Restoring Brain Rhythms: A Neurotechnology Approach to Chemotherapy-Induced Cognitive Impairment

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Most people know that chemotherapy can cause nausea and hair loss. However, few realize that it can also affect a person's ability to think clearly. Cancer patients describe this as "chemo brain," a side effect of cancer treatment characterized by memory problems and difficulty concentrating that can last for months or even years after the treatment ends. This condition is known as chemotherapy-induced cognitive impairment (CICI), and between 17 and 75 percent of cancer survivors report experiencing these symptoms. Despite how common it is, there is still no specific treatment (Janelsins et al., 2014). Because of this, researchers continue to investigate what happens in the brain during chemotherapy. Scientists know that chemotherapy can cause inflammation and damage brain cells, yet research suggests that it may also affect the functioning of astrocytes, a type of brain cell that helps keep other brain cells working properly. When these cells are disrupted, the brain can struggle with memory and other cognitive functions, contributing to the symptoms of chemo brain.

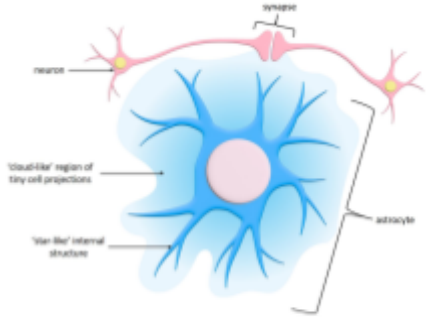

Figure 1: An astrocyte interacting with neurons and synapses (EurekAlert, 2022)

For much of history, astrocytes were viewed as simple cells whose main role was to hold neurons in place, but that understanding has changed. Scientists now know that astrocytes play important roles in the brain, including regulating communication between neurons, delivering nutrients to brain cells, maintaining chemical balance, and operating the brain's glymphatic system, a network that removes toxic proteins from the brain (Nedergaard & Goldman, 2020).

These functions are very important because they must occur at specific times and in the correct order. Astrocytes are regulated by genes, including BMAL1, PER1/2, CRY1/2, and CLOCK, which control when these cells remove waste, regulate neurotransmitters, and manage inflammation. When this system functions properly, the brain remains healthy. When it is disrupted, these processes change, and regions such as the hippocampus and prefrontal cortex, which are responsible for memory and decision-making, are some of the first to be affected (Lananna et al., 2018). This may help explain why chemotherapy can lead to cognitive problems.

Some chemotherapy drugs commonly used including methotrexate, cisplatin, and doxorubicin can generate a condition called reactive astrogliosis, in which astrocytes enter an inflammatory state. During this process, the gene BMAL1 is affected, disrupting many of the astrocytes' functions (Bhattacharya et al., 2022). As a result, the brain becomes less efficient at removing harmful proteins such as amyloid-beta and tau, the same proteins linked to Alzheimer's disease. In addition, the regulation of glutamate, a chemical that allows neurons to communicate, becomes affected. These changes can affect brain circuits involved in memory and learning, especially in the hippocampus.

Proposed Neurotechnological Solution:

Light is one of the main signals the brain uses to keep the body running on a regular schedule. Special cells in the eyes, called intrinsically photosensitive retinal ganglion cells (ipRGCs), detect light and send that information to a region of the brain called the suprachiasmatic nucleus (SCN). The SCN then sends signals throughout the brain and body, helping regulate sleep, hormones, and the activity of cells such as astrocytes.

Astrocytes depend on these signals to do their jobs properly. When these signals become disrupted, astrocytes may not work as efficiently, which can contribute to problems with memory and attention. Scientists have found that exposure to certain types of light, especially blue light, can help restore disrupted biological rhythms (LeGates et al., 2014). Thus this means that if chemotherapy disrupts the normal functioning of astrocytes, maybe light therapy could help restore it.

As a result, a possible solution is a closed-loop light therapy system. A closed-loop system monitors what is happening and adjusts its response automatically. A thermostat is an example because it measures the temperature in a room and changes the heating when necessary. A similar system could be designed for cancer patients. A device such as a wristband could track sleep, heart rate, and body temperature. Using this information, the device could determine whether a patient's biological rhythms are becoming disrupted during chemotherapy. If they are, the system could provide light therapy through a light generating device to help restore normal function.

