PARAVENTRICULAR THALAMUS PROVIDES A POLYSYNAPTIC BRAKE ON LIMBIC CRF NEURONS TO SEX-DEPENDENTLY BLUNT RISKY ALCOHOL DRINKING AND AVOIDANCE BEHAVIOR

Olivia Levine, PhD

Weill Cornell Medicine New York, NY 10065

Abstract:

Bed nucleus of the stria terminalis (BNST) neurons that synthesize and release the stress neuropeptide corticotropin-releasing factor (CRF) drive binge alcohol drinking and anxiety, behaviors that are primary risk factors for alcohol use disorder (AUD) and comorbid neuropsychiatric diseases more common in women than men. Here, we show that female C57BL/6J mice binge drink more than males and have greater basal BNSTCRF neuron excitability and synaptic excitation. We identified a dense VGLUT2+ glutamatergic synaptic input from the paraventricular thalamus (PVT) that is anatomically similar in males and females. These PVTBNST neurons release glutamate directly onto BNSTCRF neurons but also engage a large BNST interneuron population to ultimately provide a net inhibition of BNSTCRF neurons, and both components of this polysynaptic PVTVGLUT2-BNSTCRF circuit are more robust in females than males. While chemogenetic inhibition of the general PVTVGLUT2 neuron population suppressed binge alcohol drinking in both sexes, chemogenetic inhibition specifically of the PVTBNST projection promoted this behavior in females without affecting males; chemogenetic activation of the pathway was sufficient to reduce avoidance behavior in both sexes in anxiogenic contexts. We also show that withdrawal from repeated binge drinking produces a female-like phenotype in the male PVT-BNSTCRF excitatory synapse without altering the function of PVTBNST neurons per se. Our data describe a complex and unique behavioral role of the feedforward inhibitory PVTVGLUT2-BNSTCRF glutamatergic circuit that is more robust in females and undergoes sex-dependent alcohol-induced plasticity.

Biography:

Olivia completed her PhD in neuroscience in June 2020 at Weill Cornell Medicine and will start her MD at Sackler School of Medicine in fall 2020. She plans to become a psychiatrist while continuing researching the underlying brain mechanisms of neuropsychiatric disorders. In her spare time, she is a science writer for both technical and laymen articles that have been published on sites such as Technology Networks.

Publication of speakers:

1. Maurer, Raimond & Mitchell, Olivia. (2020). Older peoples' willingness to delay social security claiming. Journal of Pension Economics and Finance. 1-16. 10.1017/S1474747219000404.
2. Mitchell, Olivia & Utkus, Stephen. (2020). Target Date Funds and Portfolio Choice in 401(k) Plans. SSRN Electronic Journal. 10.2139/ssrn.3535910.
3. Lusardi, Annamaria & Mitchell, Olivia & Oggero, Noemi. (2020). Understanding Debt in the Older Population. SSRN Electronic Journal. 10.2139/ssrn.3537858.
4. Horneff, Vanya & Maurer, Raimond & Mitchell, Olivia. (2020). Putting the Pension Back in 401(k) Retirement Plans: Optimal versus Default Deferred Longevity Income Annuities. Journal of Banking & Finance. 114. 105783. 10.1016/j.jbankfin.2020.105783

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