

Background



Narcolepsy is a sleep disorder that is categorized by daytime sleepiness and sometimes sudden attacks of sleep, or cataplexy. There are two subtypes of narcolepsy: type 1, narcolepsy with cataplexy, and type 2, narcolepsy without cataplexy. Scientists do not fully understand the **pathogenesis** (how a disease develops), but they have discovered evidence that narcolepsy is caused by the loss of hypocretin-producing neurons. **Hypocretin** helps regulate sleep-wake cycles, and without it, the patient is susceptible to falling asleep at any given time. My goal is to understand what the prevailing theory of the cause of narcolepsy is by interviewing experts in the field.

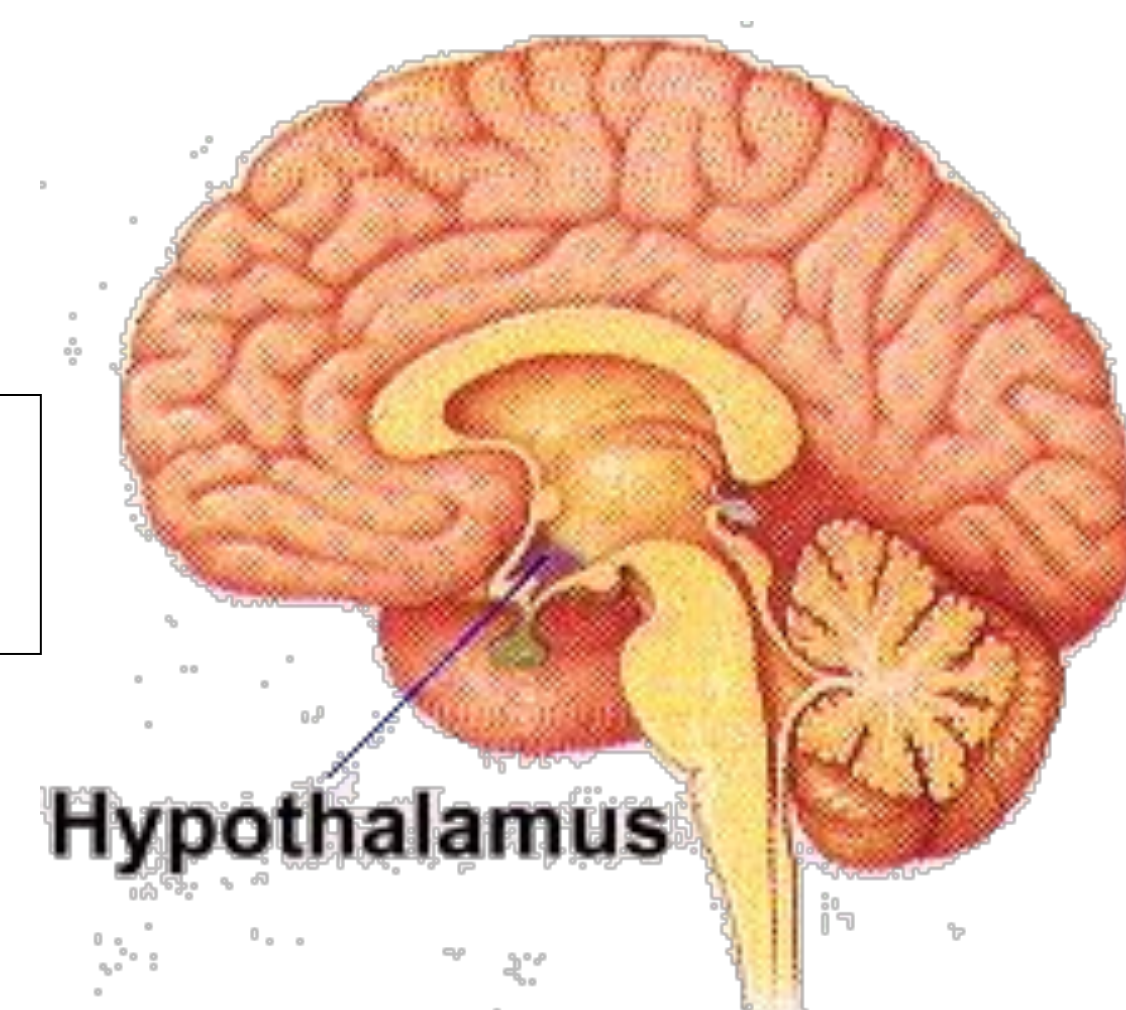


Fig 1: hypothalamus - where hypocretin-producing neurons are

DISTRIBUTION OF SLEEP STAGES OVER A 24 HOUR PERIOD:

