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SUBJECTIVE SLEEP DISTURBANCE AND COGNITION: A MULTI-CENTER STUDY FROM NEAR

NEAR MEETING, 22 SEPT 2020

JOHAN SKOOG

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Background

- Ongoing project started 2016 on subjective sleep disturbance and dementia/cognition
- 2 previously publishe
  SWEOLD

alzheimer's association | Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

Featured Article

Sleep disturbances and dementia risk: A multicenter study

Shireen Sindi, Ingemar Kåreholt, Lena Johansson, Johan Skoog, Linnea Sjöberg, Hui-Xin Wang, Boo Johansson, Laura Fratiglioni, Hilkka Soininen, Alina Solomon, Ingmar Skoog, Miia Kivipelto

First published: 17 July 2018 | https://doi.org/10.1016/j.jalz.2018.05.012

ELSEVIER

Sleep Medic

Volume 52, December 2018

Original Article

Sleep disturbances and later
multi-centre study

Shireen Sindi [a, b, c], Lena Johansson [d], Johan Skoog [d, e], Alexander Darin Mattsson [a], Linnea Sjöberg [a, b], Hui-Xin Wang [a, b, f], Laura Fratiglioni [a, b, g], Jenni Kulmala [b, h], Hilkka Soininen [i, j], Alina Solomon [b, i], Boo Johansson [e], Ingmar Skoog [d], Miia Kivipelto [b, c, h, i], Ingemar Kåreholt [a, k]

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https://doi.org/10.1016/j.sleep.2017.11.1149

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Sleep and dementia

- Risk factor for dementia

… early symptom?

- Bidirectional relation?

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Risk factor for dementia?

- Insomnia in midlife was associated with a higher risk for dementia (fully adjusted hazard ratio (HR) = 1·24, 95% confidence interval (95% CI) = 1·02 -1·50)
- Long sleep duration (more than 9 hours) was associated with an increased dementia risk at age 70 (adjusted OR = 3·70, 95% CI = 1·52 – 9·02)

Sindi, S; Skoog, J; M. Kivipelto, et al. 2018

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Risk factor for lower MMSE-score?

- Midlife nightmares and insomnia were associated with lower MMSE scores (fully adjusted β = -0.28, 95% CI = -0.49 to -0.07 and β = -0.20, 95% CI = -0.39 to -0.01), although the latter association was attenuated after adjusting for lifestyle/health-related confounders.
- Late-life sleep disturbances were associated with lower MMSE scores after 3-11 years (fully adjusted β = -0.12, 95% CI = -0.24 to -0.01).

Sindi, S; Skoog, J; M. Kivipelto, et al. 2018

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Aim

- To investigate the association between subjective sleep disturbance and cognitive level and change in 4 population-based studied from Sweden and Finland
- Work in progress…

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Databases and collaborators

- H70 – Johan Skoog, Timothy Hadarsson Bodin
- KP & SNAC-K – Erika Jonsson Laukka, Linnea Sjöberg
- GÅS/SNAC-S – Marieclare Overton
- CAIDE – Shireen Sindi, Ingemar Kåreholt

- NEAR – Alexander Darin-Mattsson

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Harmonization vs meta-analyses

- Analyses were harmonized in the two previous studies using dementia and MMSE-score as outcomes in all studies
- Coordinated analysis (separated analyses for each study using the same statistical model)
- Multilevel modelling (growth curves)

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Cognition

Variables	H70	GÅS/SNAC-S	CAIDE	KP	SNAC-K	How variables were treated in the previous multi-center s
Outcome						
language/ordflöde	Wordfluency Animals	Word fluency Animals		category fluency-food items-phase II	Category Fluency	
Memory	12 Object free recall	Recall (16 words)	immediate word recall (10 word)	composit score free recall of random words lists - P2	Recall	
	Picture Memory - recognition	Recognition (16 words) recognised words (hits) minus false hits		composit score face recognition - hits minus false alarms - old/new faces - P2	Recognition	
Speed/attention	Figure Identification	Pattern comparison (mean of correct	Stroop test part 1/ Letter digit substitution test	Trail making test: Test A time in seconds	Patterns, digit cancellation	
Executive	Logical reasoning	Digit span backwards	Stroop test part 2	digit span backward p2		
		TMT-B (completion time measured in seconds for the 12 correct connections)		trail making B-time in seconds-phase II	TMT-B	

= perfect match

= comparable

= adequate comparison

= Search for more variables!

