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The Impact of Long-term Social Housing on Biconditional Association Task Performance and Neuron Ensembles in the Anterior Cingulate Cortex and CA3

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The Impact of Long-term Social Housing on Biconditional Association Task Performance and Neuron Ensembles in the Anterior Cingulate Cortex and CA3

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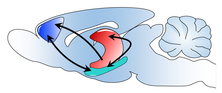
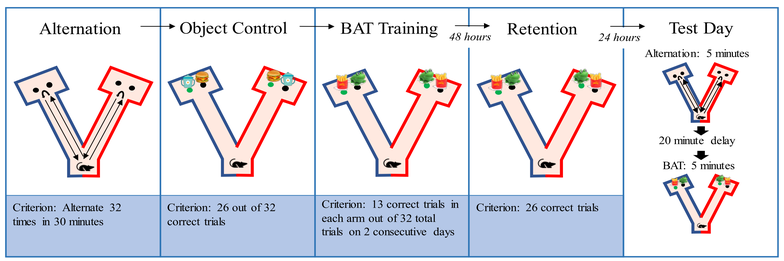
The mechanisms by which social behavior could protect against cognitive aging is unclear and use of a rodent model will help elucidate associated cognitive and neural substrates

- Cognitive decline and changes in neuronal activity are hallmarks of advancing age across species.
- The Biconditional Association Task (BAT) presents an effective means to demonstrate cognitive decline due to aging in rats.
- The prefrontal cortex (PFC) and medial temporal lobe (MTL) are among the first regions to show functional decline with advancing age.
- Altered activity in the PFC and MTL is associated with poorer BAT performance in aged rats.
- Successful human agers have more positive relationships with others and morphological differences in the anterior cingulate cortex (ACC) of the PFC than older adults with more cognitive difficulties.
- **We investigate the differences in performance on BAT and the corresponding neuronal activity between socially housed (SH) and non-socially housed (NSH) aged rats in comparison to individually housed young control (YC) rats.**



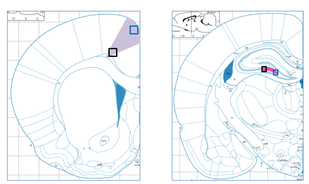
After 2 years of social or non-social housing, in old age rats were tested on the Biconditional Association Task (BAT) and their brains were imaged for neuronal activation using catFISH

9 aged SH rats with environmental enrichment	9 aged NSH rats with environmental enrichment	8 YC non-socially housed rats without environmental enrichment



BAT is an alternation style maze in which making the correct choice requires rats to associate a specific object with its location in the maze

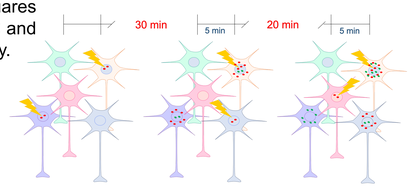
1. Double catFISH → 2. Imaging → 3. Cell counting



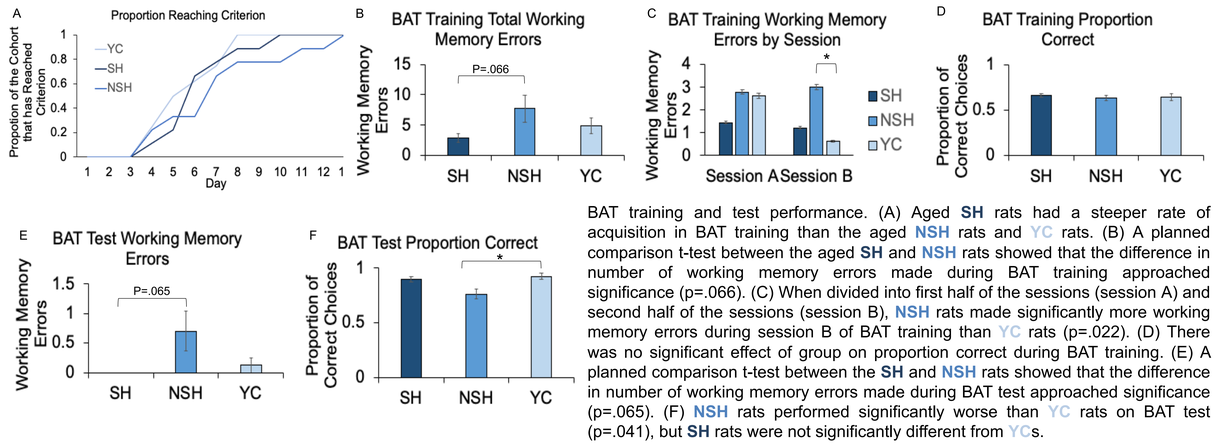
1. Brain tissue was processed for double **Cellular Compartmental Analysis of Temporal Fluorescent *in situ* Hybridization (catFISH)** by labeling expression of two immediate early genes Arc and Homer.

