associated with DS in mid-life. However, birthweight have a significant direct effect on CIQ or DS. Overall, birthweight had a small standardized indirect effect on DS that was mediated by latent MedS in mid-life.

Conclusions Here, birthweight accounts for the relationship between mid-life metabolic syndrome and information processing speed. Childhood cognitive ability remains the predominant influence on mid-life processing speed.

P5.128 New discoveries in the brain renin angiotensin system in Alzheimer's disease

Noura ALMulhim

Authors Noura AL Mulhim, Scott Miners, Patrick Kehoe

Affiliations Dementia Research Group, Bristol Medical School, University of Bristol

Introduction The classical brain RAS axis (ACE-1/Ang-II/AT1R) exerts damaging effects in the brain in both animal and human studies. Hyperactivity of this axis contributes to the pathogenesis of Alzheimer's disease (AD). Alternative RAS pathways ((ACE-2/Ang(1-7)/MasR) and (APN/Ang-IV/IRAP)) have recently been discovered that counter-regulate the damaging effects of classical RAS signalling whilst are also implicated in boosting learning and memory. However, the involvement of these alternative RAS pathways in relation to AD pathogenesis remains unclear. We have measured brain angiotensins and their receptors involved in the alternative RAS signalling in relation to AD in a well-characterised cohort of post-mortem brains.

Methods and Materials Human post-mortem brain tissue was obtained from the South West Dementia Brain Bank, University of Bristol, with local Research Ethics Committee approval. The AD cases (n=72) and the age-matched controls (n=48) were matched closely for age-at-death and post-mortem delay. The levels of Ang(1-7) and Ang-IV were measured in the mid-frontal cortex (Brodmann area 8/9) by ELISA. The expression and distribution of MasR, and insulin-regulated aminopeptidase (IRAP) (Ang-IV receptor) were determined by ELISA and immunohistochemistry. Pre-existing data on Ang-II level, and amyloid β level (by ELISA) and Tau load (field fraction analysis), Braak staging information was also available for analyses.

pharmacologically, are associated with the pathogenesis of AD.

P5.129 Identification of different cognitive evolution patterns among the population associated with specific brain imaging profiles

Anaïs Rouanet

Authors Anaïs Rouanet, Rob Johnson, Brian Tom, Sylvia Richardson

Affiliations MRC Biostatistics Unit, Cambridge University

Introduction Cognitive decline is known to be heterogeneous among the population. The aim of this work was to identify meaningful clusters in the population, i.e. homogeneous sub-groups in terms of cognitive evolution and anatomic features. Such a model can facilitate the identification of individuals likely receptive to a treatment for clinical trial organization, or early identification of the subjects at risk of dementia, thus providing a useful tool for clinical decision-making in a precision medicine framework.

Methods and Materials Profile regression, a clustering method, allows to identify clusters based on longitudinal cognitive tests. Each cluster is associated with both a specific cognitive evolution and a specific profile of covariates (such as brain imaging features). A variable selection procedure allows to highlight variables relevant to the clustering structure. A notable advantage of this method is its ability to directly learn the number of clusters from the data.

Results We apply the model on a sample from the North American Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort data. We focus on the Mini-Mental State Examination cognitive test, collected every six months up to 12 years, as a proxy measurement of cognitive evolution. The results provide graphical representations of both the different cognitive patterns observed in the sample and the associated brain imaging profiles and clusters are described in terms of brain imaging features.

Conclusions This methodology offers a flexible tool to analyze simultaneously different types of data in order to gain insight on the heterogeneity of Alzheimer's disease. In the future, it will be applied to DPUK cohorts.