

## Abstract

Chronic stress in mice induces a variety of anxiety- and depressive-like phenotypes at the neuronal, circuit, and behavioral levels. More specifically, social and hedonic-like states are dramatically impaired across many psychiatric disorders, though the underlying mechanisms sufficient to precipitate or alleviate such impairments remain largely unknown.

Here, we utilize an activity-dependent and inducible tagging strategy to modulate dorsal dentate gyrus (dDG) cells of the hippocampus (HPC) cells processing positive, neutral, or negative memories prior to chronic immobilization stress exposure. We hypothesized that chronic negative memory stimulation would impair social behavior and decrease hedonic-like activity, while positive memory stimulation would promote social behavior and increase hedonic-like activity.

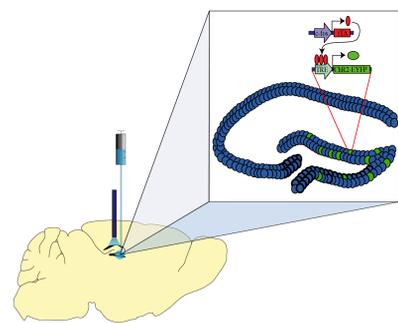
We find that chronically stimulating dDG cells processing a valence-specific experience is sufficient to affect social but not anxiety-like behaviors. Furthermore, chronic reactivation of positive and negative memories modulates the behavioral response to chronic stress. We also find that chronic memory stimulation followed by chronic immobilization stress differentially affects body weight.

Our current experiments examine whether reactivating discrete positive and negative dDG ensembles elicits changes in social and hedonic behavior. In addition, our ongoing research interrogates the dorsoventral axis of the HPC by determining whether activation of vDG positive and negative ensembles also influences behavior and bodyweight.

Together our results connect chronic memory modulation with discrete maladaptive behavioral states and provide insight into the specificity of the behavioral effects induced by HPC ensemble reactivation.

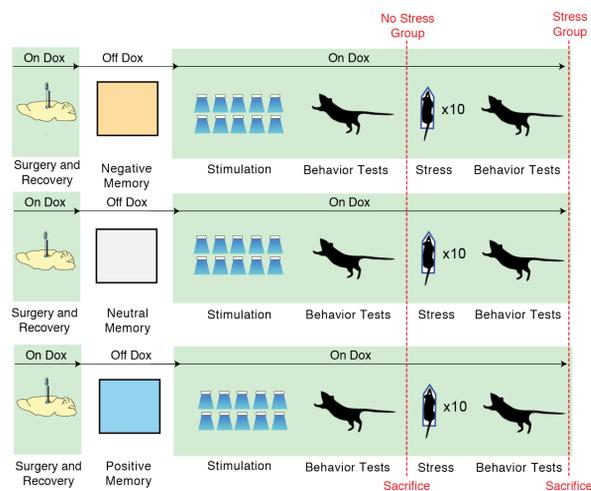
## Methods

### Activity-dependent Tagging of Hippocampal Cells



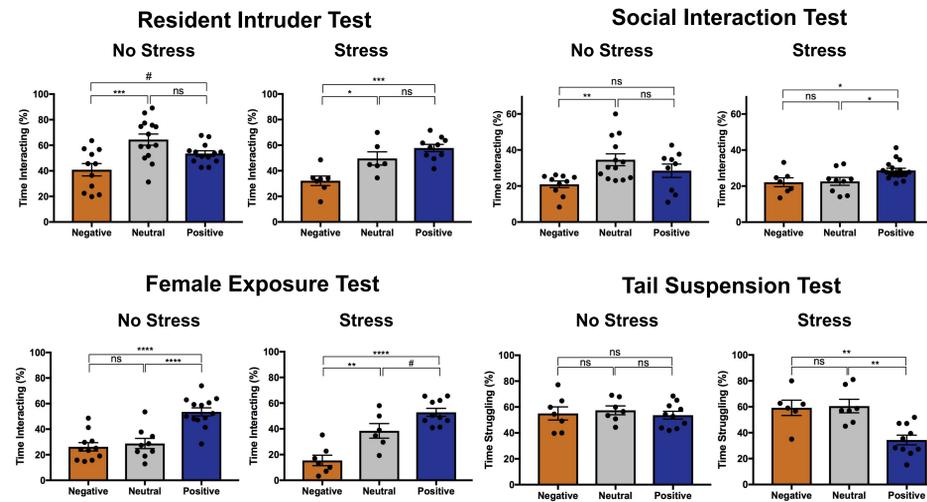
- When taken off doxycycline (dox) diet, tetracycline transactivator (Tta) binds to tetracycline response element (TRE), leading to expression of *ChR2* only in active (*cFos+*) cells
- Dox system allows opening/closing of labeling window
- Cells active during a particular memory (*ChR2+*) can be manipulated at later time point

