volumetric, PET, and cognitive test score data from ADNI. **Results:** The one-factor model did not fit the MRI volumetrics; PET and volumetrics did not covary at either baseline or 12 month visits and both outcome types exhibited evidence of two factors (each). **Conclusions:** A one-factor model does not fit the volumetric data; PET and volumes were independent, i.e., a one-factor model is also not appropriate for these two outcomes. Three factors are implied by Braak & Braak (1991); since synapse failure may precede atrophy, broadening from one- to three-factor modeling has implications for the timing and targeting of interventions. However, three one-factor models are unlikely to capture neurodegeneration. Atrophy, synapse failure, and tangle formation will need individualized statistical models, particularly for longitudinal design and analyses. A hypothetical structural equation model capturing the three Braak & Braak features and statistical features of ADNI variables is presented; normal brain aging is also represented.

P3-219 PLASMA 7-PROTEIN BIOMARKER MOLECULAR SIGNATURE DO NOT DISCRIMINATE ALZHEIMER'S DISEASE FROM NATURAL AGEING

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Background: Certain cytokines and other signaling proteins in plasma are reported to differentiate not only patients with Alzheimer disease (AD), but also converters from mild cognitive impairment to AD from the normal elderly. A set of 18 proteins of hematopoiesis, immune responses, apoptosis and neuronal support are dysregulated in presymptomatic AD. A subsequent analysis identified 5 proteins with the same overall discriminative potential. **Methods:** We simultaneously measured plasma concentrations of seven signal molecules (EGF, G-CSF, IL1a, IL3, TNFa from the suggested protein subset and additionally IL1b, IL6) using LabMAP Luminex technology in 34 AD patients fulfilling NINCDS-ADRDA criteria and 47 normal control seniors (NC). Cognitive status was evaluated with the Addenbrooke's Cognitive Examination. **Results:** Concentrations of IL1a,b, IL3, IL6 were bellow detection limits in more than half of all samples. We did not find significant differences in the concentrations of the remaining molecules (EGF, G-CSF, TNFa) between those in AD and those in NC. **Conclusions:** We did not confirm promising plasma signaling protein signature measured via Luminex technology as an AD indicator.

P3-220 TRANSTHYRETIN AND Aβ IN ALZHEIMER'S DISEASE

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Background: Transthyretin (TTR) is involved in preventing Aβ fibrilization, both by inhibiting fibril formation and disrupting Aβ fibrils. Chronic infusion of anti-TTR antibody into the hippocampus of transgenic mice led to increased local Aβ deposits, tau hyperphosphorylation and apoptosis. Antibodies against Aβ have also been shown to participate in Aβ fibrilization and deposition. We have showed that dissociated Aβ antibody levels and the dissociation Δ (dissociated minus non-dissociated) may be useful tools for the reliable and early diagnosis of disease as well as for providing an assessment of disease progression. The aim of our study is to assess the levels of antibodies against Aβ and correlate this level with TTR levels in the sera of AD patients to further understand the role of TTR - Aβ interplay in the ethiopathogenesis of the disease. **Methods:** The current research is a part of a large population-based study. 52 AD patients were examined. Normal control subjects were recruited from the same population. *Aβ antibody and TTR levels in human sera:* The technique for the *in vitro* dissociation of Aβ antibodies has been previously described in detail (Gustaw et al., 2008, J Neurochem). Sera collected from newly diagnosed AD patients and age-matched controls were analyzed for antibodies against Aβ both before and after dissociation by ELISA. Results were presented as O.D. TTR level in (ug/ml) was measures by The Prealbumin Enzyme-Linked Immunosorbent Assay (ELISA; Immunodiagnostik AG, Germany). *Statistical Analysis:* Results were analyzed using Kruskal Wallis Runk Summ Test and Pearson Product Moment Correlation. **Results:** *TTR levels in the controls were higher than in AD patients ($p = 0.012$). Moreover when the AD group was stratified according to the length of neurodegenerative process (time from diagnosis) newly diagnosed patients (< 1y from diagnosis) had a statistically significantly lower level of TTR as compared to controls and to the rest of AD patients (control = 228 vs AD< 1y from diagnosis = 276, AD >1y from diagnosis = 357). In our population of newly diagnosed Alzheimer's patients low TTR levels corresponded significantly with higher antibody levels against Aβ measured after dissociation (CC: -0.4; $p < 0.05$).* **Conclusions:** Our observation suggests a protective role for TTR in AD pathogenesis.

P3-221 PLASMA INFLAMMATORY MARKERS CORRELATE WITH SEVERITY IN ALZHEIMER'S DISEASE

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Background: Biomarkers that reflected disease severity would be immensely useful in clinical trials of disease modification therapies. Peripheral markers would be especially welcome as a complement to the imaging and CSF markers currently under investigation. As inflammation plays a critical role in AD, as the inflammatory response might be expected to worsen with disease activity and as an inflammatory signature is readily detectable in plasma and has already been suggested as a marker of AD, we reasoned that an inflammatory signature would be a good marker of disease severity. **Methods:** A total of 311 subjects including normal elderly, MCI and AD, from the AddNeuroMed study from six European countries, were included in this analysis. Plasma samples were analyzed using Luminex xMAP cytokine and inflammatory protein assays. The panel included the following 27 cytokines: IL-1β, IL-1ra, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12 (p70), IL-13, IL-17, Eotaxin, FGF basic, G-CSF, GM-CSF, IFN-γ, IP-10, MCP-1, MIP-1α, MIP-1β, PDGF-BB, Rantes, TNFα and VEGF. We used as measured of disease severity, cognition at the point of blood sampling using the ADAS-cog and MMSE together with volumetric MRI as a measure of brain atrophy. **Results:** We identified ten inflammatory proteins that showed significant correlation with whole brain atrophy. Of these, three also showed correlation with cognition. Follow on studies showed, in addition, that a number of cytokines correlated not only with baseline but with longitudinal measures of severity and three - IL-4, IL-17 and G-CSF - were differentially altered in people with fast versus slow decline as well as showing correlation with volumetric MRI measures of atrophy. **Conclusions:** These findings demonstrate an inflammatory signature in plasma, not only of disease per se but of the severity of AD as measured either by imaging evidence of the degree of atrophy or clinical measures of cognitive impairment. These data add to others suggesting that plasma biomarkers might be developed as markers not only for diagnostic utility but for use as outcome measures in clinical trials.