

women=1,583(78.8)) met inclusion criteria. Sex modified the association between APOE ϵ 2 and cognitive decline in NHW ($\beta=0.097$, 95% CI: 0.023–0.172, $p=.01$) but not NHB participants ($\beta=-0.011$, 95% CI: -0.153–0.131, $p=.9$). In sex-stratified analyses of NHW participants, APOE ϵ 2 (vs. ϵ 3/ ϵ 3) carriage was associated with attenuated cognitive decline in men ($\beta=0.096$, 95% CI: 0.037–0.155, $p=.001$), but not women ($\beta=-0.001$, 95% CI: -0.044–0.043, $p=.97$). In analyses comparing men and women APOE ϵ 2 carriers, men exhibited slower cognitive decline than women ($\beta=0.120$, 95% CI: 0.051–0.190, $p=.001$). Analyses performed separately in NACC and ROS/MAP revealed the same pattern of male-specific APOE ϵ 2 protection in NHW participants in both data sources.

Conclusions: In light of the longstanding view that APOE ϵ 2 protects against AD and dementia, our results provide evidence that APOE ϵ 2 is associated with attenuated cognitive decline in men but not women among NHW adults. This male-specific protection may contribute to sex differences in AD-related cognitive decline. Our findings have important implications for understanding the biological drivers of sex differences in AD risk, which is crucial for developing sex-specific strategies to prevent and treat AD dementia.

Categories: Dementia (Alzheimer's Disease)

Keyword 1: apolipoprotein E

Keyword 2: aging disorders

Keyword 3: dementia - Alzheimer's disease

Correspondence: Jennifer Rabin, Sunnybrook Research Institute, University of Toronto, jennifer.rabin@sri.utoronto.ca

2 Predictors of Memory Deficits in Patients with Subjective Cognitive Decline, Mild Cognitive Impairment, and Alzheimer's Disease – Do Disease Severity Moderate the Association?

Knut A Hestad^{1,2,3}, Knut Engedal^{4,5}, Bjørn Heine Strand⁶, Per G Farup^{1,7}

¹Department of Research, Innlandet Hospital Trust, Brumunddal, Norway. ²Faculty of Health and Social Sciences, Inland Norway University of Applied Sciences, Elverum, Norway.

³Department of Psychology, Norwegian University of Science and Technology,

Trondheim, Norway. ⁴Norwegian National Advisory Unit on Ageing and Health, Vestfold County Hospital Trust, Tønsberg, Norway.

⁵Department of Geriatric Medicine, Oslo University Hospital, Oslo, Norway. ⁶Department of Chronic Diseases and Ageing, Norwegian Institute of Public Health, Oslo, Norway.

⁷Department of Clinical and Molecular Medicine, Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology, Trondheim, Norway

Objective: Age, sex, education, memory, and the APOE ϵ 4 allele are related to Alzheimer's disease (AD) risk. Recently it was suggested that low body mass index (BMI) contributes to the development of AD. The objective of this study was to examine how delayed recall of a word list was influenced by demographic variables, APOE and BMI in people with memory problems, and to investigate whether the impact of these variables was smaller at higher disease severity levels.

Participants and Methods: The participants were 1206 patients in the Norwegian NorCog registry diagnosed with either subjective cognitive decline (SCD) ($n=274$), mild cognitive impairment (MCI) ($n=444$), or AD ($n=488$). ANOVAs and hierarchical regression were applied to examine whether the delayed recall part of the 10-word test of the CERAD-WL was associated with age, sex, education, APOE (ϵ 4/non- ϵ 4) and BMI. Analyses were run separately for SCD, MCI and AD patients.

Results: There were significant bivariate differences ($p<.001$) between the three patient groups for all variables; the AD patients were older, less educated, more were women, more had APOE ϵ 4 alleles, and they had lower BMI. For the SCD group, 34% of the total variance (R^2) of the dependent variable was explained. All independent variables except BMI ($p=.07$) had a significant contribution in the prediction. For MCI, 18% of the total were explained. All variables except education and sex showed significant contribution to R^2 . For the AD group, R^2 was 13%. Sex and BMI did not contribute significantly.

Conclusions: As expected, the performance on CERAD-WML was influenced by age, education and sex in the SCD group, whereas the associations between memory function and the three demographic variables were less clear among patients with MCI and AD. ApoE genotype influenced on the CERAD-WML

results among all patients, whereas BMI only influenced on the results among patients with SCD and MCI. Our findings do not support that BMI is associated with delayed recall of memory in AD.