### Behavioral Analysis Following Chronic Reactivation of Tagged Cells

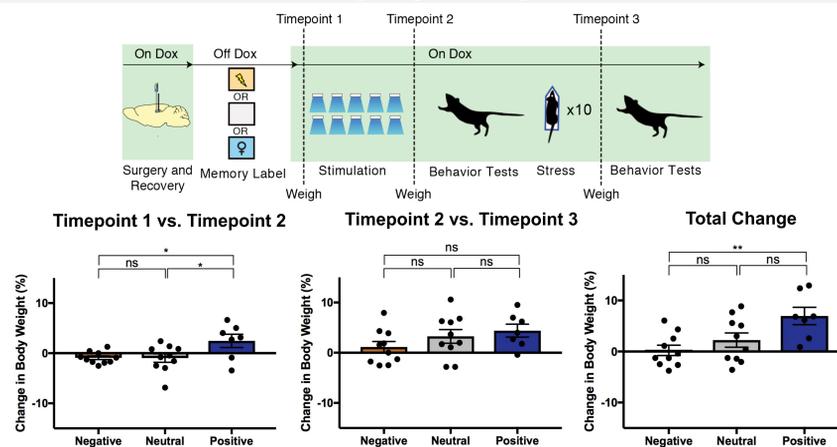


## Chronic Reactivation of Tagged dDG Cells Modulates Behavior and Bodyweight

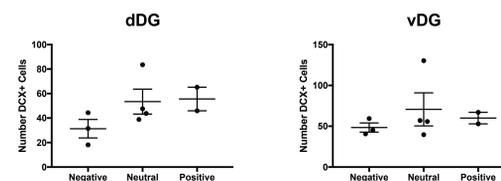
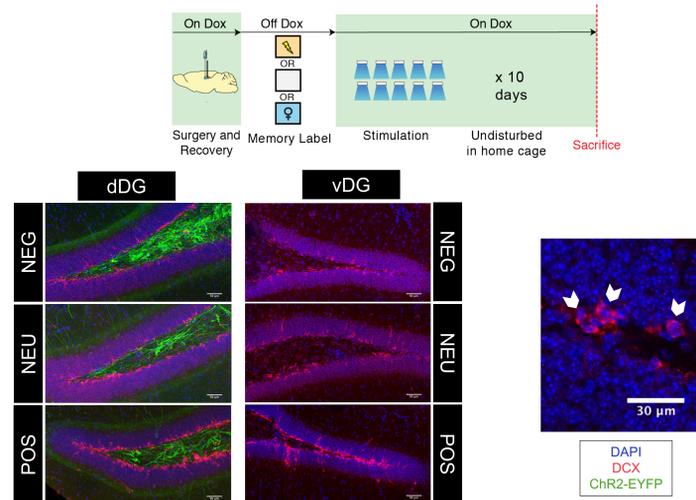
### Social and Hedonic Behavior