= Have it. Should be defined

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Cognition

- Composite scores including at least 2 tests for each domain (language, memory, speed/attention, executive function)
- A composite score for global cognition including data on at least half of the domains

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Sleep variables

Exposure	H70	GÅS/SNAC-S	CAIDE	KP	SNAC-K
Initial insomnia	Trouble initiating sleep	Do you have trouble falling asleep?			Do you have trouble falling asleep?
General insomnia??			General question insomnia		
Terminal insomnia	Wake up early in morning?	Do you wake up early?	3. I wake up 1-2 hours earlier than usual and it's hard for me to fall back asleep 4. I wake up early in the	Do you wake up early?	Do you wake up early? Trouble falling back asleep
Reduced sleep	Reduced sleep (CPRS)	Reduced sleep (CPRS)		Reduced sleep (CPRS)	
Sleep duration	Sleep duration	How many hours do you usually sleep at night during a typical day? Number of hours			Short sleep durationTired during the day
Hypnotics?	ATC-codes	ATC-codes	ATC-codes	ATC-codes	ATC-codes

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Models (Multilevel modelling) (at baseline)

Covariates	
Model 1	
Age	years
Sex	dichotomous
education	continuous
Model 2	
Model 1 +hypnotics	From medical registry (ATC-codes)
Model 3	
Model 2 + depressive sympton	self-reported: add variables on low mood and loss of interest, then use it as a continuous variable
Model 4	
Model 3+lifestyle	
Smoking	0=never or previous, 1=current
Alcohol consumption	Continuous (e.g. units, grams)
Physically inactive	1=none, 0=any activity
Cohabitant status	0= living with someone (including institutions); living alone = 1
Model 5	0-5 Number of CVDs. 1 point for each CVD.
Model 4 + CVs	
Stroke	Ischemic or hemorrhagic
Myocardial infarction	
Artrial fibrilation	
Diabetes	
heart failure	
Hypertension	Preliminary suggestion: Use systolic and diastolic variables separate and continuous
Model 6	
Model 5+APOE	0= No APOE4 alle; 1= any allele

