pathology that leads to social withdrawal. The current findings go some way towards elucidating this issue.

**P3-540**  
**EFFECT MODIFICATIONS OF THE ASSOCIATION BETWEEN SERUM MERCURY LEVEL AND MILD COGNITIVE IMPAIRMENT BY SMOKING STATUS**  
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**Background:** With population aging, dementia, the highest burden of disease among the elderly Korean, has been increased. Alzheimer’s disease (AD) is the most common type of dementia. Trace metal toxicity has been associated with the AD. In the progression of mild cognitive impairment (MCI) to AD, however, the etiologic roles of metals still need investigation. **Methods:** Study population was composed of 4 cohorts. 50 MCI and AD cases recruited from a hospital patient cohort were compared with 155 normal controls from other cohorts. Logistic analysis was used to estimate odds ratios (ORs) for case including MCI and AD. Regarding MCI and AD as ordinal variables, generalized logit and cumulative logit model were used. **Results:** The geometric mean (± interquartile ranges) for mercury (Hg) among controls were higher (2.3 ± 2.4 μg/L) than that among cases (2.1 ± 1.7 μg/L). With adjustment of age, sex, BMI, smoking and education level, in all 3 models, any ORs were statistically significant. The p-values for the interaction between smoking and Hg, however, were significant in three models. Stratified by the smoking status, while OR (95% confidence interval) of Hg, in the logistic model, was 1.16 (1.03-1.31) among non-smokers (NS) and 0.12 (0.02-0.77) among smokers. In the generalized logit model, however, OR for AD was 1.24 (p = 0.0074) among NS. Among smokers, OR was 4.96 (p = 0.046) for MCI. In the multinomial cumulative logit model, although proportional odds assumption was not satisfied, due to the small size, the interaction was still significant; 1.12 (1.001-1.25) among NS and 0.22 (0.07-0.68) among smokers. **Conclusions:** Serum Hg level, with an interaction with smoking status, accounts for the progression from normal to MCI significantly.

**P3-541**  
**DIABETES: AN IMPORTANT MODIFIABLE RISK FACTOR FOR DEMENTIA?**  
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**Background:** Dementia and type 2 diabetes (T2D) are both highly prevalent and major public health concerns. Despite T2D being linked to increased dementia risk, there is still much unknown. This study looks at the relationship between T2D, APOE ε4 genotype and dementia risk. **Methods:** We used the Genetics of Diabetes Audit and Research in Tayside Study (Go-DARTS) cohort in Scotland. Approximately 18,000 individuals provided a blood sample and consent to link genetic information to their electronic healthcare record. At recruitment, 10,077 patients had T2D. Incident all-cause dementia cases were ascertained from redeemed dementia-specific medication prescriptions, hospital discharge and cause of death ICD 9 and 10 coding and validated case notes from referral to psychiatry of old age. Cox proportional hazards was used to determine incident all-cause dementia risk by diabetes status and APOE ε4 genotype (chronological age as the times scale). We adjusted for age at recruitment, gender and APOE ε4 genotype. A competing risk model for all-cause death was analysed in view of expected earlier mortality in those with T2D. **Results:** Of 15,693 participants, 54.9% (n = 8610) had diabetes. The mean age was 65.9 years (SD +/-10.7) for those with T2D and 61.6 (SD +/-12.2) for those without. Of those with APOEε4, 36.9% (n = 2319) had diabetes and 37.8% did not have diabetes. There was no significant statistical association between diabetes and APOE ε4. Incident all-cause dementia (including dementia recorded on death certificates) occurred in 7.3% (n = 1145). Competing risk regression models, with all cause death as the competing event, showed that compared to individuals who were neither T2D nor had APOE ε4 genotype, the hazard ratio was 2.7 (95% CI 2.3-3.3); for those with both T2D and APOE ε4; 1.4 (95% CI 1.2-1.6) for those with T2D alone; and 2.1 (95% CI 1.7-2.6) for those with APOEε4 alone. **Conclusions:** These findings show that combined T2D and APOE ε4 genotype is associated with increased risk of dementia. This shows that in a large cohort, in addition to APOE ε4 genotype, T2D has an important additive risk. As T2D is preventable and treatable this could be an important modifiable dementia risk.

**P3-542**  
**CORONARY HEART DISEASE AND RISK FOR COGNITIVE IMPAIRMENT OR DEMENTIA: A SYSTEMATIC REVIEW AND META-ANALYSIS**  
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**Background:** Accumulating evidence suggests an association between coronary heart disease and risk for cognitive impairment or dementia, but no study has systematically reviewed this association. For that reason, the aim of the present systematic review and meta-analysis is to summarize the available evidence on the association between coronary heart disease and risk for cognitive impairment or dementia. **Methods:** Medline, Embase, PsycINFO, and...
CINAHL were searched for all publications until 8th January 2016. Articles were included if they fulfilled the inclusion criteria: (1) myocardial infarction, angina pectoris or coronary heart disease (combination of both) as predictor variable; (2) cognition, cognitive impairment or dementia as outcome; (3) population-based study; (4) prospective (≥1 year follow-up), cross-sectional or case-control study design; (5) ≥100 participants; and (6) aged ≥45 years. Two reviewers independently screened all abstracts and extracted information from potential relevant full-text articles. We pooled estimates from the most fully analyzed data. Meta-analysis of 10 prospective cohort studies showed that coronary heart disease was associated with increased risk of cognitive impairment or dementia (OR = 1.45, 95% CI = 1.21-1.74, p < 0.001). Between-study heterogeneity was low (I² = 25.7%, 95% CI = 0.64, p = 0.207). Similar significant associations were found in separate meta-analyses of prospective cohort studies for the individual predictors (myocardial infarction, angina pectoris). In contrast, meta-analyses of cross-sectional and case-control studies were inconclusive. Conclusions: This meta-analysis suggests that coronary heart disease is prospectively associated with increased odds of developing cognitive impairment or dementia. Given the projected worldwide increase in the number of people affected by coronary heart disease and dementia, insight into causal mechanisms or common pathways underlying the heart-brain connection is needed.

