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Gut Bacteria and Alzheimer's Disease: from dysbiosis to beta-amyloid plaques

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Background

- Alzheimer's disease (AD) is characterized by beta-amyloid (Aβ) deposits, neuro- and peripheral inflammation
- Inflammation could be the cause of AD and Aβ could act as antimicrobial peptide against bacterial lipopolysaccharide (LPS)[1]
- Gut microbiota (GMB) is one of the possible source of inflammation
- Mice models of AD with no GMB display less Aβ deposit[2]
- We previously demonstrated a higher abundance of the genus *Escherichia* in association with higher peripheral inflammation and Aβ plaques[3]
- *Escherichia* is one of the LPS-producing bacteria

Aims

I) To find a signature in GMB composition in AD patients
II) To evaluate the presence of LPS in peripheral circulation

Methods

Sample
We collected stool and blood samples from:
- 10 amyloid negative controls with no cognitive impairment (HC)
- 34 cognitively impaired amyloid positive patients (Aβ+)

Stool analyses
- DNA isolation from stool samples
- Bacterial 16S DNA amplification and indexing
- DNA sequencing

Blood analyses
- Separation of serum from whole blood
- Serum LPS evaluation with a chromogenic assay

Statistical analysis
- Mean percentage in stool bacteria at phylum level
- Genera abundance differences among groups were analysed by generalized linear models for zero inflated distributed data. Genera with significant abundance difference between groups were detected by FDR post-hoc correction.

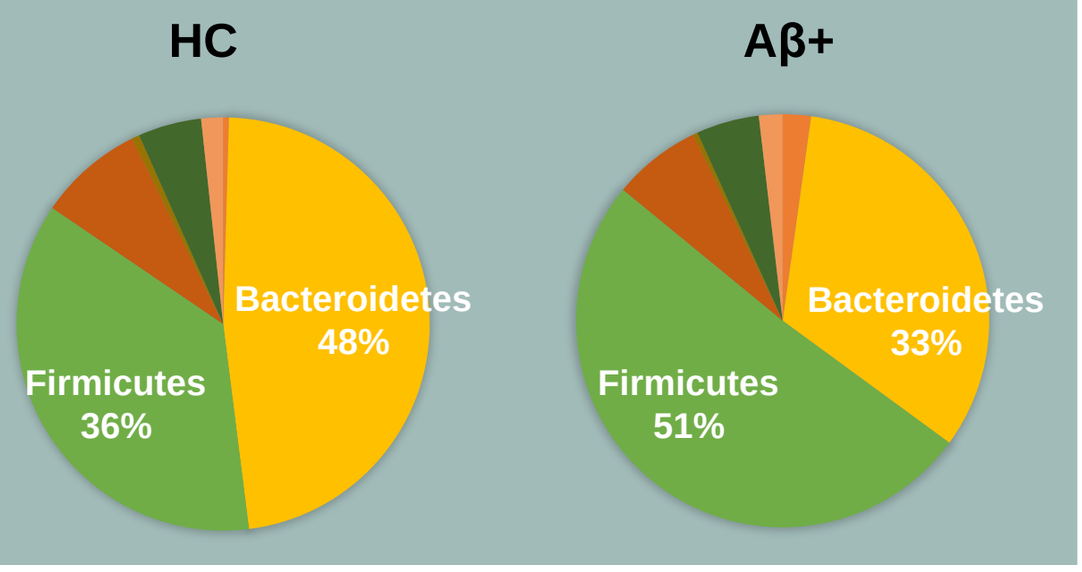
Results

I.a) Metagenomic analyses on stool DNA revealed a higher abundance of the phylum Firmicutes and a lower abundance of the phylum Bacteroidetes in the AD group as compared to HC