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Preliminary results SNAC-K

	Memory		Language		Speed		Executive function		Global cognition	
	(recall, recognition)		*(category fluency)*		*(patterns, digit cancellation)*		*TMT-B (time)*		*composite score*	
	n	Est. (95% CI)	n	Est. (95% CI)	n	Est. (95% CI)	n	Est. (95% CI)	n	Est. (95% CI)
Sleep latency – Model 1	1456		1485		1392		1142		1419	
Level at age 72		-0.05 (-0.18; 0.09)		0.04 (-0.10; 0.17)		0.06 (-0.07; 0.19)		0.13 (-0.05; 0.31)		-0.02 (-0.11; 0.08)
Slope		-0.01 (-0.04; 0.01)		-0.01 (-0.03; 0.01)		-0.01 (-0.03; 0.01)		**0.03 (0.00; 0.06)***		-0.01 (-0.03; 0.00)
Waking up at night – Model 1										
Level at age 72		-0.03 (-0.14; 0.08)		0.04 (-0.07; 0.15)		0.08 (-0.02; 0.19)		0.03 (-0.12; 0.17)		0.02 (-0.06; 0.10)
Slope		-0.00 (-0.02; 0.02)		-0.00 (-0.02; 0.02)		-0.01 (-0.02; 0.01)		0.02 (-0.01; 0.04)		-0.00 (-0.02; 0.01)
Problems falling back asleep – Model 1										
Level at age 72		-0.05 (-0.18; 0.09)		0.04 (-0.10; 0.17)		0.06 (-0.07; 0.19)		0.13 (-0.05; 0.31)		-0.02 (-0.11; 0.08)
Slope		-0.01 (-0.04; 0.01)		-0.01 (-0.03; 0.01)		-0.01 (-0.03; 0.01)		**0.03 (0.00; 0.06)***		-0.01 (-0.03; 0.00)
Waking up early – Model 1										
Level at age 72		-0.08 (-0.22; 0.05)		-0.06 (-0.20; 0.08)		0.05 (-0.08; 0.19)		0.09 (-0.09; 0.28)		-0.05 (-0.15; 0.05)
Slope		0.01 (-0.01; 0.03)		0.00 (-0.02; 0.02)		-0.01 (-0.03; 0.02)		0.01 (-0.02; 0.04)		-0.00 (-0.02; 0.02)
Feeling tired and napping – Model 1										
Level at age 72		**-0.34 (-0.64; -0.04)***		**-0.31 (-0.62; -0.01)***		-0.23 (-0.53; 0.08)		**0.76 (0.36; 1.16)****		**-0.40 (-0.62; -0.18)****
Slope		-0.02 (-0.09; 0.05)		**-0.06 (-0.12; -0.00)***		**-0.07 (-0.13; -0.02)****		-0.02 (-0.11; 0.08)		**-0.05 (-0.10; -0.01)***
Short sleep duaration – Model 1										
Level at age 72		-0.07 (-0.19; 0.06)		-0.00 (-0.13; 0.12)		0.07 (-0.05; 0.19)		0.08 (-0.09; 0.25)		-0.01 (-0.11; 0.08)
Slope		-0.00 (-0.03; 0.02)		0.00 (-0.02; 0.02)		0.00 (-0.02; 0.02)		0.01 (-0.02; 0.04)		0.00 (-0.01; 0.02)

Model 1: adjusted for age, sex, education

Significant result *p < 0.05
Significant result **p < 0.01

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Preliminary results H70

H70 – results – Sleep latency

	Memory		Language		Speed		Executive function		Global cognition	
	(12 object recall, thurstone)		*(category fluency)*		*(psif)*		*(srb2)*		*composite score*	
	n	Est. (95% CI)	n	Est. (95% CI)	n	Est. (95% CI)	n	Est. (95% CI)	n	Est. (95% CI)
Sleep latency - Model 1	781		893		801		774		807	
Level at baseline		**-0.52 (-0.94; -0.10)**		-0.74 (-1.63; 0.16)		**-1.25 (-2.21; -0.30)**		**-0.93 (-1.71; -0.15)**		**-0.74 (-1.23; -0.24)**
Slope		-0.01 (-0.06; 0.04)		-0.03 (-0.12; 0.06)		0.06 (-0.07; 0.19)		0.01 (-0.09; 0.11)		0.00 (-0.05; 0.06)
Sleep latency – Model 2	750		861		769		746		775	
Level at baseline		**-0.58 (-1.05; -0.11)**		-0.71 (-1.71; 0.30)		**-1.21 (-2.26; -0.16)**		-0.76 (-1.62; 0.09)		**-0.67 (-1.23; -0.11)**
Slope		-0.01 (-0.06; 0.04)		-0.03 (-0.12; 0.06)		0.05 (-0.08; 0.18)		0.02 (-0.09; 0.12)		0.00 (-0.06; 0.06)
Sleep latency – Model 3	731		832		745		726		750	
Level at baseline		**-0.48 (-0.96; -0.00)**		-0.72 (-1.75; 0.31)		-0.80 (-1.86; 0.26)		-0.68 (-1.54; 0.18)		**-0.60 (-1.64; -0.03)**
Slope		-0.01 (-0.07; 0.04)		-0.03 (-0.12; 0.06)		0.03 (-0.10; 0.16)		0.01 (-0.09; 0.11)		-0.00 (-0.06; 0.06)
Sleep latency – Model 4	731		832		745		726		750	
Level at baseline		-0.45 (-0.93; 0.02)		-0.61 (-1.63; 0.42)		-0.75 (-1.81; 0.32)		0.60 (-1.47; 0.26)		-0.54 (-1.10; 0.02)
Slope		-0.01 (-0.07; 0.04)		-0.03 (-0.12; 0.06)		0.03 (-0.10; 0.15)		0.01 (-0.10; 0.11)		-0.01 (-0.07; 0.05)

