Sleep and Cognition in Old Age

Birth Cohort Differences, Dementia, and Biomarkers of Alzheimer's Disease

Johan Skoog

Psykologiska institutionen, 2020

Avhandlingen för avläggande av filosofie doktorsexamen i psykologi, som med vederbörligt tillstånd av samhällsvetenskapliga fakultetsstyrelsen vid Göteborgs universitet kommer att offentligen försvaras fredagen den 4 december 2020, klockan 9:00 i sal F1, Psykologiska institutionen, Haraldsgatan 1, Göteborg.

Fakultetsopponent: Professor Matthias Kliegel
University of Geneva, Switzerland

Föreliggande uppsats grundar sig på följande artiklar:

I. Skoog, J., Jonsson, H., Sigstrom, R., Ostling, S., Falk, H., Waern, M., Thorvaldsson, V., Skoog, I., & Johansson, B. (2019). Do later-born birth cohorts of septuagenarians sleep better? A prospective population-based study of two birth cohorts of 70-year-olds. Sleep, 42(1-8). https://doi.org/10.1093/sleep/zsy204

II. Skoog, J., Backman, K., Ribbe, M., Falk, H., Gudmundsson, P., Thorvaldsson, V., Borjesson-Hanson, A., Ostling, S., Johansson, B., & Skoog, I. (2017). A longitudinal study of the Mini-Mental State Examination in late nonagenarians and its relationship with dementia, mortality, and education. Journal of the American Geriatrics Society, 65(6), 1296–1300. https://doi.org/https://doi.org/10.1111/jgs.14871

III. Sindi, S., Kåreholt, I., Johansson, L., Skoog, J., Sjöberg, L., Wang, H. X., Johansson, B., Fratiglioni, L., Soininen, H., & Solomon, A. (2018). Sleep disturbances and dementia risk: A multicenter study. Alzheimer's & Dementia, 14(10), 1235–1242. https://doi.org/https://doi.org/10.1016/j.jalz.2018.05.012

IV. Skoog, J., Zetterberg, H., Blennow, K., Kern, S., Johansson, B., Skoog, I. & Thorvaldsson, V. (2020). *A population-based study on sleep and CSF-markers of Alzheimer's disease: The influence of the APOE ε4 allele.* Manuscript submitted for publication.

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Abstract

Johan Skoog (2020). *Sleep and Cognition in Old Age; Birth Cohort Differences, Dementia, and Biomarkers of Alzheimer's Disease*. Department of Psychology, University of Gothenburg, PO Box 500, SE-405 30 Gothenburg, Sweden.

The focus for this thesis is on two major determinants of health and wellbeing in older people, namely subjective sleep disturbance and cognition. Data were drawn from the H70 Birth Cohort Studies, comprising representative samples of older people living in Gothenburg, Sweden. In **Study I**, we examined birth cohort differences regarding prevalence of insomnia (i.e., difficulties initiating sleep, maintaining sleep, and early morning awakenings) in two cohorts of 70-year-olds born three decades apart and followed over nine years. The later-born cohort showed lower prevalence of insomnia at age 70 compared with the earlier-born cohort. However, the prevalence of insomnia increased with age in the later-born but was stable in the earlier-born cohort. In **Study II,** we investigated cognitive status and change measured by the Mini-Mental State Examination (MMSE) among 97-year-olds followed over three years. We found that MMSE scores at baseline were related to dementia at baseline, but not to development of dementia during follow-up. Those who died during the three-year follow-up had lower MMSE scores than those who survived. Furthermore, participants with more education had higher MMSE scores, but there was no association between education and cognitive change. In **Study III,** which was a multicenter study, including additional samples from Stockholm and Finland, we investigated whether poor sleep in midlife and late life was associated with an elevated risk of developing dementia in late life. We found that midlife insomnia and late-life terminal insomnia (i.e., early morning awakenings) and long sleep duration were associated with a higher late-life dementia risk. In **Study IV,** we investigated if poor sleep was related to cerebrospinal fluid (CSF) markers of Alzheimer's disease (AD) and if these associations were moderated by possession of the apolipoprotein (*APOE*) ε4 allele. We found that reduced sleep, increased sleep and taking sleep medication were associated with markers of amyloid plaque accumulation (amyloid β 42/40 ratio). However, among *APOE*ε4-carriers, reduced sleep was also associated with markers of AD-related neurodegeneration (total tau, phosphorylated tau) and synaptic dysfunction (neurogranin). **Conclusions:** The main findings from the thesis imply that age-related increases in the prevalence of insomnia are postponed to higher ages in later-born cohorts. Education can still account for individual differences in cognitive performance even at these advanced ages but might not protect against cognitive decline. Different types of sleep problems may play varying roles during the life course concerning dementia risk where insomnia could potentially be more important in midlife while terminal insomnia or long sleep duration may be more critical later in life. In addition, sleep may play a vital role in the early processes of AD by potentially decreasing clearance or increasing production of amyloid β. A better understanding of sleep disturbances and cognition in old age may guide clinicians in making health care decisions and when designing person-oriented interventions that improves health and wellbeing in future older generations.

Keywords: Subjective sleep disturbance, cognition, dementia, epidemiology

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