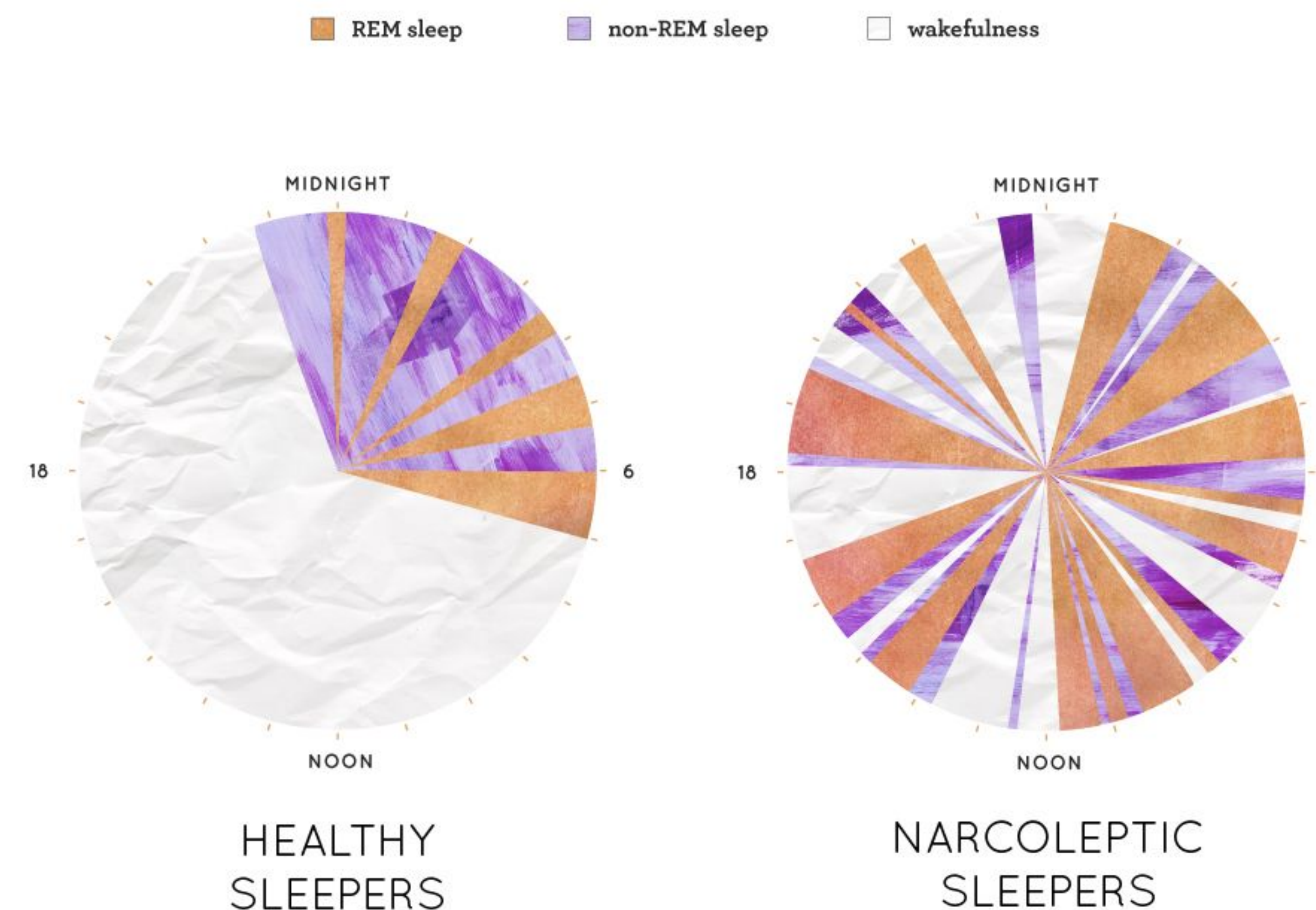


Fig 3: Narcoleptic sleepers fall into non-REM and REM sleep irregularly during the day, while also having disturbed sleep during the night.

