

Human/Human trials: Nutraceuticals and non-pharmacological interventions

Effect of a probiotic administration on inflammatory profile and clinical features in patients with Alzheimer's disease

Elisa Mombelli¹ | Nicola Lopizzo¹ | Moira Marizzoni¹ | Peppino Mirabelli² |
Delia Luongo³ | Marco Salvatore² | Giovanni B. Frisoni⁴ | Annamaria Cattaneo^{1,5}¹ IRCCS Istituto Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy² IRCCS SDN, Naples, Italy³ I.B.B.- CNR Via Mezzocannone, Napoli, Italy⁴ Memory Clinic and LANVIE-Laboratory of Neuroimaging of Aging, University Hospitals and University of Geneva, Geneva, Switzerland⁵ King's College London, London, United Kingdom**Correspondence**

Annamaria Cattaneo, IRCCS Istituto Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy.

Email: annamaria.cattaneo@kcl.ac.uk**Abstract**

Background: Increasing evidence shows that the gut microbiota (GMB) may affect the inflammatory status and influence the pathogenesis of several brain disorders, including Alzheimer's Disease. Moreover, it has been suggested that probiotics may have potential beneficial effects on the immune system via microbiome composition, influencing in turn also cognitive performances.

Method: Sixty-two old subjects with normal cognitive performance and 37 AD patients were recruited and stool and blood samples were collected. Moreover, the group of AD patients received a probiotic administration for three months and stool and blood samples were collected again at the end of the treatment. Plasma levels of a panel of pro-inflammatory cytokines were measured by using the High Sensitivity 9-Plex Human ProcartaPlex™ Panel (IFN- γ , IL-1b, IL-2, IL-4, IL-6, IL-10, IL-12p70, IL-17A and TNF α , Thermo Fisher Scientific) on Luminex Bio-Plex® 200™ system. Moreover, we also measured the plasma levels of C-Reactive Protein (CRP) using the CRP Human Instant ELISA Kit (Thermo Fisher Scientific). Bacterial composition of fecal samples was inferred using 16s sequencing; the levels of the short chain fatty acids acetate, propionate, valerate and butyrate were measured by mass spectrometry and adhesion molecules by FACS.

Result: We found higher levels of the pro-inflammatory cytokines IL-6, IFN gamma, TNF-alpha, IL-1beta, and il12p70 and of IL-2 and lower levels of the anti-inflammatory cytokine IL-10 in AD patients as compared to control subjects (all $p < 0.05$). Moreover, we found a positive correlation between MMSE score and the levels of pro-inflammatory cytokine IL-6 ($p = 0.03$, $r = 0.56$). Interestingly, the three months treatment with the probiotic composition was able to significantly reduce the level of IL-6 ($p = 0.03$) and increase the levels of IL-10 ($p = 0.023$). Bioinformatic analyses on the 16s sequencing data as well as on the SCFAs and endothelial markers are ongoing.

Conclusion: Inflammatory status is higher in AD patients as compared to control subjects and it correlates with cognitive performances. Interestingly probiotic composition is able to push down the inflammatory status in patients, possibly via changes in microbiome composition. Probiotics may be beneficial in delaying neurodegeneration and cognitive deficits in subjects at risk of developing Alzheimer Disease.