Going Back for Seconds?

An examination of forebrain neural activity that regulates behavioural expressions of pleasure in mice

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ABSTRACT

- The purpose of our study is to explore how pleasure is regulated by forebrain neural circuitry. More specifically, we are looking in the Nucleus Accumbens, where opiod receptors are thought to play an important role in hedonic reponses following a reward.
- The Nac receives excitatory glutaminergic inputs from various brain regions. It is still unclear which pathways are responsible for modulating specific behaviours, but they are believed to act in concert, influencing an animal's motivation to pursue rewards.
- With specific brain manipulations, these behavioral responses can change quite markedly. By administering intracranial injections of various drugs directly into the Nac, as well as by using optogenetic techniques to stimulate or silence specific pathways, we attempt to discover which systems are likely candidates for hedonic neural substrates.

BACKGROUND

- The circuitry in question has been mostly studied in rats. Our hope is to determine which brain regions mediate these effects in mice. However, accurately assessing increased pleasure in any nonverbal animal is no easy feat. One relatively tractable approach is to study their consummatory behaviour.
- When drinking, mice will typically produce a rhythmic set of licks that can be grouped into bursts (or bouts). Also, following a burst, mice will exhibit affective facial reactions and behaviours (such as tongue protrusions, paw shakes, and paw licks). Analysis of these behavioural responses can provide an index of pleasure generated by consumption.
- Our main goal in this study is to determine which manipulations in the Nac will produce measurable hedonic reactions.

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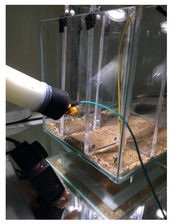
METHODS

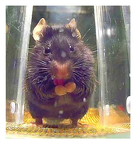
Lickometry



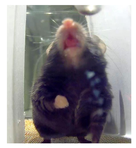
- A contact-sensitive lickometer measures each lick to the nearest 0.01s and a computer records the data
- A lick burst is defined as a minimum of 3 licks, ending when there is a delay of one second between licks
- 8 male mice
- **Test 1**: Average licks per burst and total licks are compared across different concentrations of sucrose solution

Orofacial Analysis

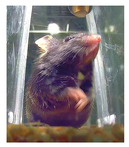
- 8 male mice
- Mice are videotaped after each lick burst. Tongue protrusions, paw shakes, and paw licks are scored manually and compared across different drug conditions
- **Test 1**: 0.2µl bilateral infusion of DAMGO (0.625µg/µl) directly into NAc
- **Test 2**: 0.2µl bilateral infusion of Muscimol (250ng/µl) directly into NAc



Paw licks

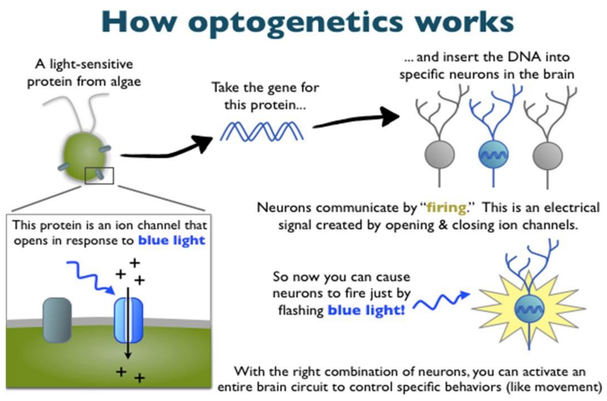


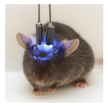
Midline tongue protrusion



Paw shakes

Optogenetics





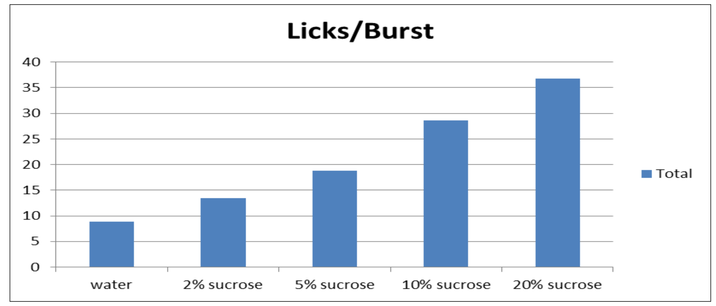
- 9 male mice
- a fiber optic cord -> NAc bilaterally
- An excitatory opsin sensitive to 273 nm light; ChR2 (AAV5-CaMKIIa-DIO-eGFP) virus delivered bilaterally into the hippocampus

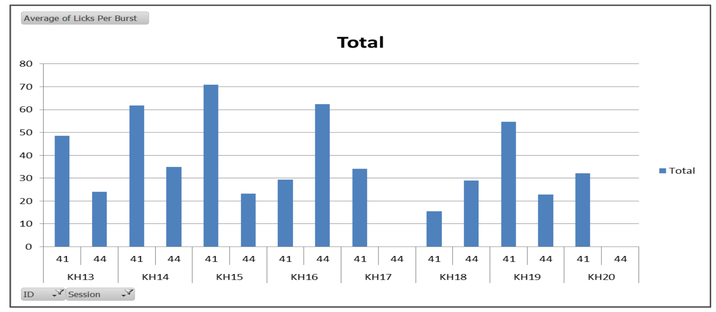
Behavioural task: We measured the number of licks per burst, while consuming 15% sucrose, of food-restricted mice with and without stimulation

Test: Stimulation protocol: 3ms, **during a burst**

- DAY 1: 6 stimulations per lick
- DAY 2: 3 stimulations per lick
- DAY 3: 2 stimulations per lick
- DAY 4: 1 stimulation per lick
- DAY 5: 1 stimulation every other lick

RESULTS





DISCUSSION

- We identified an increase in licks per burst and total licks with higher concentrations of sucrose solutions. This effect was consistent with the analysis of orafacial expressions, where we observed an increase in tongue protrusions, paw shakes, and paw licks.
- An increase in licks per burst were observed after bilateral intracranial injections of Muscimol, a selective agonist for GABAA receptors, however this effect was not seen with injections of DAMGO, a selective agonist for mu-opiod receptors. These effects were most pronounced when cannulae placement was most rostrodorsal.
- Animals ceased consummatory behaviour during the periods of optogenetic excitation of the HPC-NAc pathway
- This study is part a bigger project to gain a mechanistic understanding of pleasure systems in the brain. The hope is that these insights might help find better treatments for affective disorders.

REFERENCES

- Berridge, K. C. (January 01, 2000). Measuring hedonic impact in animals and infants: microstructure of affective taste reactivity patterns. *Neuroscience and Biobehavioral Reviews, 24*, 2, 173-198.
- Berridge, K. C., Kringelback, M. L, (May 6,2015) Pleasure Systems in the brain. *Neuron. 86(3):646-664*
- Dwyer, D. M. (2012). Licking and liking: The assessment of hedonic responses in rodents. *The Quareterly Journal of Experimental Psychology, Vol. 65, Iss. 3)*