2. The CA3 region of the hippocampus and the ACC were imaged for each rat. Regions quantified (ACC: light purple, CA3: pink). Black and blue squares indicate deep and superficial areas of the ACC and distal and proximal areas of the CA3 respectively.

3. Cells were counted for expression of Arc and Homer. *Arc* and *Homer* subcellular location allows for the characterization of neuronal activity during 2 distinct epochs of behavior.

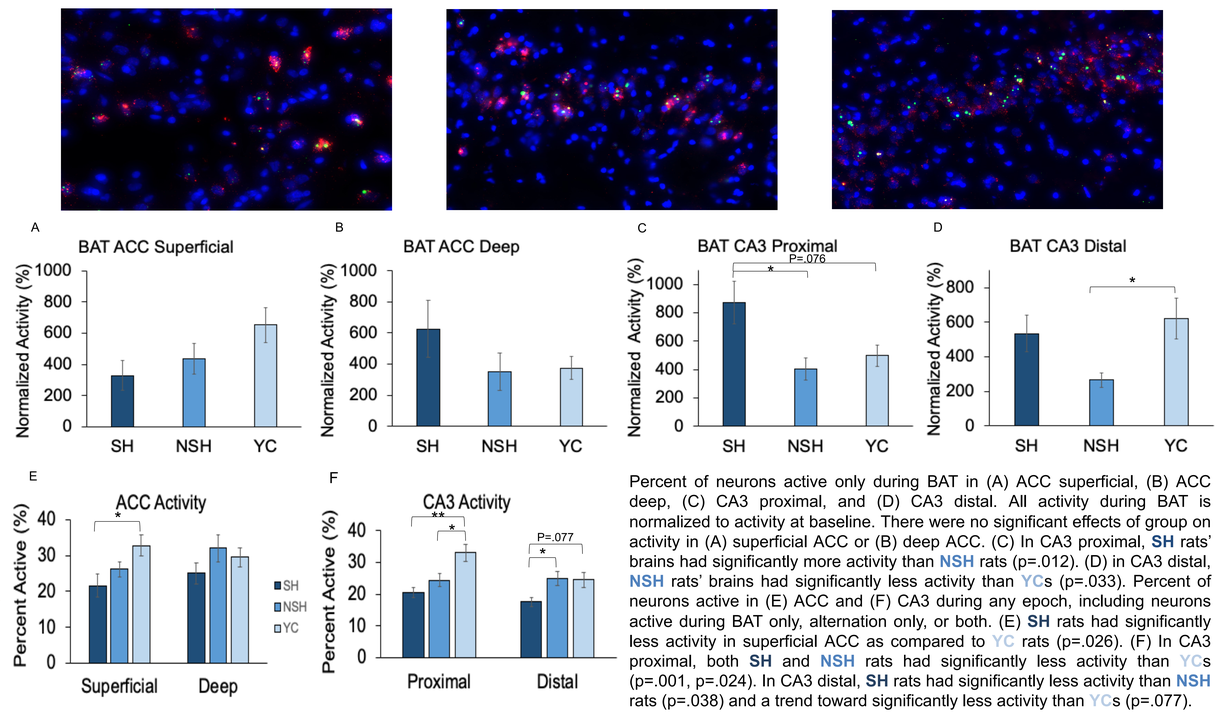


Aged NSH rats but not aged SH rats were significantly impaired on BAT performance compared to YC rats



