

Learning for Life Week 2 Summary 10-3-18

Topic: New Discoveries About Sleep and Its Impact on the Brain

Speakers: Fred Turek PhD and Phyllis Zee MD, PhD

A theme that permeated both presentations today was the reciprocal feedback loop between the brain and the peripheral body cells, organs and systems. The focus was on sleep and the body's circadian clock and how critical these processes are in health and disease.

The brain's "master clock" is located in the suprachiasmatic nucleus (SCN). Fred referred to this as the "control room". But, as we heard last week, there are clock genes in all major tissues and organs which also have internal rhythmicity. They communicate with the SCN through neural and hormonal mechanisms. Understanding that so many of the body's functions are regulated by circadian clocks helps us begin to understand why certain diseases may be outcomes of disruptions of the clocks. Fred illustrated this by telling us about the process by which a genetic mutation was discovered in a mouse whose sleep/wake rhythm was dysfunctional. These mice were more likely to be obese, have prediabetes and early heart disease. Additional experiments in mice involving the timing of meals demonstrated that eating during the "wrong time" of the day led to weight gain. This has significant implications in the treatment of obesity, and we are understanding that it is no longer just about what we eat, but also when we eat. The circadian clocks determine a tremendous number of metabolic and cellular functions. We are just beginning to understand the implications. For a summary of the relationship between the central and peripheral clocks, see an article written by one of our Gastroenterology Fellows, Keith Summa, and Fred Turek in *Scientific American*: THE CLOCKS WITHIN US. By: Summa, Keith C., Turek, Fred W., *Scientific American*, 00368733, Feb2015, Vol. 312, Issue 2

Phyllis then spoke about the clinical implications of circadian clocks and sleep. She described two major systems:

1. The **homeostatic** drive for sleep where substrates build up during the day in the brain and increase your drive for sleep. These are then washed out via the cerebral spinal fluid and the lymphatic system overnight, reducing the drive for sleep and resulting in waking up.
2. The **circadian** system which is pervasive in our brain and peripheral organs (see above) and subject to genetic and metabolic disruptions leading to behavioral changes and disease.

Thirty percent of adults get insufficient sleep. After 18 hours of sleep deprivation, a person functions at the same level as someone who is under the influence of alcohol beyond the legal limit for driving. Sleep consolidates learning and memory, and we have already heard how it serves a critical function to wash out the toxins and substances that build up in the brain over the daytime. The implications for elderly patients with cognitive decline and dementia are obvious. Deep sleep or slow wave sleep is particularly important. Phyllis described the research she has been involved with deep sleep can be enhanced through "pink noise" machines linked to brainwaves.

We learned about the importance of timing of sleep, and how light pollution in modern cities is going to impact the quality of sleep.

Take Home Points

1. Circadian clocks are in the brain and in all the peripheral organ systems, and they play a critical role in health and disease in ways that we are just beginning to understand.
2. Circadian rhythms affect metabolic pathways that lead to obesity, heart disease, cancer, dementia and many other conditions.

The time that you eat may just as important as what you eat. Don't eat after dark if you are trying to lose weight.

3. Research in this area is exploding and Northwestern is at the forefront. Given the implications, there are many varied organizations interested in this- from NIH to the Department of Defense.