The Impact of Acute Trazodone Administration on Sleep in Mice

Implications for Alzheimer's Disease Therapy

PRESENTER:

Mayuko Arai

Department of Psychology

BACKGROUND:

- Alzheimer's Disease (AD) patients often experience sleep disruptions, in addition to behavioural and cognitive deficits.
- Trazodone, an antidepressant drug with sleep-promoting properties, is currently being evaluated as a potential therapy for restoring beneficial sleep in Alzheimer's disease.
- Yet, few studies have investigated how the impacts of trazodone on sleep benefit cognitive function and neuropathological characteristics of AD.
- Aim 1: Establish the translational method to administer trazodone reliably in mice.
- Aim 2: Assess the effects of acute trazodone administration on sleep in mice.

METHODS

Subject : C57BL/6 (wild-type) mice (n = 24)

1. Identify the type and amount of highly palatable food to mix with trazodone to facilitate self-administration of the drug.
2. Assess the effects of trazodone on sleep, using electroencephalogram (EEG) recordings.

RESULTS

- Animals can be trained to ingest the drug mixed with strawberry yogurt-based treat consistently within 5 min immediately before the resting phase of the day.
- Trazodone dose-dependently increases non-rapid eye movement (NREM) sleep at the expense of rapid eye movement (REM) sleep, accompanied by an increase in slow wave power.

Trazodone dose-dependently **increases non-rapid eye movement (NREM)** sleep and **slow wave power.**

Figure 1

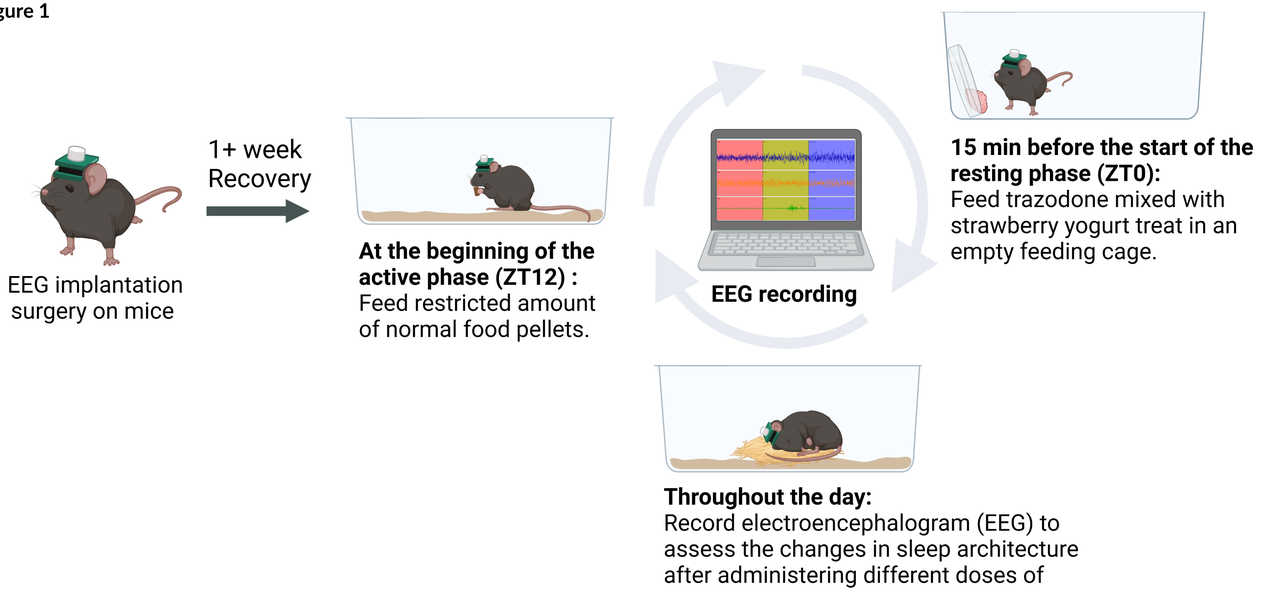
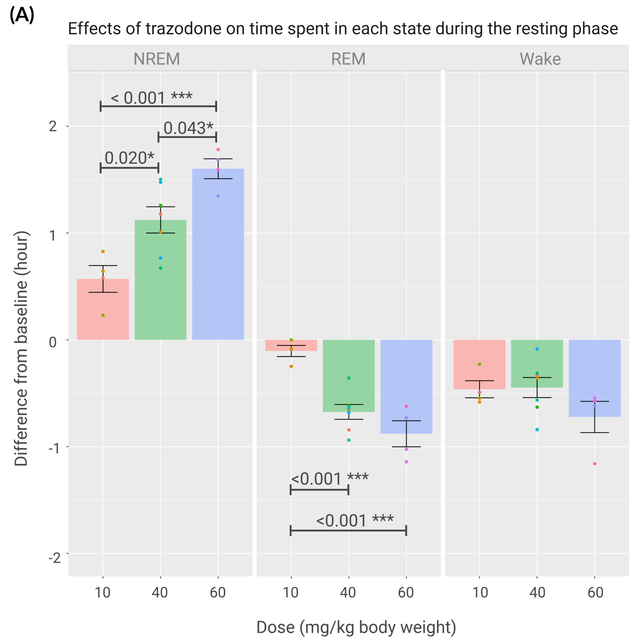
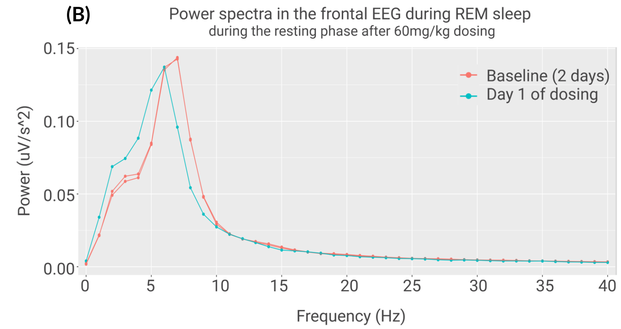