### Bodyweight Change

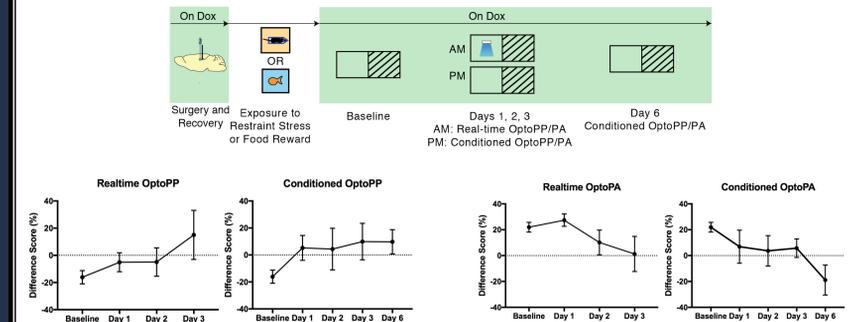


### Neurogenesis

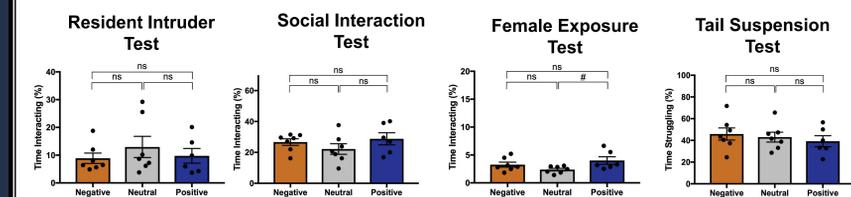


## Chronic Reactivation of Food Reward/Immobilization Stress affects Place Preference/Aversion, but does not affect Behavior

### Eliciting Optogenetic Place Preference and Aversion

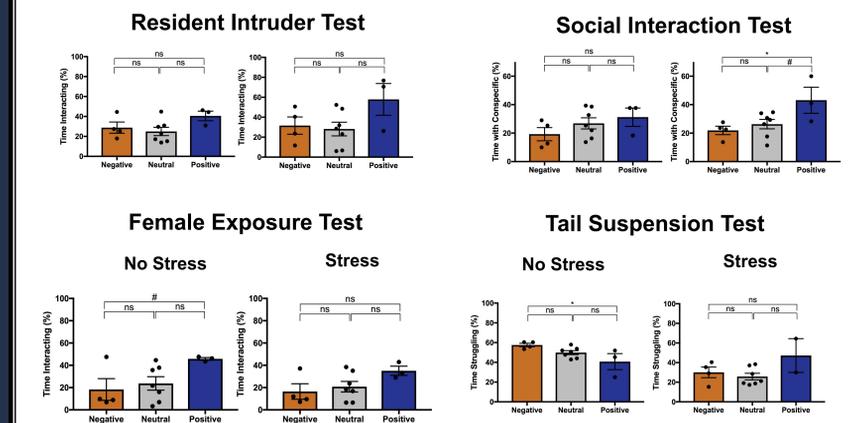


### Effect of Chronic Reactivation on Hedonic and Social Behavior

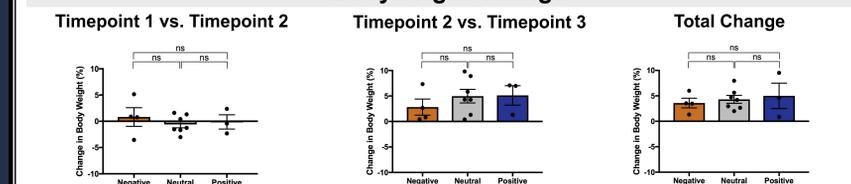


## Future Directions – Chronic Reactivation of Tagged vDG Cells

### Social and Hedonic Behavior



### Bodyweight Change



## Conclusions

- Chronic optogenetic stimulation of dDG cells encoding a negative or positive experience is sufficient to affect social and hedonic behavior and percent change in body weight in an experience-dependent manner.
- Animals exposed to chronic stress following chronic memory stimulation show valence-specific differences in social and hedonic behaviors, as well as percent change in body weight.

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