Sleep, Circadian Rhythms, and Aging: New Avenues for Improving Brain Health, Physical Health and Functioning

Current State-of-the-Art Report: It's Not What We Know, But What We (Think We) Want to Know

Michael V. Vitiello, PhD University of Washington

State-of-the-Art Mandate

- List the two to four most important questions that you believe need to be addressed within the next five years for optimal advancement of sleep research/medicine in the context of sleep and aging.
- Answers will be summarized and presented at the beginning of the meeting and then discussed towards the end of the meeting to determine how they align with the meeting presentations and what future research directions might prove most fruitful.

Responses

- 54 Attendees
 - 5 Program Committee
 - 10 Faculty/Presenters
 - 3 NIH Staff
 - 36 Attendees*
- 149 Responses

Method

- General review and identification of key words/terms
- Key word/term searches
- Cluster responses
- Synthesize responses
- Organize/structure (but not prioritize) responses
- Review for potential gaps, omissions, etc.
- Report out...

Key Words / Terms

- Sleep 175 (Duration, Quality, Disturbance, Need, Disorders ~9/ea, Nap 2, Fragmentation 2 / Architecture 3, Cycle 1, Slow Wave 1)
- Circadian 22, Rhythm 13
- Age 33, Aging 23, Older 53 / Age-related 9
- Function 29
- Cognitive 26, Brain 8, Learning 1, Memory 1
- Treat/Treatment 18, Intervention 11
- Risk 16 (risk factor 2)
- Apnea 15, Hypoxemia 2
- Dementia 12, Neuro 8, Amyloid 4, Molecular 3, Inflammation 3

Key Words / Terms

- Insomnia 11
- Normal 9
- Consequences 8
- Disease 8, Illness 5
- Pharm 6, Hypnotic 2, Sedative 1
- Behavioral 5
- Glymp 4, CSF 1
- Metabolic 4, Cardio 4, Sympatho-vagal 1
- Falls 2

Key Words / Terms

- Costs 2
- Biomarkers 2
- Race 2, Ethnicity 1 / Disparities 2 /Gender 1
- PLM 1
- Co-morbid 1
- Biological 1, Physiological 1, Physiologic 1
- Hypocretin 1
- No mentions Gene/Genetic, RCT, Trial, Sex, REM, EEG/QEEG

Observations

- No clear predominance of key words and terms.
- No clear predominance of specific research questions.
- Suggested research questions were typically siloed by the contributor and their expertise or interest.
 - This in retrospect is not surprising given that aging is a broad research area and program committee members, faculty and participants were specifically chosen to represent a wide range of interests within that broad arena.
- Rarely were both bench <u>and</u> bedside questions raised by a single respondent.
- Often the general impact of sleep in the context of aging was a constant although the end point to be determined varied.

Organization / Structure

- N.B. Both aging and sleep/CRs are very complex phenomena.
- N. B. It is important to recognize that sleep and circadian rhythms and their disruptions can be both causes and effects, and sometimes both. Such complexity may not always be noted.
- This Conference explores the impact of sleep and circadian rhythms on brain health (B) and bodily/physical health (P) and general function (F).
- A research goal could well be common to all three domains.
- An attempt was made to organize research goals from "bench to bedside" across these three domains, noting commonalities.
- The number of overarching goals was kept to ~10.

Sleep and Aging - <u>Overarching</u> Research Questions

1. What are the mechanisms by which sleep (normal, insufficient, disturbed) effects normal aging (e.g.; cognitive function (B), P, F)?

- Are they reversible?
- If so when?

2. What are the mechanisms by which sleep (normal, insufficient, disrupted) effects diseases typically co-morbid with aging (e.g.; neurodegenerative (B), cardio and cerebrovascular (P), metabolic (P), other...)?

- Are they reversible?
- If so when?

Sleep and Aging - <u>Overarching</u> Research Questions

- 3. What is "normal" sleep across the older adult life span?
- 4. Does the "need" to sleep change with age?
- 5. Is the impact of habitual sleep duration (both long and short) on health (B, P, F) a function of age?
- 6. Do the mechanisms by which sleep disorders (e.g.; apnea, insomnia, CRDs) impact health (B, P, F) vary by age?

Sleep and Aging - <u>Overarching</u> Research Questions

7. What are efficacious/effective methods to improve sleep in older adults and do they also improve other measures of health, e.g.; ameliorate co-morbid illnesses such as depression, pain syndromes, cognitive impairment, etc. (B, P), and function (F)?

• What are the potential savings in healthcare utilization and costs?

8. What are the roles of sleep, hypnotics, nocturia, delirium and institutionalization on function, falls (F) and cognitive impairment (B) in older adults and what are the implications for prevention?

• What are the potential savings in healthcare utilization and costs?

9. Are any of the above modified by sex, race, ethnicity, SES, etc.?

Exercise for the Tuesday Afternoon Session

- These overarching goals will be restated.
- Small groups will discuss them in .
- The groups will then report out as to:
 - Would you modify any of these overarching research goals, and if so how?
 - Would you eliminate any and if so which?
 - Would you add any and if so what would they be?
 - Which two of the group's final list are particularly high priority?
 - Which one or two of the group's goals might be considered "low hanging fruit"?

1. What are the mechanisms by which sleep effects normal aging, are they reversible and if so when?

2. What are the mechanisms by which sleep effects diseases typically co-morbid with aging, are they reversible and if so when?

- 3. What is "normal" sleep across the older adult life span?
- 4. Does the "need" to sleep change with age?
- 5. Is the impact of habitual sleep duration on health a function of age?
- 6. Do the mechanisms by which sleep disorders impact health vary by age?
- 7. What are the best methods to improve sleep, do they also improve other measures of health and what are the healthcare utilization and cost savings?

8. What are the roles of sleep, hypnotics, nocturia, delirium and institutionalization on function, falls and cognitive impairment and what are the implications for prevention? What are the healthcare utilization and cost savings?

9. Are any of the above modified by sex, race, ethnicity, SES, etc.?