Model 1: adjusted for age, sex, education
Model 2: adjusted for age, sex, education, hypnotics
Model 3: adjusted for age, sex, education, hypnotics, smoking, living along, alcohol consumption
Model 4: adjusted for age, sex, education, hypnotics, smoking, physical inactivity, living alone, alcohol consumption, diabetes, heart disease, cerebrovascular disease

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Preliminary results SNAC-GÅS

GÅS-results –duration (normal sleep = 7-8 hours, long sleep = 9 + hours)

	Episodic memory		Language		Speed of processing		Executive functioning		Global cognition	
	(16 word recall, recognition)		*(category and occupation fluency)*		*(pattern comparison and digit cancellation)*		*(Trail Making Test B, seconds)*		*composite score*	
	n	Est. (95% CI)	n	Est. (95% CI)	n	Est. (95% CI)	n	Est. (95% CI)	n	Est. (95% CI)
Normal vs. Long sleep- Model 1	1053		1100		1042		783			
Level at 72		**-0.18 (-0.35; -0.02)**		**-0.18 (-0.34; -0.02)**		**-0.19 (-0.35; -0.03)**		0.29 (-0.07; 0.50)		**-0.21 (-0.33; -0.09)**
Slope		-0.01 (-0.03; 0.04)		-0.02 (-0.05; 0.01)		**-0.04 (-0.07; -0.01)**		0.02 (-0.02; 0.07)		-0.01 (-0.04; 0.02)
Normal vs. Long sleep – Model 2										
Level at 72		**-0.18 (-0.35; -0.02)**		**-0.18 (-0.34; -0.03)**		**-0.19 (-0.34; -0.03)**		**0.29 (-0.07; 0.50)**		**-0.21 (-0.33; -0.09)**
Slope		0.01 (-0.03; 0.04)		-0.02 (-0.05; 0.01)		**-0.04 (-0.07; -0.01)**		0.02 (-0.02; 0.07)		-0.01 (-0.04; 0.02)
Normal vs. Long sleep - Model 3										
Level at 72		**-0.19 (-0.36; -0.03)**		**-0.17 (-0.33; 0.01)**		**-0.18 (-0.33; -0.02)**		**0.28 (0.06; 0.49)**		**-0.20 (-0.32; -0.08)**
Slope		-0.01 (-0.02; 0.04)		-0.02 (-0.04; 0.01)		**-0.05 (-0.08; -0.01)**		0.02 (-0.02; 0.07)		-0.01 (-0.04; 0.02)
Normal vs. Long sleep - Model 4										
Level at 72		-0.09 (-0.27; 0.08)		-0.06 (-0.25; 0.11)		-0.10 (-0.26; 0.07)		0.13 (-0.09; 0.34)		-0.10 (-0.22; 0.03)
Slope		-0.06 (-0.07; 0.04)		**-0.02 (-0.05; -0.01)**		**-0.04 (-0.07; -0.01)**		0.02 (-0.02; 0.17)		-0.01 (-0.05; 0.02)

