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Elevated Amyloid-β and Tau Levels in the Brain are Associated with a Reduced Abundance of Neuroprotective Gut Bacteria

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Sunday, July 16, 2023 : 12:00 AM - 4:55 PM

Monday, July 17, 2023 : 12:00 AM - 4:55 PM

Tuesday, July 18, 2023 : 12:00 AM - 4:55 PM

Wednesday, July 19, 2023 : 12:00 AM - 4:55 PM

Theme

Basic Science and Pathogenesis

Abstract

Background: Recent research suggests that differences in the gut microbiome composition may contribute to the pathogenesis of neurological disorders, including Alzheimer's disease (AD). Animal studies have shown that fecal microbiota transplantation reduces amyloid plaques in mouse AD models. However, whether the buildup of Aβ and tau deposits in the brain are associated with shifts in the human gut microbiota composition is understudied.

Method: We used stool specimens and neuropathological measures from 140 middle-aged individuals (**Table 1:** mean age 56, 54% Female) from the Framingham Heart Study (FHS) to assess the link between the gut microbiome composition and Aβ Positron Emission Tomography (Aβ-PET) in a global composite brain measure, and tau-PET deposits in the rhinal cortex and the inferior temporal cortex. We quantified gut microbiome composition using 16S rRNA sequencing. We performed multivariable association and differential abundance analyses, adjusting for age, sex, body mass index, and other confounders.

Result: Multivariable association results (**Figure 1**) indicated significant associations (adjusted p-value < 0.001) between both Aβ-PET and tau-PET levels with abundance of genera *Butyricicoccus* and *Ruminococcus.* Moreover, differential abundance analysis (**Figure 2)** showed that these bacteria have lower than expected abundance in individuals with elevated Aβ-PET and tau-PET measures (Aβ-PET, Ruminococcus: OR = 0.89, [0.88, 0.91]; Butyricicoccus: OR = 0.77, [0.72, 0.81]); (tau-PET in the rhinal cortex: Ruminococcus: OR = 0.82, [0.8, 0.83]; Butyricicoccus: OR = 0.91 [0.88, 0.94]); (tau-PET in the inferotemporal cortex:, Ruminococcus: OR = 0.79 [0.78, 0.81]; Butyricicoccus: OR = 0.83 [0.81, 0.86]). Conversely, we observed an increased abundance of genera *Cytophaga* (tau-PET in the rhinal cortex, OR = 1.78, [1.15, 2.75]) and *Alistipes* (tau-PET in the rhinal cortex, OR = 1.19, [1.17, 1.22]) in individuals with high Aβ-PET and tau-PET levels. Finally, functional analysis showed that *Butyricicoccus* and *Ruminococcus* are butyrate-producing bacteria harboring neuroprotective effects.

Conclusion: We showed that elevated measures of Aβ-PET and tau-PET in the rhinal and the inferior temporal cortex are associated with a reduced abundance of butyrate-producing *Butyricicoccus* and *Ruminococcus* in the gut of middle-aged individuals from the FHS. As these bacteria harbor neuroprotective effects, further studies are needed to elucidate underlying mechanisms and assess their therapeutic potential.

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