Analysis and Evaluation



Because there is **no consensus** on the pathogenesis of narcolepsy, it was difficult for the professors interviewed to answer my questions exactly and specifically. However, they gave their opinions based on the limited data available, and were able to provide an abundance of information.

Much of the conversations were focused on the autoimmune aspect of narcolepsy. There has been **evidence** supporting this hypothesis, such as the **HLA predisposing gene**, so many professors believe in it. However, because it has not been proven, some are not confident.

Conclusions, Implications, and Next Steps



Based upon the data collected, current research is centered mostly on **animal research**, while some others did human research on the **effect of drugs and medications**. Many professors are not currently working on narcolepsy projects because they do not have enough funding and are unable to successfully continue their research. However, the ones who are actively conducting research focus their research on working with animal models, such as zebrafish, dogs, and mice, or on studying the effects of different medications.

I also noticed that while the idea of narcolepsy as an autoimmune disease is not fully supported by evidence, many professors believe this hypothesis and are working to prove it.

My goal is to pursue opportunities for laboratory research this summer with one of the professors I interviewed. I would like to use animal models to further explore the role of hypocretin in the regulation of normal sleep cycle and how narcolepsy is triggered. This research would help researchers understand what drugs and medications would best cure this disease.

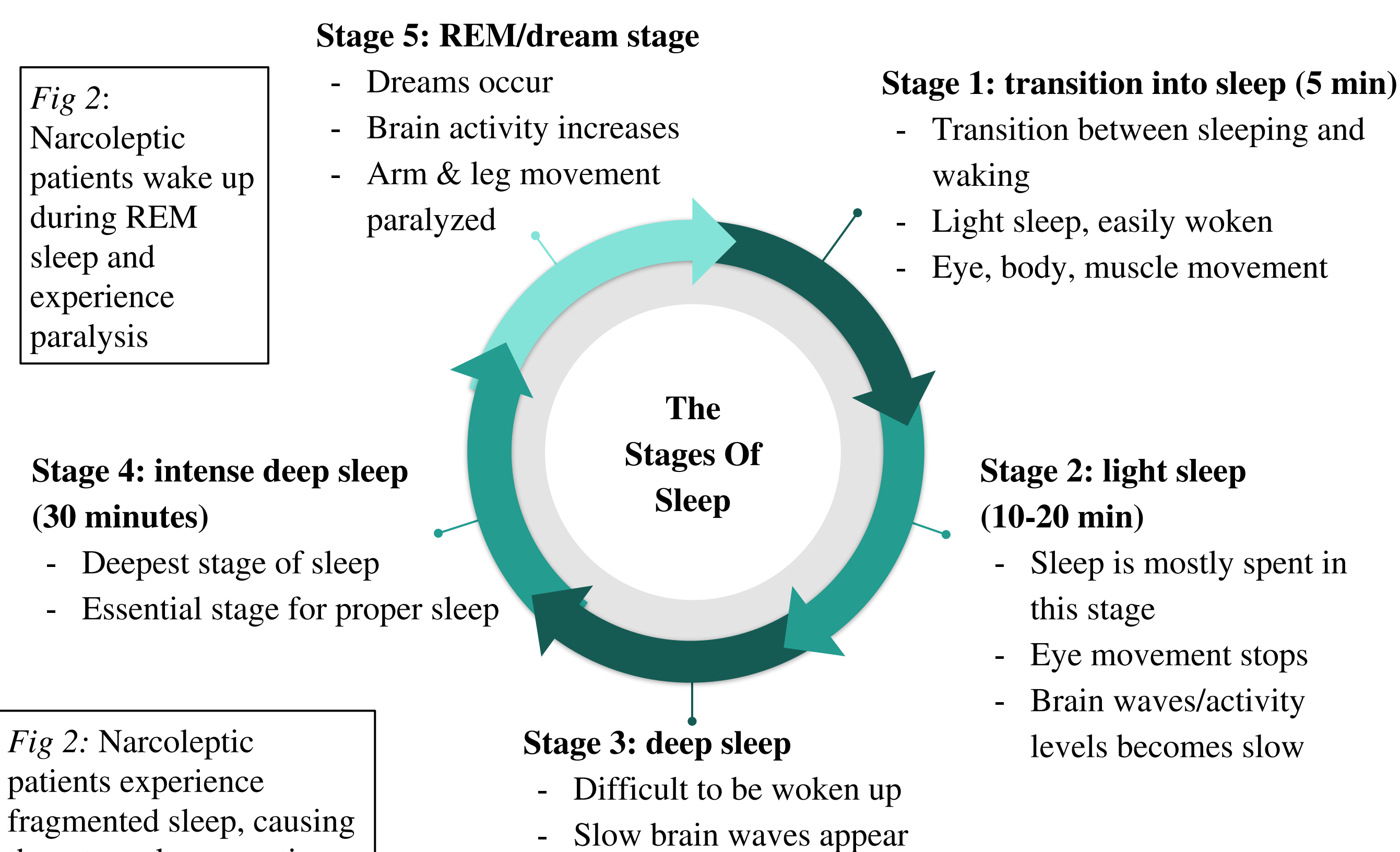


Fig 2: Narcoleptic patients wake up during REM sleep and experience paralysis

Fig 2: Narcoleptic patients experience fragmented sleep, causing them to wake many times during the night.

Data and Findings



60% of professors interviewed believe narcolepsy is an autoimmune disease

- however, only a hypothesis they are working to prove it
- professors from Stanford are more confident than those from Harvard

100% of professors interviewed believe animal models reflect human disease