BAT training and test performance. (A) Aged **SH** rats had a steeper rate of acquisition in BAT training than the aged **NSH** rats and YC rats. (B) A planned comparison t-test between the aged **SH** and **NSH** rats showed that the difference in number of working memory errors made during BAT training approached significance (p=.066). (C) When divided into first half of the sessions (session A) and second half of the sessions (session B), **NSH** rats made significantly more working memory errors during session B of BAT training than YC rats (p=.022). (D) There was no significant effect of group on proportion correct during BAT training. (E) A planned comparison t-test between the **SH** and **NSH** rats showed that the difference in number of working memory errors made during BAT test approached significance (p=.065). (F) **NSH** rats performed significantly worse than YC rats on BAT test (p=.041), but **SH** rats were not significantly different from YCs.

Across both epochs, aged SH rats showed less neuronal activation in superficial ACC and in both proximal and distal CA3 as compared to YCs



Percent of neurons active only during BAT in (A) ACC superficial, (B) ACC deep, (C) CA3 proximal, and (D) CA3 distal. All activity during BAT is normalized to activity at baseline. There were no significant effects of group on activity in (A) superficial ACC or (B) deep ACC. (C) In CA3 proximal, **SH** rats' brains had significantly more activity than **NSH** rats (p=.012). (D) In CA3 distal, **NSH** rats' brains had significantly less activity than YCs (p=.033). Percent of neurons active in (E) ACC and (F) CA3 during any epoch, including neurons active during BAT only, alternation only, or both. (E) **SH** rats had significantly less activity in superficial ACC as compared to YC rats (p=.026). (F) In CA3 proximal, both **SH** and **NSH** rats had significantly less activity than YCs (p=.001, p=.024). In CA3 distal, **SH** rats had significantly less activity than **NSH** rats (p=.038) and a trend toward significantly less activity than YCs (p=.077).

Socially housing rats likely protects against cognitive decline and changes in neuronal activation due to advancing age

Behavioral conclusions:

- Aged **SH** rats made fewer working memory errors during BAT training and test than **NSH** rats demonstrating that social housing may confer benefits to working memory in advanced age.
- **NSH** rats had significantly less correct trials on BAT test as compared to YCs; however, **SH** rats did not perform significantly differently than YCs suggesting that social housing may partially protect against decline in cognitive flexibility in advanced age.

Neuronal activation conclusions:

- **NSH** rats had significantly less proximal CA3 neuronal activation during BAT than **SH** rats and significantly less distal CA3 neuronal activation during BAT than YCs which may be related to more working memory errors and lower proportion correct on BAT by **NSH** rats.
- YCs had higher levels of cell activity in superficial ACC, distal CA3, and proximal CA3 during any epoch as compared to aged rats. Although neuronal activation often increases with age, changes in neuronal activation in the CA3 during BAT with advancing age have not been studied. Since aged rats received enrichment while YCs did not, higher levels of neuronal activation observed in the brains of YCs may also be due to a lack of social, physical, and cognitive enrichment.
- **NSH** rats had significantly more neuronal activation in distal CA3 during any epoch than **SH** rats suggesting that socially housing rats throughout their lives likely protects against age-related increases in neuronal activation in distal CA3.

Future directions:

- Further investigation is needed to determine the mechanisms that may be affected by sociality in aged rats and whether there are additional changes in neuronal activation in other brain regions not examined here.
- Further studies should be designed to include young controls that receive environmental and cognitive enrichment to determine whether lack of enrichment is a valid explanation for the higher levels of neuronal activity in YC rats as compared to aged rats observed in this study.

Acknowledgements

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