

Sleep research, from molecules and circuits to behavior

October 26 2015, by Jeremy Borniger



The Society for Neuroscience 2015 annual meeting was rife with research on all aspects of sleep and arousal. Indeed, several symposia and dozens of posters covered topics ranging from the most basic look at the molecules involved in sleep/wake states, to whole network systems. In this post I will cover a small sample of what I found particularly interesting at the meeting (keep in mind, though, that I was not able to get to everything!).



A particularly interesting minisymposium was entitled "Disrupted Sleep: From Molecules to Cognition" chaired by Eus Van Someren. A complete summary of all the talks can be found here. Derk-Jan Dijk, from the University of Surrey in the UK presented some very interesting data on what happens to the transcriptional profile of cells in human blood when sleep is disrupted. Normally, he said, ~6.4% of the blood 'transcriptome' shows a circadian pattern of transcription. When sleep is restricted or mistimed, however, the rhythmic day-night difference in transcription of genes drops down to $\sim 1\%$. Many of these genes are involved in metabolic and immune pathways, important for maintaining homeostasis and health. Chiara Cirelli spoke on the ultrastructural changes that occur on the subcellular level in response to sleep disruption. She and her team have found that when sleep is restricted, mitochondria seem to enlarge and alter their shape, and lysosomes become more active as well. Furthermore, sleep disruption increased the prevalence of lipofuscin, a lysosomal byproduct that is usually associated with normal and advanced aging. Astoundingly, they were even able to discriminate between animals that had normal sleep/wake cycles and those with disrupted sleep just on the basis of changes in subcellular architecture with $\sim 75\%$ accuracy!

Michael Chee further discussed behavioral changes associated with sleep loss, focusing on vigilance. He showed that there are people that seem to be resistant to the reducing effect of sleep disruption on vigilance. It would be useful to be able to tell who was susceptible to the negative effects of sleep loss, as many important jobs inherently disrupt sleep (e.g., air traffic controller, night-shift ER personnel, etc...). If vigilance is impaired in these populations, that could result in serious accidents and potential loss of human life. He discussed how heart rate variability, an easy to measure proxy of autonomic nervous system function, could discriminate between people who were vulnerable to the vigilancereducing effect of sleep disruption and those who were not.



Outside of this event, other talks focused more on the circuitry involved in normal sleep/wake states. For example, William Wisden chaired a session on how the hypothalamus controls behavior, where much emphasis was on sleep. He showed that the circadian clock in histamineproducing neurons alters sleep architecture, because a component of the circadian clock (Bmal1) suppresses the transcription of histidine decarboxylase, the rate-limiting enzyme in the histamine synthesizing pathway. When this clock component is missing, it leads to altered histamine signaling and therefore altered sleep/wake states. Finally, Antoine Adamantidis showed recent work demonstrating that a novel circuit exists using the neurotransmitter GABA. This circuit from the lateral hypothalamus to the thalamic reticular nucleus promotes arousal. The theme to these talks was the emphasis on optogenetic and DREADD techniques to activate/deactivate specific populations of cells with temporal and spatial precision.

This year's SfN meeting provided an arena to discuss new evidence for the detrimental effects of <u>sleep disruption</u>, from altered subcellular ultrastructure to changes in fMRI readouts and ultimately behavior. Additionally, new research was presented on the basic components of natural sleep, with special emphasis on the lateral hypothalamus and integrative networks involving numerous neurotransmitter systems connecting the brainstem to the cortex through thalamic relays. I am excited to see what the future holds and can't wait until next year's meeting!

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