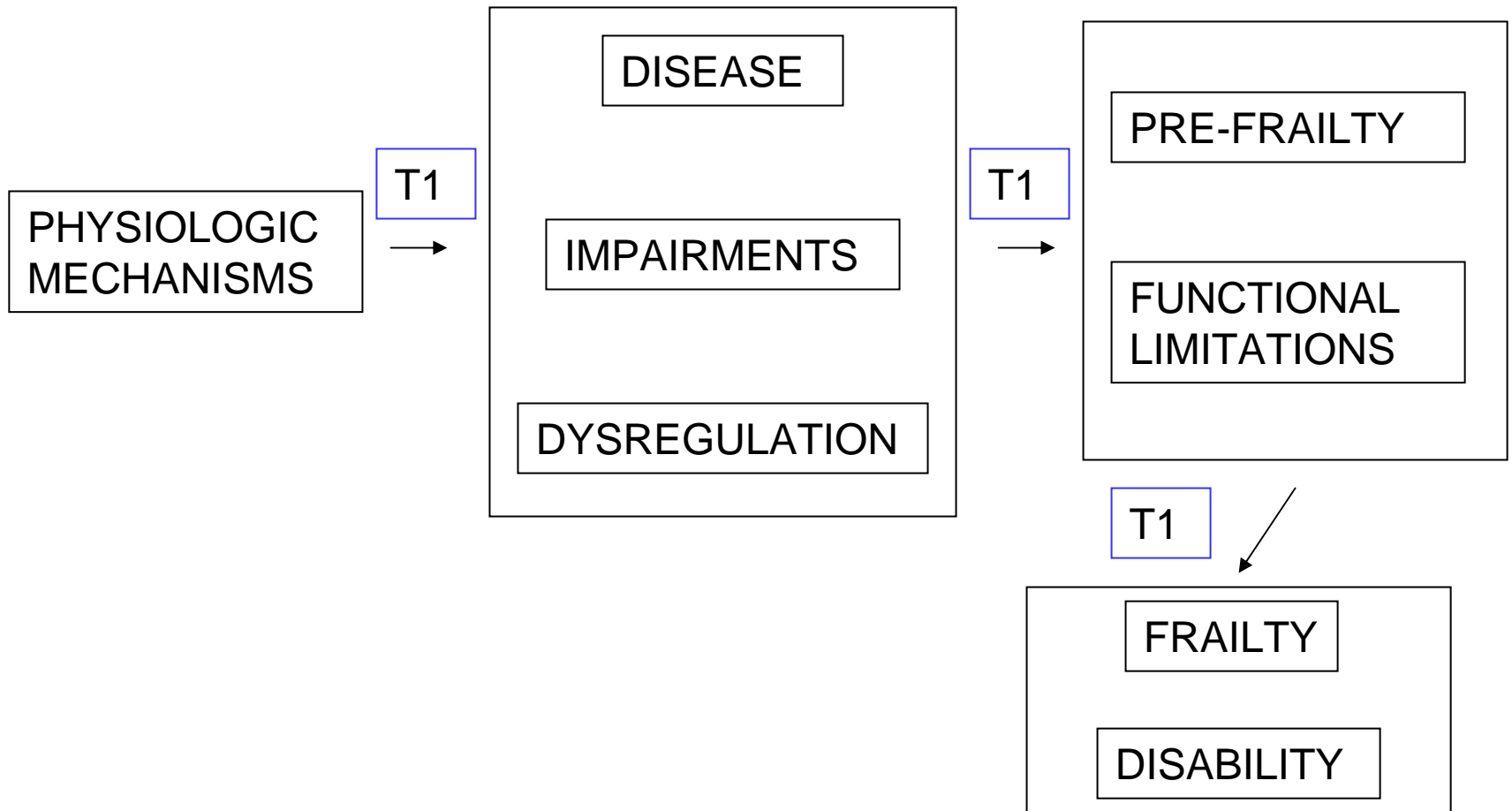


Summary discussion

JHU OAIC Retreat
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T1 Translation



Where do we stand with sleep?

T1

- Intervention trials (or, interventions)?
 - SWS stimulation increases GH—but reduced in older adults

Where do we stand with sleep?

T1

- Pathway links?

- Evidence:

- Highly **associated with age**: complaints, insomnia, changes in architecture, circadian rhythm—**loss of complexity**?
 - **Nocturnal growth hormone, evening cortisol changes** with age (some gender issues; other neuroendocrine?—leptin, ghrelin, glucose sensitivity assoc with sleep deprivation)
 - Also: direct affects of sleep on **GH axis**; tie to HPA axis
 - **Hypothesis: shift in anabolic / catabolic balance**
 - Chronic stress **affects sleep**; cortisol association, catecholamines
 - Sleep stage modulation of autonomic nervous system fn
 - Lower distal-proximal **skin temperature** difference associated with lower sleep latency

Where do we stand with sleep?

