

Related factors of cognitive decline in community-dwelling elderly people are gender (male), alcohol consumption, smoking and employment (past). Thus, it is important that related factors open to change such as alcohol consumption, and smoking are more important factors to consider in cognitive decline. In conclusion, changing the above related factors that are closely related to lifestyle is very important in preventing cognitive decline in community-dwelling elderly people. Consequently, we must provide assistance and education to the elderly which will help them make changes in such related factors.

P3-528

PROSPECTIVE ASSOCIATIONS BETWEEN VITAMINS, METABOLITES, AND OVERALL DEMENTIA IN THE OLDEST-OLD



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Background: Vitamins A, D, E and Beta-carotene may have a protective function for cognitive health. However, results from previous studies investigating the association with dementia are inconclusive and longitudinal studies are few. **Methods:** We included 1,388 non-demented participants, 65 Alzheimer's disease (AD) dementia participants and 12 vascular-dementia participants from the AgeCoDe study, a prospective multicenter-cohort of elderly (75+) general-practitioner patients in Germany. We aimed to cross-sectionally and longitudinally investigate whether plasma levels of vitamin A, Beta-carotene, vitamin D, vitamin E, Trolox Equivalent Antioxidant Capacity (TEAC) and Oxidative-LDL (Ox-LDL) are associated with clinically diagnosed AD-dementia and overall dementia in the oldest old over a follow-up time of 7 years. **Results:** In a logistic regression model, vitamins and metabolites were analyzed categorically. Participants with high levels of vitamin E had a lower odds for overall dementia as compared to participants in the reference group (normal range: 5.5-18.0 mg/L) after adjustment for age, sex, ApoE e4, education, BMI, physical activity, smoking, creatinine, cholesterol, triglycerides, blood pressure and depression (OR 0.41(95%CI 0.19;0.86)). This same finding was observed for AD-dementia (OR 0.41(95%CI 0.18;0.91)). The other vitamins and metabolites were unrelated to current diagnosis. During a follow-up time of 7 years 173 individuals of the non-demented participants developed AD-dementia and 29 vascular-dementia. Subjects with vitamin D deficiency (<20 ng/mL) were at a high risk for both overall-dementia (HR 2.82(95%CI 1.19;6.67)) and AD-dementia (HR 3.62(95%CI 1.38;9.50)). Subjects in the highest TEAC tertile, as compared to the lowest, were at increased risk for AD-dementia (HR 1.52(95%CI 1.01;2.30)). **Conclusions:** Cross-sectionally, we observed low vitamin E levels in patients with dementia. However, no such association was observed in longitudinal analyses, which is in line with previous studies. Changes in diet around dementia onset might affect the bioavailability

of vitamins and metabolites. Vitamin D deficiency and high TEAC increased the risk to develop all-cause dementia. Our study supports the advice for more sun exposure and vitamin D supplementation in those with vitamin D deficiency. The unexpected finding about high TEAC being a risk factor for AD dementia, rather than a protective factor, may be related to findings that a high level of antioxidant-capacity may turn into a prooxidant-capacity under certain conditions.

P3-529

A SYSTEMATIC REVIEW OF MENDELIAN RANDOMIZATION STUDIES INVESTIGATING CAUSAL ASSOCIATIONS BETWEEN RISK FACTORS AND DEMENTIA



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Background: Very little is known about the causal nature of the associations between established risk factors, e.g. education and smoking and dementia risk. We have therefore conducted a systematic review of Mendelian randomization (MR) studies investigating causal links between risk factors and dementia or dementia-related outcomes. **Methods:** We searched five databases from inception to March 2016 using a search strategy including subject headings and free text terms relevant to dementia, cognition and MR. Forward and backward citation searches of included publications were also conducted. We included MR studies investigating the association between any risk factor and global cognitive function, all-cause dementia or dementia subtypes, excluding non-genetic studies, genetic studies other than MR and animal studies. Two reviewers independently screened titles and abstracts, reviewed full-texts and assessed the quality of included studies. **Results:** Fourteen MR studies investigating a variety of risk factors (education, lifestyle factors, cardiovascular factors and related biomarkers, diabetes related and other endocrine factors, and telomere length) and dementia-related outcomes met our inclusion criteria. Most studies received an overall rating of good quality, however sample size and statistical power were rated low in half of the studies. Shorter telomeres were causally associated with an increased risk of Alzheimer's disease (AD, odds ratio per standard deviation decrease of telomere length = 1.36 (1.12, 1.67), p = 0.002). There was also some suggestion of a causal association with smoking quantity and metabolic risk factors including systolic blood pressure, fasting glucose, insulin sensitivity and high-density lipoprotein cholesterol. Causal associations between several risk factors and dementia-related outcomes were investigated in one study only. Moreover, survival and diagnostic bias or pleiotropic effects cannot be excluded. **Conclusions:** There was convincing genetic evidence to support a causal association between telomere length and AD. Inconclusive evidence for other risk factors or tentative evidence for smoking quantity and selected metabolic markers may result from insufficient statistical power. Further well designed MR studies are needed to investigate the causality of the associations between risk factors and dementia where randomised controlled trials are unethical or impractical.