- animal models help researchers look at anatomy of hypocretin system
- helps them research and understand autoimmune component

100% of professors asked believe zebrafish models are transferable to mammals

- professors believe that zebrafish are easier to work with
- can easily see neurological development
- light activation is used to test

20% of professors interviewed are actively conducting narcolepsy research

- because of insufficient funding, only one professor is actively conducting research
- may be b/c of lack of awareness raised for the disease and the fact that it is not fatal

Methods



Grounded Theory:

Interviews:

1. Literature research: I found professors knowledgeable in the field.
2. Email: I reached out to professors to ask for availability and consent.
3. Publication Research: I researched the interviewees' publications in order to formulate questions relating to their expertise.

Acknowledgements/References



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Works Cited:

About narcolepsy. (n.d.). Retrieved August 29, 2017
 Black, J. (2018, February 11). Personal Interview.
 Brown, R. (2017, December 11). Personal Interview.
 Division of Sleep Medicine at Harvard Medical School Staff. (2013, July 19). The science of narcolepsy. Retrieved September 8, 2017
 Elbaz, I., Yelin-Bekerman, L., Nicenboim, J., Vatine, G., & Appelbaum, L. (2012, September 12). Genetic ablation of hypocretin neurons alters behavioral state transitions in zebrafish. Retrieved February 27, 2018
 "Interview to Dr. Gerrit Jan Lammers, 1st European Narcolepsy Day." *Neurologia*
 Kapella, M. C., & Carley, D. W. (2017). Narcolepsy. Retrieved October 3, 2017
 Kawai, M. (2018, January 25). Personal Interview.
 Leary, E. (2018, January 31). Personal Interview.
 Mayo Clinic Staff. (2015, September 1). Narcolepsy. Retrieved August 29, 2017
 McDowall, J. (n.d.). [T cell receptors]. Retrieved October 10, 2017
Narcolepsy v normal sleep [Photograph]. (n.d.).
 NIH Staff. (2017, September 5). Narcolepsy. Retrieved September 6, 2017
 NIH staff. (2017, October 17). Human leukocyte antigens. Retrieved October 21, 2017
 Ollila, H. M., Fernandez-Vina, M., Mignot, E., Ravel, J.-M., Han, F., Faraco, 2017