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Poster Presentation

The Effects of Disrupted Circadian Rhythms on Hippocampal Vascularization Following Cardiac Arrest

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Background

Approximately 565,000 people experience cardiac arrest every year. Of these, only 10.6% of cases achieve a full recovery. The recovery period is critical for the overall outcome of the patient post-ischemia. Artificial light at night (aLAN) in hospitals is necessary to allow for continual care, however, exposure to aLAN may impair patients' recovery. Nonetheless, many people are unaware of how disrupted circadian rhythms can affect their recovery. Internal circadian rhythms have a period of ~24 h, and control many physiological processes. Figure 1 is an example of some of these. These processes are entrained to roughly these time points, but can be disrupted by aLAN exposure.Prior to the invention of electrical light, circadian rhythms of individuals were entrained to precisely 24-hour days by bright light. Disruption of dark nights by exposure to aLAN increases cell death and decreases survival rate following ischemia, and in otherwise healthy mice, decreases vascular growth factors. Thus, in the present study we aimed to determine whether the return to dark nights after exposure to aLAN ameliorates hippocampal vascular damage during recovery from global ischemia.

Hypothesis

My hypothesis states that disrupted circadian rhythms by exposure to dim light at night (dLAN) exacerbates hippocampal vascular recovery after global ischemia.

Experimental Plan

We used male and female Swiss Webster mice that were 8 weeks of age upon arrival to our facilities. Following arrival, the mice were given 7 days to acclimate to the new environment. Upon completion of the acclimation period, mice underwent either a cardiac arrest or either a sham procedure used as a control. Mice were then placed in regular light-dark cycles consisting of14 hours of light and 10 hours of darkness 0 lux Or housed indLAN conditions consisting of 14 hours of light; and 10 hours of dim,5 lux,

illumination during the dark period). After one week,all groups were housed with standard, lit days, and completely dark nights.. Upon completion of the two week period, mice were injected with lectin and tissue was collected 5 minutes after the injection. The brain tissue we collected was sliced, imaged, and then analyzed using FIJI software for total area of lectin-positive staining.

Figure 2

Figure 2 is a representative image of the hippocampus that we used for analysis. The blue marker is DAPI, which labels cell bodies by binding to DNA found in the nuclei. In red, we observe lectin labelling. Lectin is a glycoprotein that binds to vasculature, and thus, in red, we observe the hippocampal vasculature. This is the stain that we quantized and used to calculate the percent total area of vasculature for our results.

Results

In the female mice that underwent CA and were housed in dLAN->LD conditions, we determined there was a significantly lower percent area fraction of lectin-positive staining in the CA1, CA2, and CA3 regions of the hippocampus when compared to the sham mice.

However, in the males, the hilus, granule cell layer, and dentate gyrus regions of the hippocampus showed increased total vascular area in the dLAN->LD group in both CA and sham mice.

Conclusions

From these results, we were able to conclude that females who experienced CA have significantly worse vascular recovery when exposed to circadian rhythm disruption. Also, in males, we can conclude that experiencing circadian disruption does not display an exacerbated vascular recovery following CA.

Future Directions

The two groups within this experiment did not allow us to make significant conclusions about the return to LD following dLAN. In the future, we would include another control group that would be housed in dLAN conditions for the entirety of the two-week period. This would enable us to achieve definitive conclusions about whether return to dark nights following dLAN exposure ameliorates or eliminates the effects of dLAN on cerebrovasculature.

Also, if you were to look at the scale difference between the male and female graphs, you could see that female mice have significantly more vasculature within the hippocampal regions. So, we propose an additional experiment that will compare

ovariectomized females to undisturbed males determining how the female sex hormones like estrogen impact the recovery of vasculature following ischemia.

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