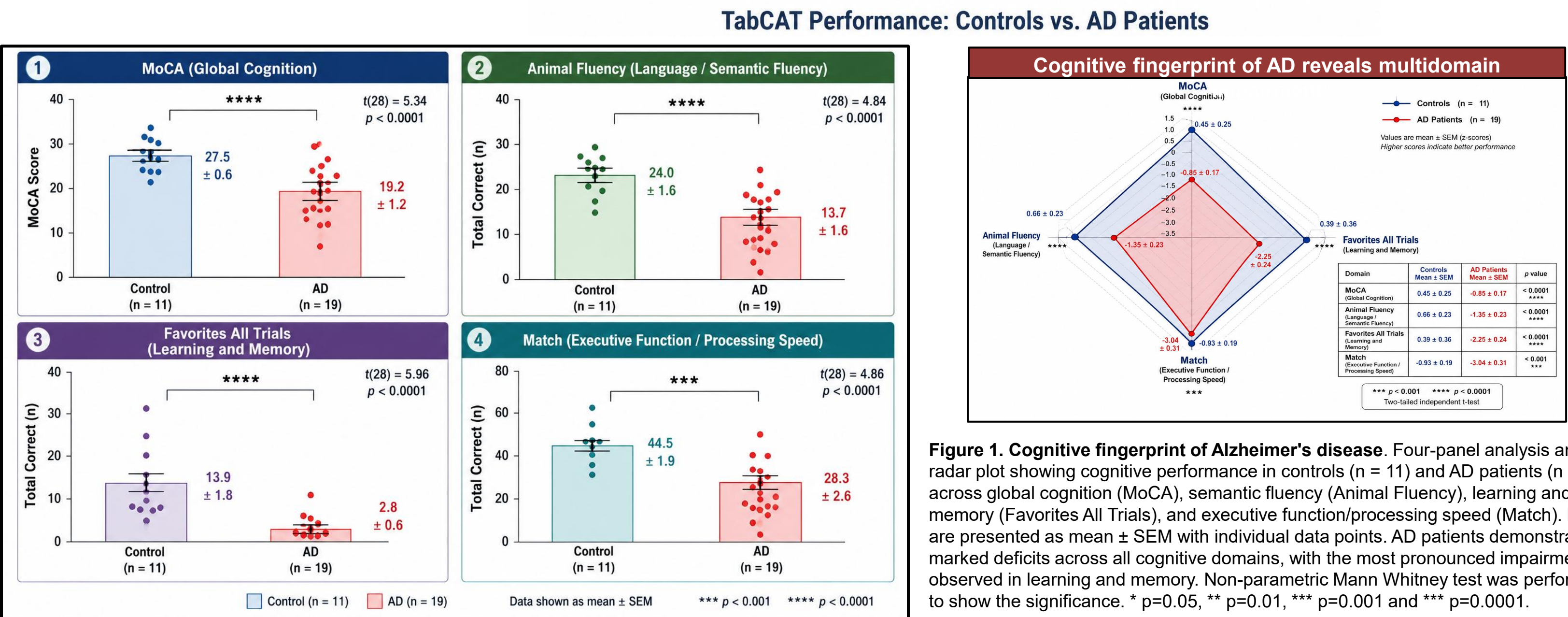


Figure 1. Cognitive fingerprint of Alzheimer's disease. Four-panel analysis and radar plot showing cognitive performance in controls (n = 11) and AD patients (n = 19) across global cognition (MoCA), semantic fluency (Animal Fluency), learning and memory (Favorites All Trials), and executive function/processing speed (Match). Data are presented as mean ± SEM with individual data points. AD patients demonstrated marked deficits across all cognitive domains, with the most pronounced impairment observed in learning and memory. Non-parametric Mann Whitney test was performed to show the significance. * p=0.05, ** p=0.01, *** p=0.001 and **** p=0.0001.