T1

- Pathway links?

- Evidence:

- Increase in **pro-inflammation** with OSA & severity (but: not a surrogate of obesity, CVD, etc.?—hypox/ oxidative stress)
- **T-cell phenotype** association with OSA; reduced immunity right after deprivation
- **Energy homeostasis** —leptin, ghrelin, glucose sensitivity assoc with sleep deprivation; also, deprivation changes chaperoning of proteins
 - (**more?**) **Links to hunger / satiety**: Orexins (induce eating)
 - **Melatonin**: tied both to sleep onset and may improve mitochondrial efficiency
 - Duration and energy expenditure: complex (“more time to expend if awake more” vs appetite, glucose, etc. pathways)

Where do we stand with sleep?

T1

- Pathway links?
 - Potential (indirect?) Evidence:
 - Major correlate of major depression
 - Associated with increased risk of future falls (issue: when the falls occurred—daytime, nighttime part)
 - Insomnia predicts CVD
 - Pain sensitivity decreases with decreased sleep...
 - But, insomnia treatment seems to affect pain
 - Etc....
 - Increased incidence of cognitive decline (but conflicting evidence)?
 - Sedentary lifestyle as a potential link (maybe not causal?)

Where do we stand with sleep?

T1

- Pathway links?
 - Gaps:
 - Relationships of architecture components to health
 - *** Very little lit on sleep and frailty
 - Quite little on sleep and immune function
 - Little direct info on sleep and energy

Where do we stand with sleep?

T2

- Practice translation studies?
 - Evidence:
 - Less resiliency to sleep deficiencies?

 - Gaps:

Where do we stand with sleep?

T3

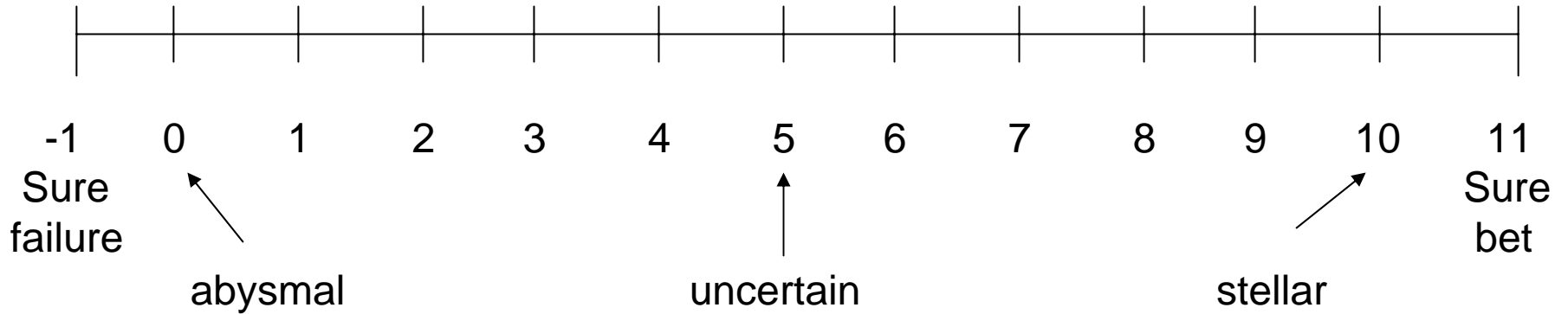
- Systems biology approach
 - Sleep is a complex process
 - Human work on transitions exists; our expertise
 - (Frailty: benefits for framework, definitions)
 - Sleep effects span multiple systems
 - Some existing work: sleep-wake rhythms
 - Homeostatic and circadian integration (offsetting mechanisms—but erodes with long awake time)
 - Multiple interacting oscillators

Where do we stand with sleep?

T3

- Practice
 - Sleep intervention
 - Lunesta: decreased insomnia; decreased depression (drugs)
 - Behavioral—sleep hygiene, cognitive therapy—effective according to NIH—but are the effects clinically meaningful?
 - Temperature: core, skin temperature manipulation associated with improved sleep architecture
 - CPAP
 - GH affects sleep in non-elderly with GH deficiency
 - Other
- Methods
 - Measurement of sleep quality
 - Phenotypes are getting there
 - Other
 - LF/HF ratio problematic re sympathetic / parasympathetic tones
 - Nonstationarity is a major challenge
 - Causal directionality
 - Sleep Heart Health is a resource

How promising is sleep as an intervention target for ameliorating frailty?



Action items

- Further assessment of the evidence base
 - Findings? Type/quality? Synthesis?
- Pilot research
- Longer view

Models other than sleep?

Action items