Categories: Dementia (Alzheimer's Disease)

Keyword 1: mild cognitive impairment

Keyword 2: dementia - Alzheimer's disease

Correspondence: Knut A. Hestad, Department of Research, Innlandet Hospital Trust, Brumunddal, Norway, Knut.Hestad@inn.no

3 Stricker Learning Span criterion validity: remote self-administration of a computer adaptive word list memory test shows similar ability to differentiate PET-defined biomarker groups as in-person Rey Auditory Verbal Learning Test performance in cognitively unimpaired individuals on the Alzheimer's continuum

Nikki H. Stricker¹, John L. Stricker¹, Aimee J. Karstens¹, Jay S. Patel¹, Teresa J. Christianson¹, Winnie Z. Fan¹, Sabrina M. Albertson¹, Ryan D. Frank¹, Mary M. Machulda¹, Walter K. Kremers¹, Julie A. Fields¹, Jonathan Graff-Radford¹, Clifford R. Jack, Jr.¹, David S. Knopman¹, Michelle M. Mielke², Ronald C. Petersen¹

¹Mayo Clinic, Rochester, MN, USA. ²Wake Forest University School of Medicine, Winston-Salem, NC, USA

Objective: The Stricker Learning Span (SLS) is a computer-adaptive word list memory test specifically designed for remote assessment and self-administration on a web-based multi-device platform (Mayo Test Drive). Given recent evidence suggesting the prominence of learning impairment in preclinical Alzheimer's disease (AD), the SLS places greater emphasis on learning than delayed memory compared to traditional word list memory tests (see Stricker et al., *Neuropsychology* in press for review and test details). The primary study aim was to establish criterion validity of the SLS by comparing the ability of the remotely-administered SLS and in-person administered Rey Auditory Verbal Learning Test (AVLT) to differentiate biomarker-

defined groups in cognitively unimpaired (CU) individuals on the Alzheimer's continuum.

Participants and Methods: Mayo Clinic Study of Aging CU participants (N=319; mean age=71, SD=11; mean education=16, SD=2; 47% female) completed a brief remote cognitive assessment (~0.5 months from in-person visit). Brain amyloid and brain tau PET scans were available within 3 years. Overlapping groups were formed for 1) those on the Alzheimer's disease (AD) continuum (A+, n=110) or not (A-, n=209), and for 2) those with biological AD (A+T+, n=43) vs no evidence of AD pathology (A-T-, n=181). Primary neuropsychological outcome variables were sum of trials for both the SLS and AVLT. Secondary outcome variables examined comparability of learning (1-5 total) and delay performances. Linear model ANOVAs were used to investigate biomarker subgroup differences and Hedge's G effect sizes were derived, with and without adjusting for demographic variables (age, education, sex).

Results: Both SLS and AVLT performances were worse in the biomarker positive relative to biomarker negative groups (unadjusted p's<.05). Because biomarker positive groups were significantly older than biomarker negative groups, group differences were attenuated after adjusting for demographic variables, but SLS remained significant for A+ vs A- and for A+T+ vs A-T- comparisons (adjusted p's<.05) and AVLT approached significance (p's .05-.10). The effect sizes for the SLS were slightly better (qualitatively, no statistical comparison) for separating biomarker-defined CU groups in comparison to AVLT. For A+ vs A- and A+T+ vs A-T- comparisons, unadjusted effect sizes for SLS were -0.53 and -0.81 and for AVLT were -0.47 and -0.61, respectively; adjusted effect sizes for SLS were -0.25 and -0.42 and for AVLT were -0.19 and -0.26, respectively. In secondary analyses, learning and delay variables were similar in terms of ability to separate biomarker groups. For example, unadjusted effect sizes for SLS learning (-.80) was similar to SLS delay (-.76), and AVLT learning (-.58) was similar to AVLT 30-minute delay (-.55) for the A+T+ vs A-T- comparison.

Conclusions: Remotely administered SLS performed similarly to the in-person-administered AVLT in its ability to separate biomarker-defined groups in CU individuals, providing evidence of criterion validity. The SLS showed significantly worse performance in A+ and A+T+ groups (relative to A- and A-T- groups) in this CU sample after demographic