Two Hallmark Pathological Features of AD-Amyloid Beta Plaques & Tau Tangles

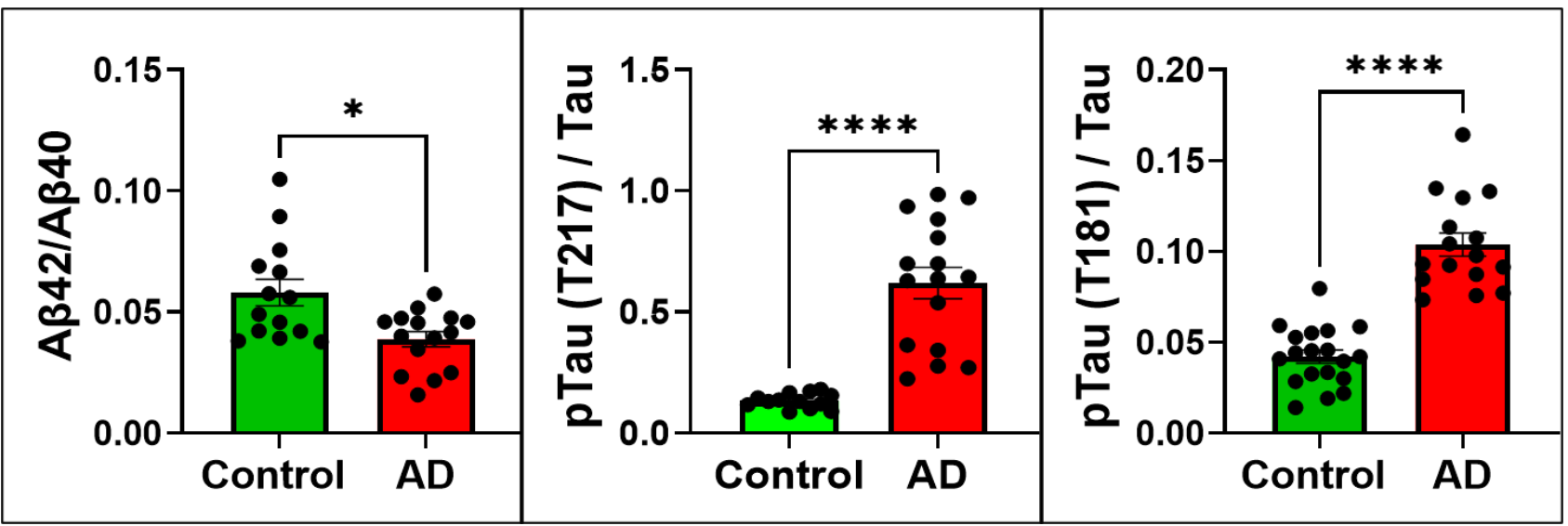
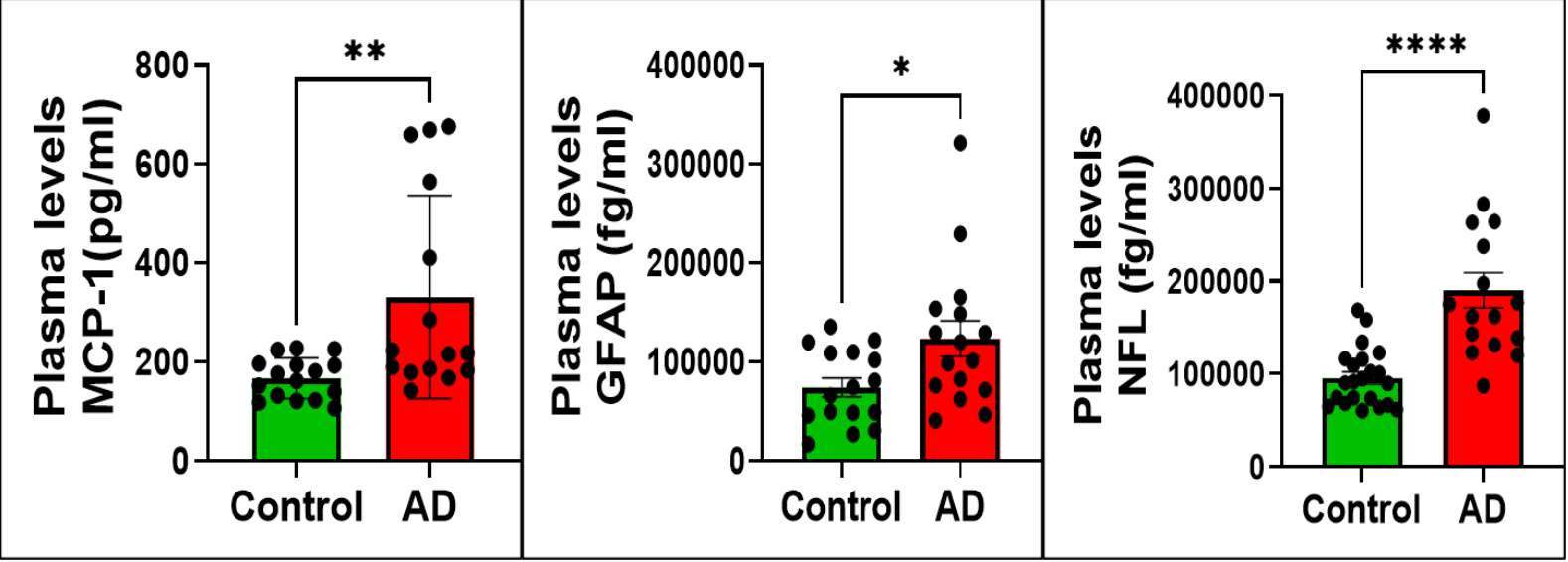


