The role of Central Amygdala GABAergic input to the Parabrachial Nucleus in food intake

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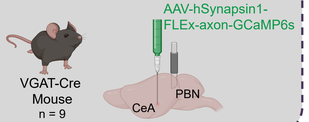
Introduction

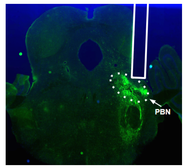
Precise management of food intake is imperative for survival. The brain integrates internal signals with external stimuli to control food intake, but the critical neural circuits involved are not fully understood. The connection between the central nucleus of the amygdala (CeA) and the parabrachial nucleus (PBN) has been implicated in regulating food intake [1-4]. However, the exact neural mechanisms and role of this pathway during consumption remain unclear. Using chemogenetic and optogenetic manipulations and fiber photometry recordings in transgenic mice, we aim to clarify the influence of the CeA-PBN neural circuitry on ingestive behavior.

Methods

Fiber Photometry Recordings

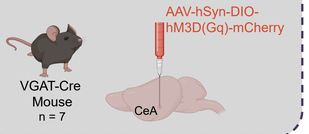
Axonal calcium signaling recording of GABAergic CeA neurons in PBN





Chemogenetic Manipulations

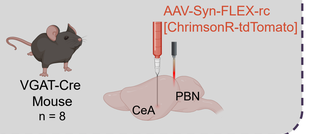
Chemogenetic excitation of GABAergic CeA neurons

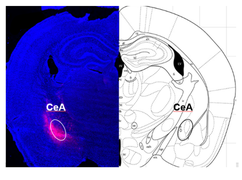


DREADDs: Designer Receptors Exclusively Activated by Designer Drugs (DREADDs). Modifies G-protein coupled receptors to react with otherwise inert ligands Clozapine N Oxide (CNO) or C21. 3mg/kg CNO/C21 (experimental condition) or equal volume saline (control condition) administered intraperitoneally prior to feeding assay.

Optogenetic Manipulations

Optogenetic stimulation of GABAergic CeA-to-PBN projecting neurons





Measured Feeding Assay: Access to food pellet for 2hrs. Pellet weighed every 30mins to measure amount consumed. Used in chemogenetic and optogenetic experiments described above.

References

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2. Douglass, A. M. et al. (2017). Central amygdala circuits modulate food consumption through a positive-valence mechanism. *Nature Neuroscience*, *20*(10), 1384–1394.
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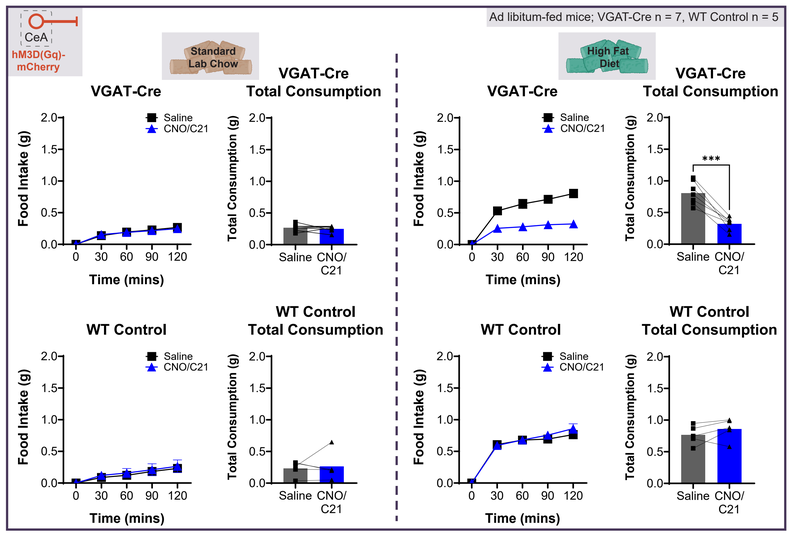
4. Wang, Y. & Sternson, S. M. (2023). Multimodal mapping of cell types and projections in the central nucleus of the amygdala. *ELife*, *12*.

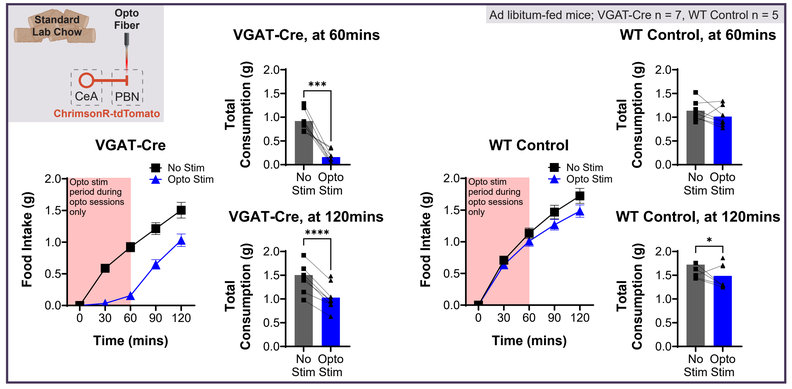
Graphics created with BioRender.com

Activity of CeA axons projecting to PBN increased during bouts of licking and running

Chemogenetic excitation of GABAergic neurons in CeA decreased high fat diet intake



Optogenetic stimulation of GABAergic CeA-to-PBN projecting neurons decreased food intake



Conclusions

- GABAergic CeA-to-PBN axonal calcium signaling increased during lick and run bouts
- Excitation of CeA GABAergic neurons reduced consumption of highly palatable food
- Selective optogenetic stimulation of inhibitory CeA projections to PBN decreased food intake

These findings highlight the CeA-PBN projection's ability to modulate food intake, potentially by restricting meal bout duration. Continued research will uncover the complete role of this pathway in regulating consumption and, more broadly, in integrating physiological signals with environmental cues to guide ingestive behaviors.

Acknowledgements

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