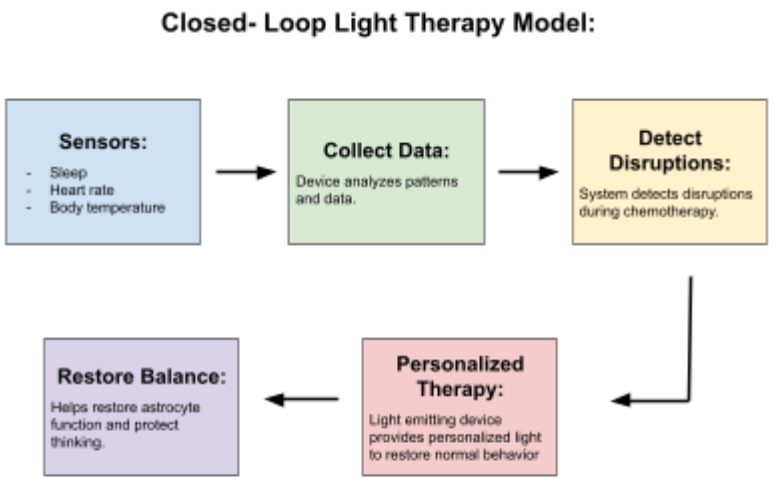

Figure 2. Proposed Closed-Loop Light Therapy Model

This approach would be non-invasive, meaning that it would not require surgery or additional medication. It could also be personalized because every patient has different biological rhythms, allowing the device to adjust to each person's needs.This idea may be especially valuable for children with cancer because their brains are still developing, making the protection of memory and learning particularly important. Although this technology has not yet been developed specifically for chemo brain, many of its components already exist. Scientists are already studying devices that monitor biological rhythms, and light therapy is already used to treat some medical conditions. Combining these technologies may provide a new way to reduce the cognitive side effects of chemotherapy and improve the lives of cancer patients.

Concerns:

Like any new medical technology, closed-loop light therapy also raises important ethical questions. Because this system would monitor information such as sleep patterns and heart rate, protecting

patient privacy would be essential, this is especially important in pediatric cancer patients, who may not be old enough to consent to how their personal data is collected.

People's biological rhythms can also change based on age, sex, genetics, and other factors. If the algorithms used to personalize light therapy are developed using data from only a small group of patients, the technology may work better for some people than for others, so to avoid this, researchers must make sure that trials include diverse populations and that patient data is managed responsibly. Addressing these concerns from the beginning will be important to making sure that closed-loop light therapy is safe and accessible to all patients who may benefit from it.

Final Thoughts:

In conclusion, chemo brain is not simply a mysterious side effect of cancer treatment, it may happen because chemotherapy disrupts some of the systems that help the brain function properly, which is why it is important to better understand and treat it. The closed-loop light therapy discussed in this paper is based on technologies that already exist and are being studied. The next step is to determine whether these technologies can be adapted to treat chemotherapy-induced cognitive impairment. By helping restore biological rhythms, neurotechnology may help offer a new way to protect the brain and improve the quality of life of cancer patients.

References:

Bhattacharya, S., et al. (2022). Astrocytes deficient in circadian clock gene Bmal1 show enhanced activation responses to amyloid-beta pathology without changing plaque burden. Scientific Reports, 12, 1827. https://doi.org/10.1038/s41598-022-05862-z

Innominato, P. F., et al. (2014). The circadian timing system in clinical oncology. Annals of Medicine, 46(4), 191–207. https://doi.org/10.3109/07853890.2014.916990

Janelsins, M. C., Kesler, S. R., Ahles, T. A., & Morrow, G. R. (2014). Prevalence, mechanisms, and management of cancer-related cognitive impairment. International Review of Psychiatry, 26(1), 102–113. https://doi.org/10.3109/09540261.2013.864260

Lananna, B. V., et al. (2018). Cell-autonomous regulation of astrocyte activation by the circadian clock protein BMAL1. Cell Reports, 25(1), 1–9. https://doi.org/10.1016/j.celrep.2018.09.015

LeGates, T. A., Fernandez, D. C., & Hattar, S. (2014). Light as a central modulator of circadian rhythms, sleep and affect. Nature Reviews Neuroscience, 15(7), 443–454. https://doi.org/10.1038/nrn3743

Nedergaard, M., & Goldman, S. A. (2020). Glymphatic failure as a final common pathway to dementia. Science, 370(6512), 50–56. https://doi.org/10.1126/science.abb8739

University of Queensland. (2022). Brain cells more active in Alzheimer's disease than previously thought. EurekAlert! https://www.eurekalert.org/news-releases/942499