and Ab1-42/Ab1-38 ratios (amyloid markers), and tau protein (a marker of neurodegeneration). All measures were related to clinical disease progression. Standardized plasma samples were collected from 318 subjects (mean age = 76.1 ± 3.5; MMSE = 28.7 ± 0.95; FCSRT = 46.05 ± 2.00). APOE genotype: ε2/ε2 [0.3%], ε2/ε3 [13.9%], ε2/ε4 [1.3%], ε3/ε3 [67.5%], ε3/ε4 [16.1%], ε4/ε4 [0.9%]. These samples were investigated for NFL, Ab1-40, Ab1-42, and tau protein by using the ultrasensitive Single-Molecule Array (Simoa) technology. Results: All data and results will be presented at the conference. Conclusions: We present a comprehensive panel of novel plasma candidate biomarkers reflecting different pathophysiological mechanisms during the preclinical stage of AD. This will help characterize initiated pathophysiological mechanisms of action driving amyloid accumulation and AD progression during the preclinical stage and support early disease detection and identification of molecular mechanisms as targets for therapeutic intervention.

**P3-166** THE USE OF QUANTITATIVE EEG AS A POTENTIAL BIOMARKER FOR COGNITIVE ENHANCERS

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Background: The quantitative electroencephalography (qEEG) is an important tool in quantifying changes in the brain activity. In animal models of cognition, synchronous EEG activity observed in a frequency range of 4 to 8 Hz (Theta) and 30 to 50 Hz (gamma) has been associated with cognitive enhancement. Neurological diseases such as Alzheimer’s disease (AD) often affect the complex neuronal network by degeneration of neurons, resulting in a slowing of the EEG signal which corresponds to increase of low-frequency spectral power bands and a decrease of higher-frequency bands. If these theta and gamma oscillations are associated with mnemonic or cognitive function, qEEG can be used as a potential biomarker for the cognition-enhancing drugs regardless of their primary biological target. Methods: Theta modulation studies were conducted in urethane anesthetized rats and mice. Electrical stimulations were applied to the nucleus pontis oralis and power of oscillatory activity was measured in hippocampus CA1 region. Modulation in oscillatory gamma activity was measured using multi-channel telemetry device (Data Sciences International). In the current study, we evaluated several drugs that were shown to have effect on the cognition in preclinical behavioral models. Results: Acetylcholinesterase inhibitor, donepezil and muscarinic receptor selective PAM induced increase in the low frequency bands like theta in anesthetized animals and gamma oscillatory power in freely moving animals. The nonselective mAChR antagonist scopolamine decreased the oscillatory power of theta and gamma in anesthetized and freely moving animals, respectively. Conclusions: These results indicate that qEEG could be an effective biomarker for the evaluation of potential cognitive enhancers in the treatment of Alzheimer’s disease.

**P3-167** TRANSCRANIAL DOPPLER ULTRASOUND: A PROMISING NON-INVASIVE BIOMARKER FOR THE DIAGNOSIS OF ALZHEIMER’S DISEASE

**Marion Ortner**, Konstantin Kotliar, Claudia Muggenthaler, Christine Hauser, Christoph Schmaderer, Hans Forstl, Alexander Hapfelmeier, Janine Diehl-Schmid, Christian Sorg, Holger Poppert. **Timo Grimmer**, 1 Klinikum Rechts der Isar, Technical University of Munich, Munich, Germany; 2 University Hospital Klinikum rechts der Isar, Technical University of Munich, Munich, Germany. Contact e-mail: t.grimmer@tum.de

Background: An increasing body of evidence shows that impaired elimination of amyloid β (Aβ) from the brain might contribute to the development of Aβ plaques in Alzheimer’s disease (AD). Although not completely understood, one of the main elimination pathways from the brain is alongside cerebral arteries. Impaired cerebral blood vessel pulsatility and subsequently reduced propulsion in this pathway could lead to the accumulation and deposition of Aβ in the brain of AD patients. Therefore, we hypothesized that there is an increased impairment in pulsatility across AD spectrum. Methods: Using transcranial Doppler ultrasound the resistance and pulsatility index (RI; PI) of the middle cerebral artery (MCA) in healthy controls (HC), patients with mild cognitive impairment (MCI) stratified by the presence or absence of biomarkers indicative for underlying AD, and Alzheimer’s dementia (ADD) were measured. Results: Between HC and ADD significant group differences of the left and right RI (p = 0.010; p = 0.030) and of the left PI (p = 0.034) with corresponding AUCs of 0.776, 0.763, and 0.718 were detected. RI and PI of the MCI groups ranged between HC and ADD. RIs and PIs were significantly (p = 0.012, p = 0.023) associated with disease severity as measured by CDR SOB. Conclusions: Our results strengthen the hypothesis that impaired pulsatility could cause impaired amyloid clearance from the brain and thereby contribute to the development of AD. Further research is needed to investigate if TCD could develop into an easy to administer, cost efficient, non invasive and widely available biomarker for AD.

**P3-168** AGE-DEPENDENT INVERSE CORRELATIONS IN CSF AND PLASMA AMYLOID-B(1-42) CONCENTRATIONS PRIOR TO AMYLOID PLAQUE DEPOSITION IN THE BRAIN OF 3XTG-AD MICE

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Background: Amyloid-β (Aβ) plays a critical role as a biomarker in Alzheimer’s disease (AD) diagnosis. In addition to its diagnostic potential in the brain, recent studies have suggested that changes of Aβ level in the plasma can possibly indicate AD onset. Methods: We selected APPsw PS1ΔM146V and TauP301L transgenic (3xTg-AD) mice. We first confirmed the absence of Ths positive amyloid plaques, dense-core plaques, in the brains of young 3xTg-AD mice with immunohistochemical staining. We then measured the

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