Autophagy is deregulated in AD and we have recently shown deregulation of autophagy in schizophrenia. Furthermore, ADNP transcripts were increased in lymphocyted from schizophrenia patients compared to matched controls (Molecular Psychiatry, 2013, [Epub ahead of print]). The aim of the present project was to evaluate ADNP and the related ADNP2 lymphocyte expression in AD. **Methods:** Peripheral lymphocytes were isolated from AD patients and age-matched controls by ficoll grandiet separation. RNA was extracted using the Trizol reagent followed by reverse transcription and quantitative real time polymerase chain reaction (PCR) for ADNP and ADNP2 RNA. Results were normalize to the TATA box transcript. **Results:** ADNP RNA was increased by ∼8-folds in AD lymphocyte samples compared to controls ($p<0.05$). This was in contrast to the transcript of ADNP2, which did not change. In comparison to schizophrenia patients (Molecular Psychiatry, 2013, [Epub ahead of print]), the increase in ADNP expression was apparently ∼3-fold greater in AD patients, and ADNP2 expression was also significantly increased in schizophrenia patients. **Conclusions:** Our results posit ADNP and ADNP2 lymphocyte expression as markers for AD and schizophrenia with differential disregulated expression in the two indications. Interestingly, previous proteomic studies identified ADNP as the only protein decreasing in AD serum, suggesting potential rapid turn-over, structural changes and/or defective translation mechanism that have been associated with cognitive deficiencies. These studies pave the path to better disease understanding, novel biomarkers and personalized medicine.

P4-275 A NOVEL CSF 16PLEX NEURODEGENERATION ASSAY

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Background: The diagnosis and management of Alzheimer's disease (AD) and related dementias remains challenging due to a lack of accurate biomarkers. Whilst changes in the cerebrospinal fluid (CSF) levels of amyloid beta and tau proteins perform well as diagnostic markers in established disease, they lack adequate sensitivity for use in early diagnosis and offer little prognostic value. To expand the utility of CSF in the management of dementia we have developed a 16plex protein assay. Uniquely, this is the first assay to benefit from our proprietary TMT-SRM Universal Reference concept. Herein, Selected Reaction Monitoring (SRM) mass spectrometry is used in combination with a bulk isotopically labelled Universal Reference Cerebrospinal Fluid. The use of SRM allows the precise selection of digested protein fragments for high sensitivity and specific measurement using a tripl e quadrupole mass spectrometer and the use of the heavy TMT-labelled universal reference enables measurement consistency across multiple studies and over time. **Methods:** In total, the assay quantifies 31 peptides from Amyloid-like protein 1, Amyloid beta A4 protein, Beta-2-microglobulin, Complement C3 alpha and beta, Chromogranin A, Complement factor H, Cystatin C, Serum amyloid P-component, Clusterin alpha and beta, Apolipoprotein E, Alpha-2-macroglobulin, Secretogranin-2, Gelsolin as well as Fibrinogen gamma. Each patient CSF sample is labelled with a light TMT tag and then spiked with the heavy TMT-labelled universal reference CSF. The lighter endogenous peptides co-elute with their equivalent heavier reference peptide and quantified by integrating the MS peak area for the light compared to heavy signals in a classical SRM workflow. **Results:** Following reproducibility testing using ten analytical repeats of 1:1 mixtures, the diagnostic utility and performance of the assay for AD was subsequently assessed in a cohort of 62 CSF samples comprising 31 cases of clinically diagnosed AD and 31 neurologically healthy age- and sex-matched controls. Statistical analysis was performed and a remarkable level of separation between AD cases and controls could be achieved (ROC AUC 0.97). **Conclusions:** The class separation of AD from controls using the CSF16plex assay gives similar performance to that obtained using any of the clinically recognised markers such as amyloid beta 1-40/1-42 ratio, total tau and pTau levels.

P4-276 EFFECT OF PS-1 E280A MUTATION OF FAMILIAL ALZHEIMER'S DISEASE ON QUANTITATIVE EEG IN ASYMPTOMATIC ADULTS

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Background: Defective genes in Presenilin-1 (PS-1) has been related with high risk in develop a familial form of Alzheimer disease (AD). The mutation PS-1 E280A has been found in a large kindred of Antioquia, Colombia. We investigated the influence of AD-associated E280A genotype on brain activity in young asymptomatic subjects. **Methods:** We examined quantitative EEG in a cohort of 30 healthy non-demented individuals divided into 15 non-carriers (age 31.5 ± 5.8 years) and 15 E280A carriers (age 28.8 ± 5.1 years) during resting and a memory task. Power spectrum was calculated in delta (0. 5-4. 0 Hz), theta (4. 0-8. 0 Hz), alpha-1 (8. 0-10. 0 Hz), alpha-2 (10. 0-13. 0 Hz), beta (13. 0-25. 0 Hz) and gamma (25. 0-50 Hz) band frequencies for four regions of interest. Changes were evaluated in different conditions by ANOVA analysis and in the bands and regions where statistical differences were found we performed a discriminant analysis (DA) through leave-one-out crossvalidation. **Results:** Theta frequencies band was significantly lower in carriers compared with controls ($p = 0.008$) during encoding. In resting condition a significant decrease was found in theta ($p = 0.0001$) and an increase in alpha-2 frequencies ($p = 0.037$) in carriers compare with controls. DA separately for these measures showed a high group discrimination (66,7%) in temporal region for theta and alpha-2 in resting condition. A paired combination of the measures showed higher discrimination (76,7%) for the encoding condition between frontal y central regions in theta. **Conclusions:** Early changes in theta frequencies were observed in the EEG recordings for both resting and memory conditions. The combination of power spectrum in the theta band for central and frontal regions during encoding process showed a high discrimination between carriers and non-carriers. Our findings could be used as clinical markers in this population but additional analysis are necessary including subjects in different phases of the disease.

P4-277 CHANGES IN BRAIN NETWORK MEASURES IN PRE-SYMPTOMATIC ALZHEIMER'S DISEASE WITH E280A PRESENILIN-1 MUTATION GENE

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Background: Studies have shown that sporadic AD is related to perturbation of the synchronization of the EEG signal. In Colombia has been reported the largest known group with familial AD characterized by the presence of the PS-1 E280A (Glu280Ala) mutation. Previous works with EEG in this kindred showed differences of the electrical sources patterns. **Methods:** 30 healthy asymptomatic subjects (15 carriers and 15 non carriers of PS-1 E280A mutation) were enrolled. We recorded EEG signals in resting condition. To analyze the functional interactions between the different EEG channels the coherence was calculated over the principal rhythms of the