AMUZA Case Study

Studying Circadian Rhythm Circuitry with Optogenetics

Studying circadian rhythms is crucial as these innate biological rhythms govern nearly every aspect of our physiology, behavior, and health. From regulating sleep-wake cycles to influencing hormone production and metabolism, circadian rhythms play a fundamental role in orchestrating the timing of biological processes. Disruptions to these rhythms have been linked to numerous health issues, including sleep disorders, mood disorders, metabolic syndrome, and even cancer. Understanding the mechanisms underlying circadian rhythms not only provides insights into basic biological processes but also holds immense potential for developing novel therapeutic interventions to improve human health and well-being.

Historically circadian rhythms have been particularly difficult to study. However, in recent years, novel tools have emerged to help dissect how circadian rhythms contribute to health and disease. Here we highlight the efforts of a researcher at Texas A&M University who is exploring novel ways of modulating circadian rhythms using wireless in-vivo optogenetics techniques. Our interview with them has been edited for formatting.

Anonymous Ph.D. Candidate at Texas A&M University.

Research Background

Amuza: What is the goal of your research? What social problem do you want to tackle?

Researcher: Our goal is to use optogenetic stimulation to adjust circadian rhythms in mice. The context for this is that in aging populations' circadian rhythms change and lead to early forms of disease. We optogenetically stimulate the suprachiasmatic nucleus (SCN) to modulate circadian rhythms and look for behavioral outcomes. In clinical populations there is a high correlation between changes in circadian rhythm and cognitive deficits.

Amuza: What are some of the biggest challenges you face during your research journey?

Researcher: Studying circadian rhythms needs to happen over at least a 24 hr period, so the nature of studying this is very chronic. We have to record the mice and manipulations over the course of days. This makes things challenging when incorporating optogenetics, especially with a tethered system that can obstruct their ability to live in the home cage.

Before Purchase

Amuza: How involved were you with researching the new system and purchasing process?

Researcher: I was the one who researched available options and made the decision to order the system.

Amuza: Did you have any other options for in vivo optogenetic stimulation/inhibition (wired or wireless)? If yes, please let me know which and why you chose TeleOpto?

Researcher: We looked into a combined optogenetics and fiber photometry system from Doric which was fairly expensive, we also looked into a tethered option from Thor Labs but the tethered configuration was not ideal for us.

Amuza: What are some key factors that led to your initial purchase of TeleOpto? What difficult challenges were you going to overcome with TeleOpto?

Researcher: A big factor was that the system seemed pretty straightforward to use. When I talked to the sales representative and went over the TeleOpto manual I was convinced it would be easy to set up. The receiver looked like it would be easy to remove and attach from the implant and light power delivery and probe customization was compatible with our overnight experiments. Additionally, the price was hard to beat, as it was much lower than competitors.

User Experience

Amuza: What benefits and features stood out to you during your research experience with TeleOpto?

Researcher: Again, it was very easy to set up and

get the system up and running. It was pretty painless to integrate a third party pulse generator to control stimulation, so compatibility with other hardware was nice. The battery life surpassed my expectation for longer term recordings.

Amuza: What type of animal model and optogenetic sensors do you use and why are they important?

Researcher: We are working with mice, specifically transgenic mice with Cre-dependent reporter gene expression of channelrhodopsin2 or other excitatory channelrhodopsins in the SCN. This allows us to artificially stimulate SCN neurons, which are involved in controlling circadian rhythms, and determine how this affects sleep/wake cycles and other behaviors.

Amuza: How was your experience using TeleOpto different from previous methods you have used for in vivo optogenetics?

Researcher: I've not had much experience with other commercially available in vivo optogenetics systems. We did try to build a custom system for both optogenetics and fiber photometry but found this challenging. The idea of a commercial kit seemed more straightforward and would save time.

Amuza: How likely are you to recommend TeleOpto to a colleague?

Researcher: I would recommend this system for more short term experiments such as drug-abuse studies, etc. While this system is an improvement over other tethered systems for circadian rhythm research, there are still some limitations. Minimal disturbance of the animals is ideal and the need for removing the receiver and charging the battery can lead to disruptions in animal activity cycles.

Amuza: How has TeleOpto improved your research? Has it helped you solve any difficult challenges you were facing in your research? Please let us know the details.

Researcher: While we did not generate positive results with this particular project, it was likely not due to the Teleopto systems ability to deliver proper light power to

the correct location. The issues likely were related to the need to handle animals in order to charge the receiver battery and power it on to begin stimulation sessions. This is why studying circadian rhythms is particularly difficult. However, we are now moving to begin using
the system with some of our drug abuse studies.

Amuza: Do you have any suggestions for improvements you would like to see in the future?

Researcher: While the battery life can last all night, it can't last multiple days, meaning the animals must be handled every day which can be challenging. It would be nice to see the battery life increased without significantly increasing the weight of the receiver.

Future Application

Amuza: Do you have any planned future applications for TeleOpto?

Researcher: We plan to move into using this system with our drug abuse models. Initial experiments are planned to implant probes in the dorsolateral striatum and place the animals in an open field and see if we can modulate locomotor activity via stimulation. If this is successful, we plan to explore modulating drinking behavior and fentanyl self-administration via modulation of striatal neuron activity.