Background:

Circadian Rhythms are physical, mental, and behavioral changes that follow a 24-hour cycle. These natural internal processes affect most living things, including animals, plants, and microbes. One example of a light-related circadian rhythm is sleeping at night and being awake during the day [1]. Although circadian rhythms are endogenous, they are adjusted to the local environment by external cues called zeitgebers (German for "time givers"), which include light, temperature, and redox cycles [2]. And has been found that the light/dark cycle of the sun has a powerful effect on the circadian clock, sleep, and alertness [3]. Lots of professional jobs require the individuals to work for extended number of hours beyond the regular 8 hours (like in some cases up to 12 hours or more a day), causing a reduced number of hours of sleep, and a disruption of their circadian rhythm.

AIM:

To build a model to verify if being exposed to unbalanced light–dark cycles by itself, could have an impact on the production of CLK (during light) and PER2 (during dark) proteins, and therefore the aging of an individual when it is continuously done for several months or even years.

Research Plan:

- Use Klotho-deficient mice because it is vertebrate mammal with circadian cycles of typically ~23.5 hrs., that has common features with human aging process such as short lifespan, hypokinesia, infertility, arteriosclerosis, osteoporosis, and brain alterations related to neurological disorders, and with an expected lifespan of around 8–9 week of age [4] [5]. Even though mice are nocturnal as contrary as human being diurnal, it can still be used by reversing light/dark cycles in the animal facility to try to provide a way to study mice during their nocturnal active phase, which may extrapolate better to human diurnal physiology [6].
- Breed 15 same age Klotho-deficient mice and place them in individual cages where the amount of food, water and light is being controlled, and their activity are recorded by individual cameras.
- Have them all available the same amount of food and water and expose them to 12/12 hours of light/dark for 2 weeks. In this way they will learn where the food and water are located inside the cage.
- Pick these 15 mice and perform a brain MRI.
- Group the mice in 3 groups of 5 mice, where their exposed to light/dark for the rest of their life will be 0/24 hrs., 12/12 hrs., and 24/0 hrs.
- Every week they will need to be sedated, weighted, and have brain MRI performed.
- Compare the weigh, brain MRI, monitored activities, as well as the lifespan of the three groups
- Verify if any of these variables have a significant difference than the rest of the groups.
- If there is one significant difference on one of the variables for the light/dark groups of 0/24 hrs., then repeat the experiment with fine tune groups of 4/20 hrs., 8/16 hrs.
- If the significant difference happens on the light/dark groups of 24/0, then repeat the experiment with fine tune groups of 20/4 hrs., 16/8 hrs.
- I would expect that the 12/12 hrs. group would be the one with the largest life span.
- Also, I would expect that the equivalent to the human's "long light and short dark" exposure would have the highest impact on any of the variables. I think that most likely there would be a

weigh and physical activity difference. And probably, there would be a shorter lifespan and a brain disease would appear sooner than the 12/12 hrs. group.

- This would indicate that there is a possible connection between sleeping few hours a day and the faster aging in humans.

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