SCI & CIRCADIAN RHYTHMS | GROWING YOUR OWN MEDS | WORKOUT ON A WALL

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SPINAL CORD INJURY BC

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Pleasure Principles

Dr. Stacy Elliott believes every person with SCI should unlock their sexual potential—and explains the steps they can take to do this

Questionable Timing

In the past, scientists have found evidence that SCI disrupts the body's internal clock. Dr. Andrew Gaudet, a University of Texas at Austin researcher and former ICORD investigator, is working hard to confirm and better understand the mechanisms and implications of this disruption—and develop strategies to lessen the impact.

The human body runs on a 24-hour biological clock known as the circadian system. It's a vital system, one that plays an important role in regulating virtually all of our body's functions.

The actions of the circadian system are triggered by light—specifically, blue light. The presence of light at the beginning of the day, for example, triggers the circadian system to tell the body that it's time to get up and get to work. As our world becomes darker each night, it tells the body that it's time to sleep and focus on the processes of replenishing our cells. These are known as circadian rhythms.

Scientists have hypothesized for decades that any injury to the spinal cord compromises our circadian system and circadian rhythms. The fact that many people with SCI report experiencing significant sleep disorders provides evidence of this. But the extent and the implications of this circadian disruption, throughout the time from acute to chronic SCI, aren't really well understood to this day.

Enter Dr. Andrew Gaudet, an assistant professor of psychology at the University of Texas, who has chosen to focus his research on the link between SCI and circadian functioning.

"It's been an interesting road that ended up merging my interests in SCI and circadian rhythms," says Gaudet, who lived in Vancouver for ten years.

His interest was first tweaked when, as an undergrad at UBC, he worked in the lab of ICORD's Dr. Matt Ramer, studying the immune response after SCI. After graduating with his PhD in 2010, he moved to Ohio State University to work with Dr. Phil Popovich, who is renowned for his work in nervous and immune system interactions after SCI.

"I completed postdoctoral research there between 2011 and 2014, studying inflammation and axon growth after SCI," says Gaudet. "In that time, I also met my future wife—a fellow researcher named Dr. Laura Fonken—on the 7th floor of our research tower, and we began collaborating on research related to inflammation of the nervous system, metabolism, and biological clocks. These studies continued at our next research positions, at University of Colorado Boulder—I was there between 2015 and 2018. This is where Laura and I collaborated, along with my supervisor Dr. Linda Watkins, in completing studies related to SCI and biological clocks."

The couple then secured their current positions as assistant professors at The University of Texas at Austin, where the focus of their research collaboration is almost exclusively circadian functioning after SCI.

"I'm developing a research program that involves SCI, and determining how biological rhythms influence post-SCI metabolism and functional recovery," says Gaudet. "My wife is an expert at neuro-immune interactions, endocrinology, metabolism, and circadian rhythms. We have lab meetings together and will continue to collaborate, which creates a unique perspective for studying issues after SCI."

This husband and wife synergy was very much in evidence with the recent publication of an animal study in the online journal eNeuro that confirms the disruption of circadian functioning in the first days and weeks after SCI delays—and suggests the disruption might actually limit recovery.

"Previous research has focused on how SCI affects other parts of the body, but this is the first study to reveal the widespread, domino-like disruption an injury might have on these rhythms that are crucial for health," says Gaudet. "It was known that SCI impairs metabolism—for instance, predisposing individuals to cardiovascular disease and increased fat mass. It was also known that circadian disruption alters metabol-

ism—for instance, eating the same amount at the wrong time of day can lead to obesity. However, no one had systematically addressed this question: does SCI disrupt circadian rhythms?"

In order to explain his research, Gaudet suggests that we think of the circadian system as a corporate structure.

"It consists of a president or CEO—the suprachiasmatic nucleus of the brain," he says. "That part of the brain only responds to light—particularly blue light—from the eyes, and sends this information to middle managers, which include certain hormones, body temperature, movement and activity, eating, and autonomic function. The middle managers integrate this information from the CEO with other information from the body—about stress, for example—in order to tell every organ and cell in the body what time it is, and what each cell should be doing. So the liver knows what time it is and is ready for food at 7 AM, whereas the liver releases stored energy and is not timed for food at 12 AM."

In their study, Gaudet and Fonken compared the rhythms of two of these middle managers, body temperature and movement/activity, in two groups of rats—one with moderate SCIs, the other uninjured. What they observed was that these rhythms almost completely disappeared immediately after injury, but gradually recovered within one to two weeks. They also assessed levels of another middle manager, the hormone corticosterone, and found that it too was disrupted soon after injury, but recovered within two weeks.

"Overall, this moderate injury disrupted rhythms in various middle managers and outputs of the circadian system," says Gaudet.

Armed with this knowledge, he next wants to push forward with research to determine if and how circadian disruption also restricts neurological recovery.

