

tent with epidemiological studies indicating that TC is a risk factor for AD. These results suggest that factors associated with lipid metabolism may be important in the development of AD even at very old ages. These findings are consistent with our recent observations of an association between AD-neuropathological lesions density and coronary artery disease.

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FOLATE LEVELS AND COGNITIVE PERFORMANCE. THE ROTTERDAM SCAN STUDY.

Lonneke M. de Lau¹, Helga Refsum^{2,3}, A. David Smith², Carole Johnston², Monique M. Breteler¹, ¹Erasmus Medical Center Rotterdam, Rotterdam, The Netherlands; ²Oxford Centre for Gene Function, Oxford, United Kingdom; ³Institute of Basic Biomedical Sciences, University of Oslo, Oslo, Norway. Contact e-mail: l.delau@erasmusmc.nl

Background: Elevated homocysteine concentrations are associated with cerebral small vessel disease, hippocampal atrophy, worse cognitive performance and an increased risk of dementia. It is unclear whether these associations are due to effects of homocysteine itself, or rather to other factors involved in homocysteine metabolism, such as folate. Recent evidence suggests that folate may have beneficial effects on cognition, independent from its effects on homocysteine levels. **Objective(s):** To examine the independent association of plasma folate levels with cognitive performance, and to evaluate to what extent this effect is through vascular mechanisms. **Methods:** In the population-based Rotterdam Scan Study, 1,033 non-demented participants aged 60-90 years underwent extensive cognitive testing and brain imaging. We constructed compound scores for psychomotor speed, memory function, and global cognitive function and scored white matter lesions and hippocampal atrophy on brain MRI scans. We evaluated the relation between folate levels and cognitive performance by means of multivariate linear regression, with plasma folate as a continuous variable (expressed per standard deviation increase) and in quintiles. To examine the role of vascular mechanisms, we also evaluated the association between folate levels and white matter lesions and hippocampal atrophy. **Results:** Increasing folate levels were associated with higher scores for psychomotor speed and global cognitive function (adjusted difference in test score per standard deviation increase in folate for psychomotor speed 0.07 (95% confidence interval (CI), 0.02-0.12), for global cognitive function 0.04 (95% CI, 0.00-0.08)), but not with memory function. Analyses in quintiles suggested a linear relationship. Higher folate levels were associated with a lower prevalence of severe white matter lesions (adjusted Odds Ratio per standard deviation increase 0.82 (95% CI, 0.69-0.98)). Adjustment for homocysteine levels only slightly diminished these associations. No relation was seen between folate levels and hippocampal atrophy. **Conclusions:** Higher plasma concentrations of folate are associated with better cognitive performance, in particular psychomotor speed, regardless of homocysteine level. A significant inverse association between folate levels and presence of severe white matter lesions was found, while no association was observed for hippocampal atrophy. These findings suggest that the effect of folate on cognition is mediated through vascular mechanisms.

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THE SEARCH FOR A SUCCESSFUL COGNITIVE AGING ENDOPHENOTYPE IN THE OFFSPRING OF VERY ELDERLY (90+) NONDEMENTED PROBANDS IN A FOUNDER POPULATION

Steven D. Edland¹, Michal Schnaider-Beer², Henriette Raventos³, Daniel Valerio Aguilar³, Luis Emilio Corrales Campos³,

Mariana Pereira Castro³, Gary W. Angelo², Hillel T. Grossman², Irina N. Bepalova², Mary Sano², Jeremy M. Silverman², ¹University of California at San Diego, San Diego, CA, USA; ²Mount Sinai School of Medicine, New York, NY, USA; ³University of Costa Rica, San Jose, Costa Rica. Contact e-mail: sedland@ucsd.edu

Background: Ascertaining families with demonstrable successful cognitive aging might help reveal rare genes associated with good cognitive functioning into very late old age. Given the genetic complexity of this desirable condition, however, validated cognitive endophenotypes (i.e., traits lying midstream between a gene and a genetically complex condition of interest) will be required for open ended gene finding strategies. Delayed recall in particular is a promising candidate endophenotype because it has shown strong heritability in AD proband families and delayed recall impairment has predicted the development of AD. **Objective(s):** To identify cognitive endophenotypes for successful cognitive aging in a founder population. **Methods:** Delayed recall, along with other tests of cognitive functions, were assessed in 27 very elderly (age 90+) nondemented (VEND) probands and 47 of their aged 60+ offspring. The families were ascertained from the Central Valley of Costa Rica (CVCR), a founder population. Two sets of CVCR comparison groups were also assessed: 1) Very elderly (aged 90+) demented (VED) probands (n=13) and their age 60+ offspring (n=28); 2) Young (aged 60-70) nondemented elderly (YND; n=15) and their age 60+ siblings (n=17). **Results:** VEND offspring, VED offspring, and YND sibling groups did not significantly differ with respect to age, sex, or years of education. Using a random effects model controlling for sex and education, delayed recall was significantly better among VEND offspring than YND siblings (P<0.005) and VED offspring (P<0.05). In addition, there were significant group by education interactions such that fewer years of education was associated with lower delayed recall scores in the YND siblings (P<0.005) and VED offspring (P<0.05), but education had no effect on VEND offspring. Similar albeit nonsignificant relationships were observed with age. **Conclusions:** The VEND offspring had higher levels of delayed recall than the VED offspring and YND siblings. In addition, whereas low education was associated with poorer performance in delayed recall in two comparison groups, no such association was present in VEND offspring. These results are consistent with the hypothesis that delayed recall in VEND offspring is a state independent trait and might be a useful endophenotype for successful cognitive aging.

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INCIDENT DEMENTIA IN WOMEN IS PRECEDED BY WEIGHT LOSS BY AT LEAST A DECADE

David S. Knopman¹, Walter A. Rocca¹, Steven D. Edland², Ruth H. Cha¹, Ronald C. Petersen¹, ¹Mayo Clinic College of Medicine, Rochester, MN, USA; ²University of California San Diego, San Diego, CA, USA. Contact e-mail: knopman@mayo.edu

Background: Several studies have shown that weight loss precedes dementia. **Objective(s):** To study the association between antecedent height and body weight and dementia using a case-control design. **Methods:** Cases of incident dementia in the 5 year period of 1990 to 1994 were identified in Rochester MN. We also identified age (\pm 1 year) and sex matched controls from the same community who were free of dementia in their matched case's year of onset (index year). Dementia and Alzheimer disease (AD) were defined using the criteria of DSM-IV. Weights were abstracted from the medical record for time periods of 1-2, 3-4, 5-6, 7-8, 9-10, 11-20, 21-30 and > 30 years prior to the index year. We also recorded height at age 40 years. **Results:** We identified 481 incident cases of primary dementia (AD, vascular dementia or another neurodegenerative disorder), of whom 345 were diagnosed as AD. There were 350 women and 131 men; 60.2% were age 80 and 4.6% were <65 at onset. For both primary dementia and AD, there were no significant differences in height between cases and controls at age 40. In addition, there were no differences in weight between cases and controls 21-30 years prior to the index year. However, women with primary dementia were nearly 6 lb lighter than