Figure 2





(A) One-way ANOVA revealed a significant effect of trazodone dose on NREM sleep length $F(2, 12) = 13.82$, $p < 0.001$, and REM sleep length $F(2, 12) = 19.21$, $p < 0.001$. Tukey's HSD was used for the post-hoc comparisons.

(B) Representative power spectra during REM sleep after a single self-administration of 60mg/kg trazodone.

DISCUSSION

- Trazodone can be administered through voluntary oral ingestion in mice
- Trazodone increases NREM sleep, but at the expense of REM sleep.

FUTURE RESEARCH

- Administer trazodone in mouse models of AD to examine its effects on sleep, memory performance, and pathological characteristics associated with AD.

REFERENCES

de Oliveira, P., Cella, C., Locker, N., Ravindran, K. K. G., Mendis, A., Wafford, K., Gilmour, G., Dijk, D.-J., & Winsky-Sommerer, R. (2022). Improved Sleep, Memory, and Cellular Pathological Features of Tauopathy, Including the NLRP3 Inflammasome, after Chronic Administration of Trazodone in rTg4510 Mice. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *42*(16), 3494–3509. https://doi.org/10.1523/JNEUROSCI.2162-21.2022

La, A. L., Walsh, C. M., Neylan, T. C., Vossel, K. A., Yaffe, K., Krystal, A. D., Miller, B. L., & Karageorgiou, E. (2019). Long-Term Trazodone Use and Cognition: A Potential Therapeutic Role for Slow-Wave Sleep Enhancers. *Journal of Alzheimer's Disease: JAD*, *67*(3), 911–921. https://doi.org/10.3233/JAD-181145

ACKNOWLEDGEMENTS

Supervised by Dr. Brianne Kent and in collaboration with Katherine Mantel, Cody Stevens, and Emad Shams. We thank Robert Gibson, Afnan Sahibzada, Manthan Vekariya, and Hillary Han for assisting in the experimentation.

Funded by NSERC Discovery Grant.

Mayuko Arai, mayuko_arai@sfu.ca

undergraduate research symposium

SFU SIMON FRASER UNIVERSITY