"Since every cell in our body contains its own clock, and this clock is linked to many other functions in our body, I would predict that circadian disruption could worsen inflammation, increase post-injury damage in the spinal cord, and harm potential repair mechanisms," he says.

But he adds that even if this is the case, it might not all be bad news—accelerating recovery of circadian rhythms soon after injury could boost the body's ability to limit further damage and to repair itself.

"If disruption of these rhythms harms recovery after SCI, efforts to restore a patient's routines—for example, optimizing daily schedules of meals, sleep, physical rehabilitation and bright light—could promote recovery," Gaudet explains. "Future studies of SCI that incorporate circadian factors could inform the development of such chronotherapies. Early after injury, there are several strategies that could be used to boost rhythms. Light is the strongest activator of the circadian system, so optimizing the amount and timing of light would be a great start: bright light in the morning—for example, having a window in the room soon after injury—and dark nights. If light at night is necessary, then it could be red light, which does not activate the circadian system. When possible in the intensive care unit, hospital staff could try to consolidate visits—studies I've read suggest that an ICU patient receives an average of 50 or more visits per night; this surely disrupts sleep at this critical time post-injury."

Other strategies could include ensuring patients eat at the optimal time of day (particularly starting with breakfast), avoid eating anything beyond early evening, exercise only during the day (ideally in the morning), and avoid extra stress. And Gaudet says there are also drugs being tested that can alter the circadian system.

"Of course," he says, "none of this would be a miracle cure, but these are easy-to-implement steps in the right direction, it could help with recovery, and

Dr. Andrew Gaudet

Circadian disruption: much more than a bad night's sleep

Probably the most well-known form of circadian disruption is jet lag. When we cross time zones rapidly, our bodies are unable to adjust rapidly to the new light cycle and we "feel bad" for several days. But long-term circadian disruption has been demonstrated to seriously impact our health.

For example, shift workers—those that work night shifts, or have rotating shifts—are exposed to long-term circadian disruption, and are predisposed to obesity, certain cancers, and metabolic disorders. People who routinely rely on artificial light to stay awake late into the night tend to snack at inappropriate times (that is, during the evening and night), which can contribute to obesity, cardiovascular issues, and metabolic syndrome. And long-term circadian disruption can result in or worsen mental health conditions such as anxiety, depression, and seasonal affective disorder.

Most able-bodied people can make a conscious decision to make life changes that reduce circadian disruption. But SCI by itself seems to cause long-term circadian disruption, and those with SCI obviously don't have the luxury of switching it off. This underscores the importance of trying to better understand the mechanisms behind SCI-related circadian disruption and develop strategies to reduce or prevent it.

it also would provide a healthier overall state for treatment with other effective therapies."

If you've been reading this and wondering what it means for you as someone who's lived with SCI for many years, we can tell you that Gaudet is also intrigued by circadian function in chronic SCI and is considering how best to study this.

"As for what relates directly to chronic SCI and circadian rhythms, some have worse sleep or sleep issues. In addition, individuals with chronic SCI can have disrupted melatonin, blood pressure, activity, and sleep/wake rhythms. The circadian-related deficit likely relates to severity and level of injury—more severe and higher injuries would likely have worsened circadian disruption. I think it would be interesting to incorporate this into my work in the future—how strengthening circadian function could influence metabolic function and overall health in chronic SCI."

In the meantime, Gaudet says it just makes sense for anyone with chronic SCI to consider their circadian system and its relation to health when making day-to-day decisions.

"Individuals with SCI are more susceptible to worsened body composition, obesity, cardiovascular disease, and metabolic issues," he says. "Our data (from the study described above) showed that SCI disrupted circadian rhythms and metabolic function in parallel. One potential take-away is that circadian health may be particularly important for people with SCI. Individuals with chronic SCI may be more sensitive to circadian disruption, which could influence overall health and metabolism. To maintain or boost circadian health, we all could focus on our lighting environment and how we're responding to the time of day. Light, eating, activity, stress, and sleep all feed in to the circadian system, so optimizing timing of these factors when possible could be useful for individuals with chronic SCI."

Visit www.gaudetlab.com to read more about Dr. Gaudet and his work. ■

Dr. Gaudet recommends:

- Getting as much bright light as possible in the morning (e.g., sitting near a window or going outside)
- Using low light and/or red light in the evening (especially an hour before bed; red light does not activate the circadian system)
- Using blue-light filters on your phone and other devices in the evening and before sleeping
- Eating a meal in the morning
- Avoiding eating anything beyond early evening or during the night
- Scheduling activity or rehabilitation for the morning to help boost rhythms
- Avoiding stressful activities in the evening, as related hormones could make the body think it is a different time of day
- Keeping a regular sleep schedule, which could be helped through the strategies above.

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