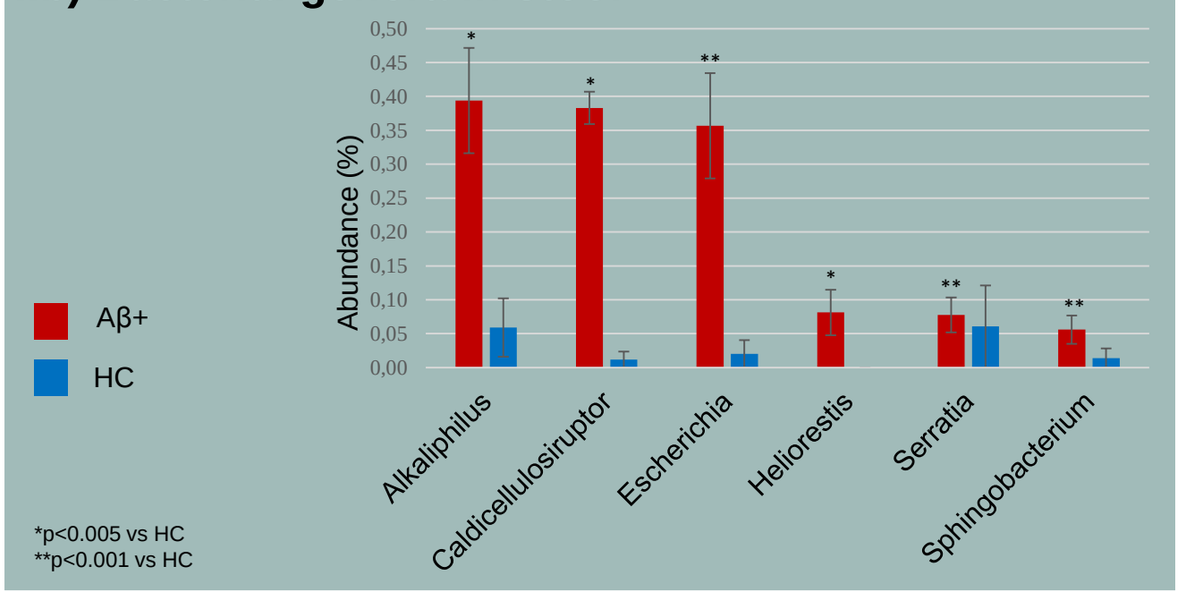
I.b) At genus level, 6 genera are significantly more abundant in the AD group as compared to HC

II) AD group display higher serum LPS level, as compared to HC

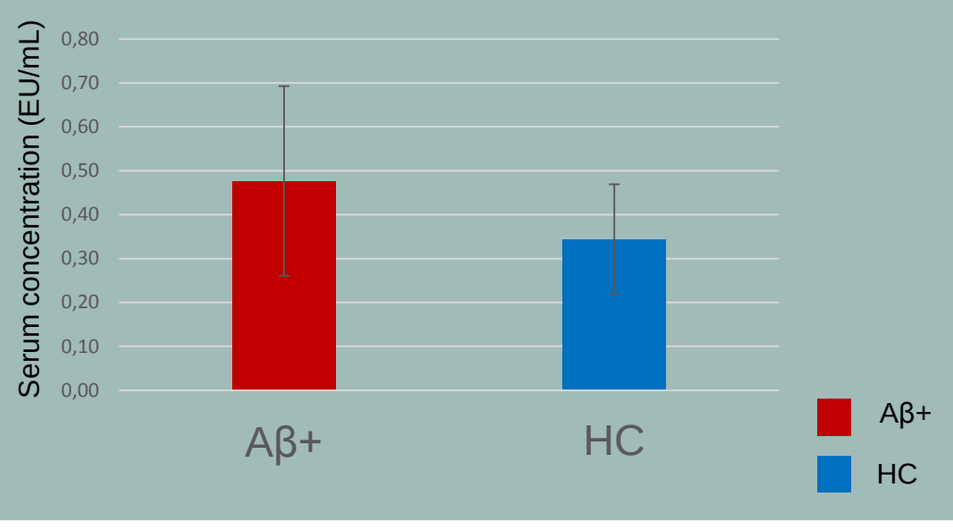
I.a) Bacterial phyla in stool



I.b) Bacterial genera in stool

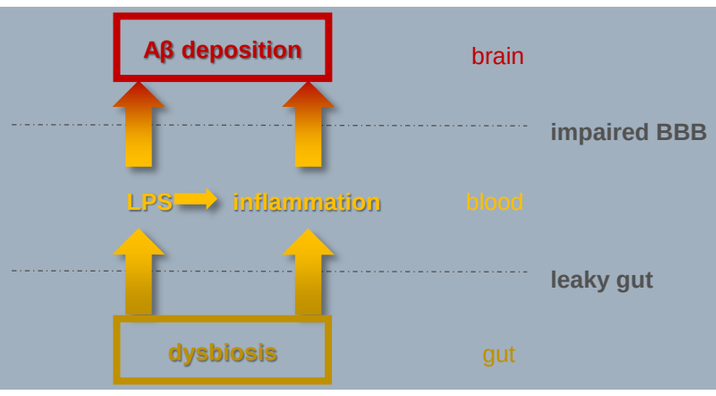


II) Serum LPS



Conclusions

Our data suggest the presence of a specific GMB composition in association with AD. This signature, maybe as consequence of a more permeable gut barrier, is also associated with higher serum levels of the bacteria component LPS, which may be able to overt inflammation and, once in the brain, to trigger Aβ deposition and AD pathology.



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