**P3-543**

**ASSOCIATION OF PSYCHOSOCIAL WORK STRESS WITH COGNITIVE DECLINE AND BRAIN STRUCTURE DIFFERENCES**

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**Background:** Evidence on the influence of psychosocial work stress on cognitive function and brain structure is limited. This study examined whether work-related stress is associated with structural brain changes and cognitive decline in old age. Methods: In a population-based prospective cohort study, 2876 dementia-free participants aged ≥60 years were followed-up for up to 9 years. A subsample (n=436) underwent brain magnetic resonance imaging (MRI) at baseline. Global cognitive function was measured by the Mini-Mental State Examination at baseline and all follow-ups. Levels of job control and demands in the longest held job over the whole working life were assessed by a validated matrix using information on occupational activities obtained by a structured interview. Data were analyzed using mixed-effects linear regression. Results: People with low levels of job control and demands exhibited greater cognitive decline (β: -0.13, 95% CI: -0.19 to -0.07, p<0.001; β: -0.10, 95% CI: -0.16 to -0.04, p<0.01), compared to those with high levels. Relative to persons who had active job strain, faster cognitive decline was found in those who had high job strain (β: -0.11, 95% CI: -0.18 to -0.05, p=0.001) and passive job strain (β: -0.16, 95% CI: -0.23 to -0.09, p<0.001). Further analysis showed that the association between job strain status and cognitive decline was only limited to young-old persons (up to 78 years) and was not significant in those aged 81+ years. MRI data showed that low levels of job demands and passive job strain were both related to smaller total hippocampal volume (β: -0.23, 95% CI: -0.39 to -0.08, p<0.01; β: -0.19, 95% CI: -0.37 to -0.01, p<0.05). Conclusions: Work-related psychosocial stress is associated with smaller hippocampal volume and may accelerate cognitive decline even in the eight decade of life, suggesting that neural alterations play a role in the work stress-cognitive decline link.

**P3-544**

**THE ASSOCIATION BETWEEN APATHY AND MILD COGNITIVE IMPAIRMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Background:** The relationship between apathy and mild cognitive impairment (MCI) remains unclear. The aims of this systematic review and meta-analysis were to investigate the incidence of apathy among people with MCI compared with people with dementia or normal cognition, and to clarify the risk of dementia among people with MCI and apathy compared with those with MCI and no apathy. Methods: A systematic search up to September 2016 was performed to identify cross-sectional and longitudinal studies in the major healthcare databases. Article screening, data-extraction and methodological quality assessment were conducted independently by two researchers. Pooled odds ratio (OR) and hazard ratio (HR) were calculated to examine the association between apathy and MCI. Results: Eleven cross-sectional studies and twelve longitudinal studies were included. The pooled odds ratios of incidence of apathy among people with dementia versus MCI, people with MCI versus normal cognition were 2.97 95%CI [2.34, 3.77] (P<0.001), and 5.68 95%CI [3.22, 10.02] (P<0.001). The pooled hazard ratio and odds ratio of conversion to dementia were 1.22 95%CI [1.14, 1.31] (P=0.002) and 2.74 95%CI [1.34, 5.61] (P=0.006) in the group of MCI plus apathy compared to those without apathy. Conclusions: The results suggest that the occurrence of apathy among people with MCI is less than those with dementia, but is more than people with normal cognition. Furthermore, apathy increases the risk of progression to dementia among people with MCI. Future studies should focus on apathy among people with MCI and dementia, and tailor interventions targeting apathy management among people with MCI, which may reduce the risk of dementia.

**P3-545**

**RE-EXAMINING THE COMPLEX RELATIONSHIP BETWEEN ALZHEIMER’S DISEASE NEUROPATHOLOGY AND COGNITION: THE ROLE OF FRAILTY**

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**Background:** The neuropathological features of Alzheimer’s disease (AD) are poorly correlated with the clinical presentation of dementia. However, dementia and frailty are closely linked: both are strongly related to advanced age and vulnerability to adverse health outcomes. It is possible that frailty interacts with neuropathological features of AD to increase vulnerability to cognitive impairment. To examine if frailty is related to AD-related dementia, after controlling for neuropathology. Methods: This was a cross-sectional analysis of data from the Rush Memory and Aging Project, a clinico-pathological study of older adults living in retirement.