**The effect of repeated stress on excitatory neurons in the female rat dorsomedial hypothalamus.**

**Background**

Over the past five years, people worldwide have experienced significant stress and uncertainty. In these times, people often turn to comfort foods, potentially as a coping mechanism (Dallman, 2003). Prolonged stress is known to trigger eating disorders (Auger et al., 2023). Davies et al. (2023) found females were at higher risk for pandemic stress-induced binge eating, and females ages 10 to 19 showed the greatest increase in eating disorder released hospitalizations (Auger et al., 2023) during this time.

Sex differences in food intake are also observed in rodent models of emotional stress-induced binge eating. A study by Anversa et al. (2019) found that female rodents with unrestricted food access, and no previous history of food restriction, ate 72% more when subjected to chronic stress than their unstressed controls. This change was not seen in male rodents with the same unrestricted food access (Anversa et al., 2019). Although there is a clear link between stress and appetite in rodents and humans, the mechanisms are poorly understood. The dorsomedial hypothalamic nucleus (DMH) is an ideal brain region to study the link between stress and appetite for two reasons. **1)** cells in the DMH have receptors that allow them to respond to stress hormones (Myers et al., 2014) and **2)** the DMH is very important in appetite and body weight regulation (Bellinger and Bernardis, 2002). The primary objective of our study is to determine the effect of repeated stress on DMH neurons of female rats.

**Experimental Design**

Once approval from the Mount Allison Animal Care Committee is obtained, female Sprague-Dawley rats will be separated into two groups, **i)** unstressed controls, and **ii)** repeated stress. Groups will have unrestricted food access, and the repeated stress group will undergo five consecutive days of 30-minutes of physical restraint, a well-established stressor (Patchev and Patchev, 2006). In both groups, we will measure food intake and take blood samples to measure levels of corticosterone (the stress hormone in rodents). Following the fifth day, both groups will be anesthetized and euthanized, then their brains will be removed. The brains will be sliced, and their neurons will be kept alive in oxygenated artificial cerebrospinal fluid. Using patch clamp electrophysiology, we will study **i)** the amplitude and frequency of action potentials (to observe the effects of stress on neuron excitability), and **ii)** excitatory and inhibitory currents (to understand how stress affects communication between neurons in the DMH). A total of ~8-10 neurons/group and ~2 neurons/brain will be used for each experiment.

**Expected Outcome**

The relationship between stress and appetite is complex, with chronic stress both increasing and decreasing food intake in rodents and humans (Torres et al., 2007). Because DMH neurons can stimulate appetite, it is possible that repeated stress will increase their excitability and enhance neuronal communication in a way that could lead to increased food intake.

**Impact & Significance**

Electrophysiology studies commonly use rats to gain insight into human brain function, but the majority of studies use male rats, despite clear sex differences in stress related changes in appetite. Our research aims to answer the question how does repeated stress in young female rats affect the synaptic transmission of neurons in the DMH that regulate appetite? By addressing this question, we will enhance our understanding of how stress affects neurons that regulate appetite in rats. Given the similarities between the human and rat brain, this research could have important implications for human health.

**References**

Anversa, R. G., Campbell, E. J., Ch’ng, S. S., Gogos, A., Lawrence, A. J., & Brown, R. M. (2019). A model of emotional stress‐induced binge eating in female mice with no history of food restriction. *Genes, Brain and Behavior*, *19*(3), e12613. <https://doi.org/10.1111/gbb.12613>

Auger, N., Steiger, H., Luu, T. M., Chadi, N., Low, N., Bilodeau‐Bertrand, M., Healy‐Profitós, J., Ayoub, A., Brousseau, É., & Israël, M. (2023). Shifting age of child eating disorder hospitalizations during the Covid‐19 pandemic. *Journal of Child Psychology and Psychiatry*, *64*(8), 1176–1184. <https://doi.org/10.1111/jcpp.13800>

Bellinger, L. L., & Bernardis, L. L. (2002). The dorsomedial hypothalamic nucleus and its role in ingestive behavior and body weight regulation. *Physiology & Behavior*, *76*(3), 431–442. <https://doi.org/10.1016/S0031-9384(02)00756-4>

Dallman, M. F., Pecoraro, N., Akana, S. F., La Fleur, S. E., Gomez, F., Houshyar, H., Bell, M. E., Bhatnagar, S., Laugero, K. D., & Manalo, S. (2003). Chronic stress and obesity: A new view of “comfort food”. *Proceedings of the National Academy of Sciences*, *100*(20), 11696–11701. <https://doi.org/10.1073/pnas.1934666100>

Davies, H. L., Hübel, C., Herle, M., Kakar, S., Mundy, J., Peel, A. J., Ter Kuile, A. R., Zvrskovec, J., Monssen, D., Lim, K. X., Davies, M. R., Palmos, A. B., Lin, Y., Kalsi, G., Rogers, H. C., Bristow, S., Glen, K., Malouf, C. M., Kelly, E. J., … Breen, G. (2023). Risk and protective factors for new‐onset binge eating, low weight, and self‐harm symptoms in >35,000 individuals in the UK during the COVID ‐19 pandemic. *International Journal of Eating Disorders*, *56*(1), 91–107. <https://doi.org/10.1002/eat.23834>

Myers, B., Mark Dolgas, C., Kasckow, J., Cullinan, W. E., & Herman, J. P. (2014). Central stress-integrative circuits: Forebrain glutamatergic and GABAergic projections to the dorsomedial hypothalamus, medial preoptic area, and bed nucleus of the stria terminalis. *Brain Structure and Function*, *219*(4), 1287–1303. <https://doi.org/10.1007/s00429-013-0566-y>

Patchev, V. K., & Patchev, A. V. (2006). Experimental models of stress. *Dialogues in Clinical Neuroscience*, *8*(4), 417–432. <https://doi.org/10.31887/DCNS.2006.8.4/vpatchev>

Torres, S. J., & Nowson, C. A. (2007). Relationship between stress, eating behavior, and obesity. *Nutrition*, *23*(11–12), 887–894. <https://doi.org/10.1016/j.nut.2007.08.008>