Figure 2: Differences in markers of AD pathology and neuroinflammation between controls and AD patients. Bar graphs showing the significant differences in the plasma levels of AD biomarkers- ratio of Aβ42/40, phosphoTau 217 and 218 over total Tau along with markers of neuroinflammation MCP-1, GFAP and NFL between controls (n = 11) and AD patients (n = 18). Data are presented as mean ± SEM with individual data points. Non-parametric Mann Whitney test was performed to show the significance. * p=0.05, ** p=0.01, *** p=0.001 and **** p=0.0001.

Neuroinflammation is the major driver of AD pathology



Alzheimer's Disease is Associated with Distinct Gut Microbial Dysbiosis

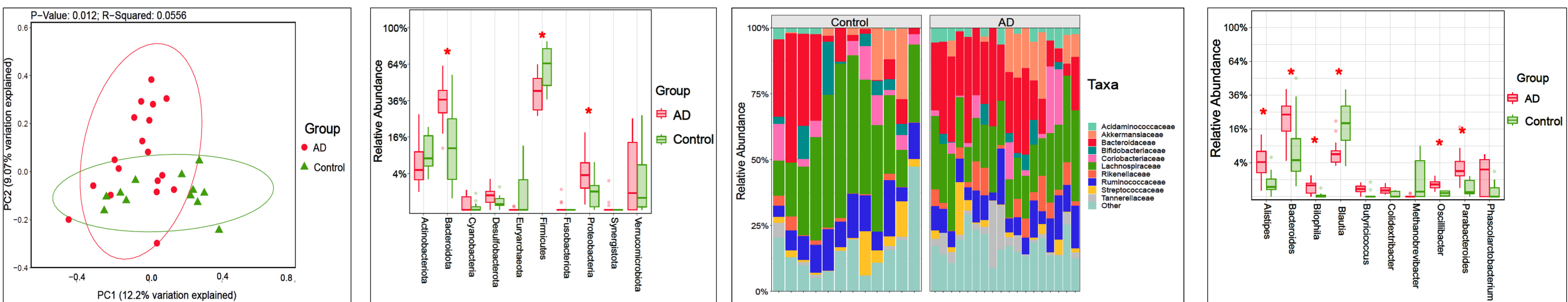


Figure 3: Differences in Gut microbial communities between controls and AD patients. PLS-DA plots showing discrimination of bacterial genera between controls (n = 11) and AD patients (n = 18). PLS-DA components 1 and 2 explain the variance between groups. Bar graphs and stack-bars showing the significant differences between % relative abundance (%RA) of bacterial phyla, families and genera between control and AD patients. Data are presented as mean ± SEM with individual data points. Non-parametric Mann Whitney test was performed to show the significance. * p=0.05, ** p=0.01, *** p=0.001 and **** p=0.0001.