Model 1: adjusted for age, sex, education
Model 2: adjusted for age, sex, education, hypnotics
Model 3: adjusted for age, sex, education, hypnotics, smoking, living alone, alcohol consumption, physical inactivity, depression
Model 4: adjusted for age, sex, education, hypnotics, smoking, living alone, alcohol consumption, physical inactivity, depression, stroke, myocardial infarction, artrial fibrilation, diabetes, heart failure and hypertension

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Conclusions

- Difficuilties to draw conclusions on sometimes conflicting results
- Possibilities to draw conclusions on sometimes conflicting results
- Opportunities to draw general conclusions on larger populations
- Time consuming to harmonize outcomes-, predictor- and control-variables
- Networking and share experience between study groups

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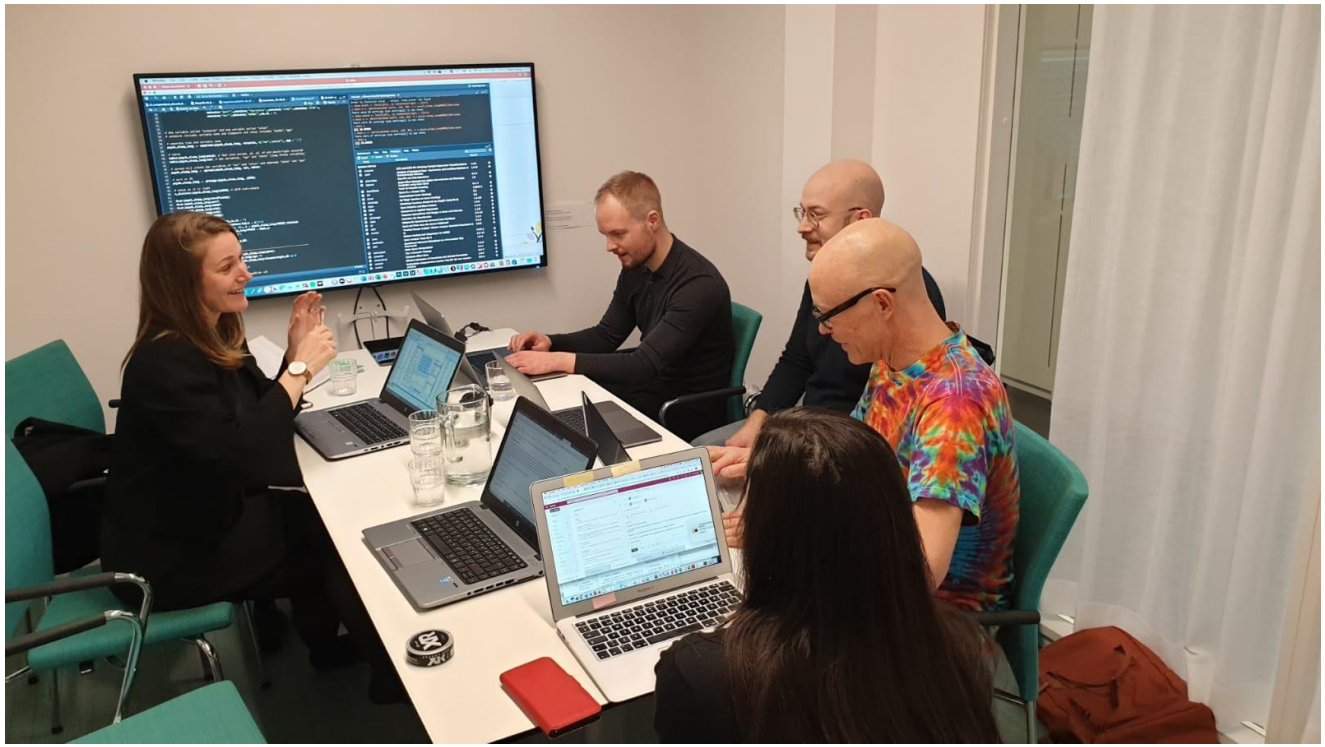
Thank you!



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