undergo continuous and complex physiological adaptations that contribute to longevity and healthy cognition. In either case, clinical or mechanistic extrapolation of relationships of CVRFs with cognitive compromise in young-old to the oldest-old might be erroneous.

**P4-009**

**CHARACTERISATION OF DEPRESSION IN DEMENTIA AND MILD COGNITIVE IMPAIRMENT**

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Background: Baseline data-analysis of a prospective Belgian study was performed to characterise significant depressive symptoms and its behavioural correlates in Alzheimer’s disease (AD) and mild cognitive impairment (MCI) patients. Methods: 200 AD (189 probable and 11 definite AD patients) and 200 MCI patients were included and behavioural and neuropsychological data were obtained using a standard battery of assessment scales and tests. Statistical analysis consisted of Mann Whitney U test for comparison of data between groups and univariate analysis. Multivariate analysis was used to develop models that accounted for the variation of depressive symptoms. Results: MCI patients showed less behavioural symptoms and were less cognitively impaired than AD patients. MCI/AD patients with significant depressive symptoms showed significantly more behavioural symptoms than patients without significant depressive symptoms. Depressive symptoms were correlated with almost all BPSD tested in AD and MCI patients. For MCI patients, a model with three behavioural symptoms (verbally agitated behaviour, physically non-aggressive behaviour, diurnal rhythm disturbances) was developed that accounted for 52.1% of variation in depressive symptoms. Conclusions: Several behavioural symptoms were correlated with depressive symptoms in MCI and AD. A model was developed that accounted for 52.1% and 46.1% of variation in depressive symptoms in MCI and in AD, respectively. The occurrence of diurnal rhythm disturbances urge to screen for depression in both MCI and AD patients.

**P4-010**

**ALZHEIMER’S DISEASE AMYLOID-ß LINKS LENS AND BRAIN PATHOLOGY IN DOWN SYNDROME**

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Background: Down syndrome (DS, trisomy 21) is the leading genetic cause of intellectual disability and the most common chromosomal disorder in humans. In DS, trillication of chromosome 21 invariably includes the APP gene (21q21) encoding the Alzheimer’s disease (AD) amyloid precursor protein (APP). Tripling of the APP gene accelerates APP expression and Amyloid peptide accumulation in the brain that invariably lead to early-onset AD neuropathology and neurocognitive sequelae. The DS phenotype complex also includes expression of distinctive early-onset cerulean cataracts of unknown etiology. Previously, we reported increased Aβ accumulation, co-localizing amyloid pathology, and disease-linked supranuclear cataracts in the ocular lenses of subjects with AD. Here, we investigate the hypothesis that related AD-linked Aβ pathology underlies the distinctive lens phenotype in DS. Methods: Ophthalmological examinations of DS subjects were correlated with phenotypic, histochemical, and biochemical analyses of lenses obtained from DS, AD, and normal control subjects. Results: Evaluation of DS lenses revealed a distinctive pattern of supranuclear opacification accompanied by accelerated supranuclear Aβ accumulation, co-localizing amyloid pathology, and fiber cell cytoplasmic Aβ aggregates (>5 to 50 nm) identical to the lens pathology identified in AD. Peptide sequencing, immunoblot analysis, and ELISA confirmed the identity and accelerated accumulation of Aβ in DS lenses. Incubation of synthetic Aβ with human lens protein promoted protein aggregation, amyloid formation, and Rayleigh light scattering that recapitulated the molecular pathology and clinical features observed in DS lenses. Conclusions: These results establish the genetic etiology of the distinctive DS lens phenotype and identify the molecular origin and pathogenic mechanism by which lens pathology is expressed in this common chromosomal disorder. Moreover, these findings confirm increased Aβ accumulation as a key pathogenic determinant linking lens and brain pathology in DS and AD.

**P4-011**

**IN VIVO DETECTION OF EARLY ALZHEIMER’S DISEASE-LINKED Aβ PEPTIDE ACCUMULATION IN THE LENS BY NON-INVASIVE QUASI-ELASTIC LIGHT SCATTERING**

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Background: Alzheimer’s disease (AD) is characterized by accumulation of Aβ peptides in the brain which begins years before the onset of cognitive symptoms. We previously reported Aβ deposition, amyloid pathology, and distinctive co-localizing supranuclear cataracts in human AD lenses. Methods: Here we developed quasi-elastic light scattering (QLS) instrumentation for quantitative analysis of Aβ in the lens and evaluated this technology in Tg2576 AD transgenic mice. Results: Tg2576 mice progressively accumulate human Aβ that forms light-scattering microaggregates within the cytoplasm of supranuclear lens fiber cells. Non-invasive QLS discriminated unanesthetized Tg2576 mice from wild-type controls by 10 months of age when lenses were still clear and the brain was free of amyloid plaque. In vitro studies were conducted to understand the relationship between Aβ aggregation and QLS light scattering signals. Conclusions: These studies demonstrated that human Aβ promoted mouse lens protein aggregation and time-dependent QLS signal changes similar to those detected in vivo. Our data indicate that QLS non-invasively detects early AD-linked Aβ accumulation in the lens.

**P4-012**

**THE INFLUENCE OF METABOLIC SYNDROME ON SIMVASTATIN THERAPY IN ASYMPTOMATIC ADULTS AT RISK FOR ALZHEIMER’S DISEASE: THE ESPRIT STUDY**

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