Distinct Microbiome-Cognition Associations in Controls and AD Patients

Correlations among All study participants

Spearman Correlation Analysis	Bacterial Families		AD Pathology Markers			Neuroinflammation Markers	
MOCA vs.	Lachnospiraceae	Tannerellaceae	Aβ42/40	pTau T217	pTau T181	GFAP	NFL
Spearman r	0.3435	-0.3888	0.5036	-0.7411	-0.6710	-0.4119	-0.5879
P value	0.0681	0.0371	0.0074	<0.0001	0.0001	0.0328	0.0013
Participants #	29	29	29	29	29	29	29

Correlations among only AD participants

Spearman Correlation Analysis	Global Cognitive performance	Memory/Executive functions (Total Correct- Z scores)				
%RA of Bacteroidaceae vs.	MOCA	Composite_BHA-CS-Short	Composite_BHA-CS-Full	FavLearn_R2	FavDelay	Favorites_AllTrials
Spearman r	0.5746	0.5088	0.6090	0.5955	0.6520	0.6789
P value	0.01	0.04	0.0044	0.0091	0.0056	0.0035
Participants #	18	18	18	18	18	18

Figure 4: Associations between gut microbiome and cognition among AD Cohort. Table showing Spearman correlations between % relative abundance (%RA) of gut bacterial families, AD pathology, neuroinflammation and cognition measure in the cohort of controls and AD patients. Non-Parametric Spearman correlation coefficient (r) and statistical significance (P < 0.05) were denoted.

COHORT CHARACTERISTICS

Table 1: Summarized Demographic at Enrollment (EN)				
Variable	Category	Control (Non-Cognitively Impaired)	AD (Alzheimer's Disease)	p value
Sample Size		11	18	
Age (Mean ± SD)		68.90 ± 8.84	72.77 ± 4.72	0.22
Gender n(%)	Female	7 (63.6%)	9 (50%)	
	Male	4 (36.3%)	9 (50%)	
Anti-Amyloid Therapy n(%)	Yes	NA	14 (77.7%)	
	No	NA	4 (22.2%)	
APOE status n(%)	E4/4		6 (33.3%)	
	E3/4		5 (27.7%)	
	E2/4		2 (11.1%)	
	E3/3		3 (16.6%)	
	ND		2 (11.1%)	
MoCA Scores (Mean ± SD)	Enrollment	28.45 ± 1.37	19.72 ± 5.41	3.30E-06

SUMMARY AND CONCLUSIONS

- AD patients exhibited impaired cognitive performance and a distinct gut microbial profile compared with controls.
- Specific microbial taxa showed strong associations with cognitive function, particularly Bacteroidaceae in AD patients.
- ❖ Microbiome-cognition relationships may provide greater insight into AD pathology than microbial abundance changes alone.
- ❖ Modulation of gut microbiota through interventions like diet, probiotics, or fecal microbiota transplantation may offer new strategies for the prevention and management of Alzheimer's Disease.

LIMITATIONS

- Cross-sectional design limits causal inference between microbiome changes and AD pathology.
- Small sample size may reduce generalizability.
- Dietary, medication, and lifestyle confounders may influence microbial composition.
- Functional and longitudinal studies are needed to validate microbiome-cognition associations.

FUTURE DIRECTIONS

- Validate findings in larger, longitudinal cohorts.
- Characterize microbial functions and metabolites involved in cognitive decline.
- Integrate multi-omics approaches to elucidate gut-brain mechanisms in AD.
- Evaluate microbiome-based biomarkers and microbiota-targeted therapeutic interventions.

CONTACT

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