Geriatric Journal Club  
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Title: Sleep Disturbance and Older Adults’ Inflammatory Responses to Acute Stress


Background:
- Stress and the inflammatory response are implicated in a wide range of disease processes that affect physical and mental health.
- Sleep disturbance is independently associated with medical and psychiatric morbidity, and inflammatory function.
- Reciprocal relationships exist between sleep and inflammatory cytokines; regulatory pathways are not well understood.

Importance:
- Chose to present this study because it examines a common late-life problem, and raises important conceptual questions about the role of sleep in the health of older adults

Specific aims:
- Examine associations between sleep disturbance and interleukin-6 (IL-6) responses to acute mental stress in older adults
- Hypotheses:
  1. Sleep disturbance in healthy older adults will be associated with larger IL-6 responses to mental stressors
  2. Negative emotional arousal and diminished cognitive function will mediate the association between poor sleep and IL-6 response in older adults
  3. Loneliness and perceived stress will also affect the association between poor sleep and IL-6 response in older adults

Methods:
- General design
  - Observational study of community-dwelling, healthy older adults

- Procedures
  - Ascertained cognitive status, and administered health, medication use, and sleep questionnaires at baseline distinguished poor vs good sleepers
  - Administered neuropsychological tests of verbal and working memory as a standardized stressor and to measure cognitive function
- Affect was assessed at 0 and 60 minutes after the completion of cognitive testing
- Venous blood for IL-6 levels was collected at 0, 20, 40, 60 minutes after cognitive testing

Sample
- Healthy men and postmenopausal women age 50 and older
- Excluded those w/health problems having immune or endocrine features (e.g., cancer, stroke, diabetes, recent surgery); smoking; dementia; EtOH excess; obesity or underweight; use of psychotropic drugs or any sedative/hypnotics.
- Final sample of 45 women, 38 men
- Mean age 61.6 years (SD=8.78, range=50-87 yrs)
- 92% white, 6% black, 1.2% Latino, 1.2% American Indian/Alaska Native

Measures/Self-report and Laboratory
- SLEEP QUALITY: Pittsburgh Sleep Quality Index (PSQI)
- NEGATIVE AFFECT: Positive and Negative Affect Schedule (PANAS)
- GLOBAL PERCEIVED STRESS: Perceived Stress Scale (PSS)
- LONELINESS: UCLA Loneliness Scale
- DEPRESSIVE SYMPTOMS: 30-item Geriatric Depression Scale (GDS)
- VERBAL MEMORY: Auditory Verbal Learning Test (AVLT)
- WORKING MEMORY: Auditory Consonant Trigram Task (ACTT)
- IL-6 assays

Statistical Approach
- Poor sleepers (PSQI>5) vs good sleepers (PSQI≤5) compared with t-tests and chi-square tests on continuous and categorical variables, respectively
- Pearson correlation coefficients to evaluate for associations between covariates and variables of interest (e.g. GDS and education level for analysis of cognitive performance)
- Regressions to control for effects of age, BMI, depression, stress and loneliness on IL-6 response between sleep groups

Results:

Participants (Table 1)
- 27% had PSQI score>5 (poor sleepers)
- Poor sleepers had more loneliness, global perceived stress, and depressive sx (but on average were not clinically depressed)
- No differences between good and poor sleepers in age, gender, BMI, antihypertensive or statin drug use, or baseline IL-6

IL-6 response to cognitive testing (Table 2, Figure 1A)
- Baseline IL-6 not associated with GDS, PSQI; did not differ by sleep group
- Signif increases in IL-6 in both groups from baseline to 60-min post-test
- Poor sleepers had signif larger increase in IL-6 from baseline to 60-min post-test after controlling for baseline IL-6, age, BMI, GDS
Affective response to cognitive testing
- Negative affect increased from baseline to immediate post-test, but returned to baseline at 60-min post-test (Fig 1B)
- Poor sleep was associated with larger increases in negative affect post-test after controlling for GDS score (Fig 1B)
- Sleep group remained a significant predictor of IL-6 change after controlling for negative affect change in response to cognitive testing stress (Table 2, regression model 2), i.e., negative affect not a mediator of IL-6 response

Other variables of interest
- No difference in immediate and delayed verbal recall (AVLT) between good and poor sleepers
- No difference on working memory scores after adjusting for age and education
- Association between poor sleep and greater IL-6 change persisted after adjustment for perceived stress and loneliness

Author’s Conclusions:
- Association between poor sleep and IL-6 response to acute stress was not explained by psychosocial factors known to be linked to immune dysregulation (depressive symptoms, perceived stress, loneliness)
- Age-related changes in both sleep and immune regulation (greater acute inflammatory stress response in addition to immunosenescence) may leave older adults more vulnerable to deleterious effects of sleep disturbance
- Poor sleep may be an independent risk factor for poor mental and physical health

Reviewer’s Comments:
- Post-test levels of IL-6 found here have been previously shown to increase risk of morbidity and mortality in older adults
- Causal pathways still unclear: does poor sleep cause increased inflammatory response, or vice versa? Other studies have linked poor sleep to higher IL-6 levels at rest.
- Small sample size to detect mediating effects of depression, perceived stress, loneliness
- PSQI is self-report instrument. Don’t know what polysomnography would show
- PSQI scores do not make a diagnosis of primary insomnia. Not known if same IL-6 response occurs in those individuals

Practice Implications:
- Sleep may be a target for interventions to modify stress-induced levels of inflammatory cytokines
- At this time, can’t claim that treatment of poor sleep quality is a way to reduce morbidity or promote successful aging