

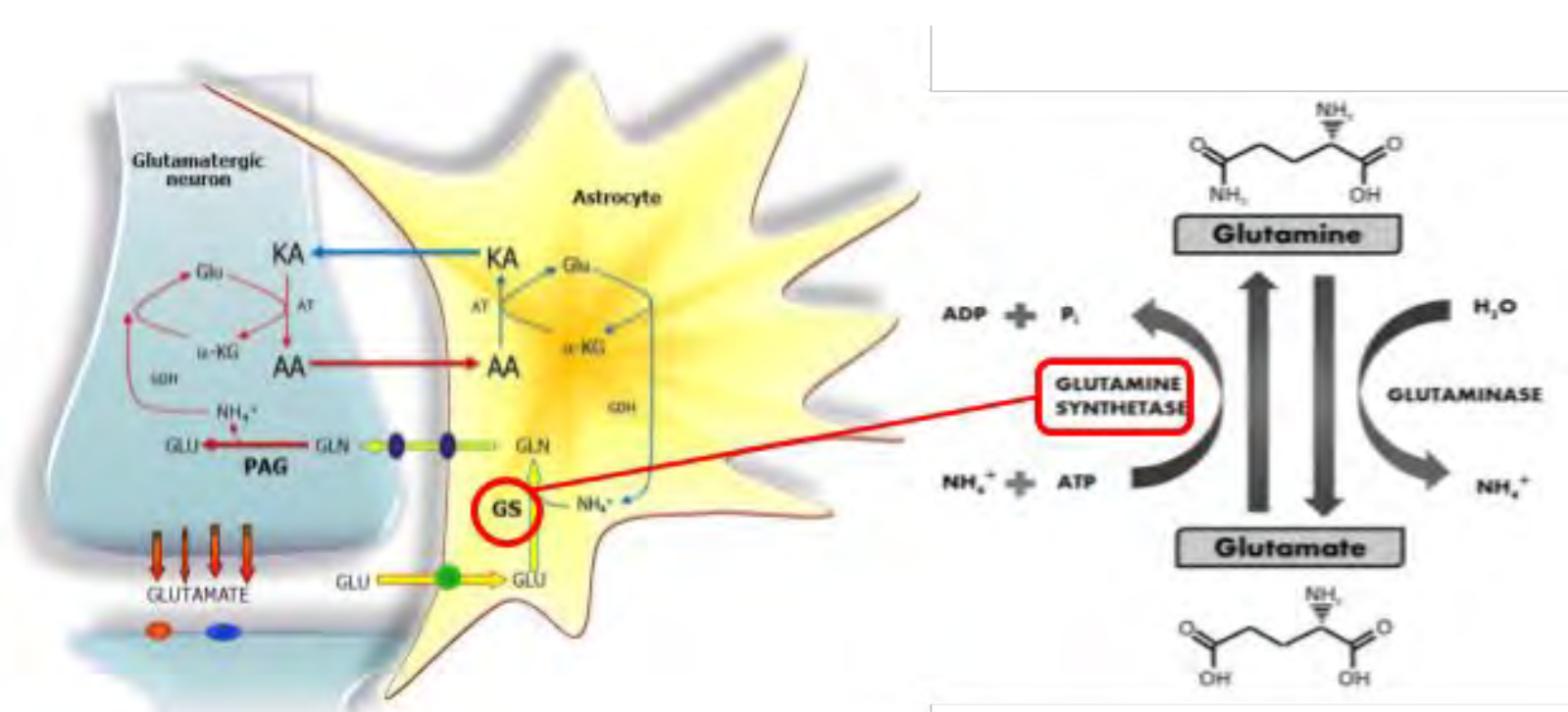
# MAY WE HAVE YOUR ATTENTION: SUSTAINED ATTENTION SHOWS BRAIN REGION SPECIFIC INCREASED ASTROCYTIC GLUTAMATE RECYCLING

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## INTRODUCTION

Astrocytes have an important role in cognition as they possess the unique ability to recycle glutamate from synapses. Dysfunctional astrocytes often contribute to neurodegenerative disorders and changes in glutamate recycling have been implicated, but the impact of these changes on cognition remains unclear. This study focuses on sustained attention, or vigilance, and how recycling of glutamate shifts with this behavior. We characterized the rat's cognitive performance based on accuracy and reaction times and assessed whether these behaviors correlated with glutamine synthetase activity. We additionally examine female rat vaginal smears to correlate estrous phases with performance. We hypothesize that having faster reaction times and a higher percentage in correct answers indicates better sustained attention and will correlate with higher glutamine synthetase levels.



## METHODOLOGY

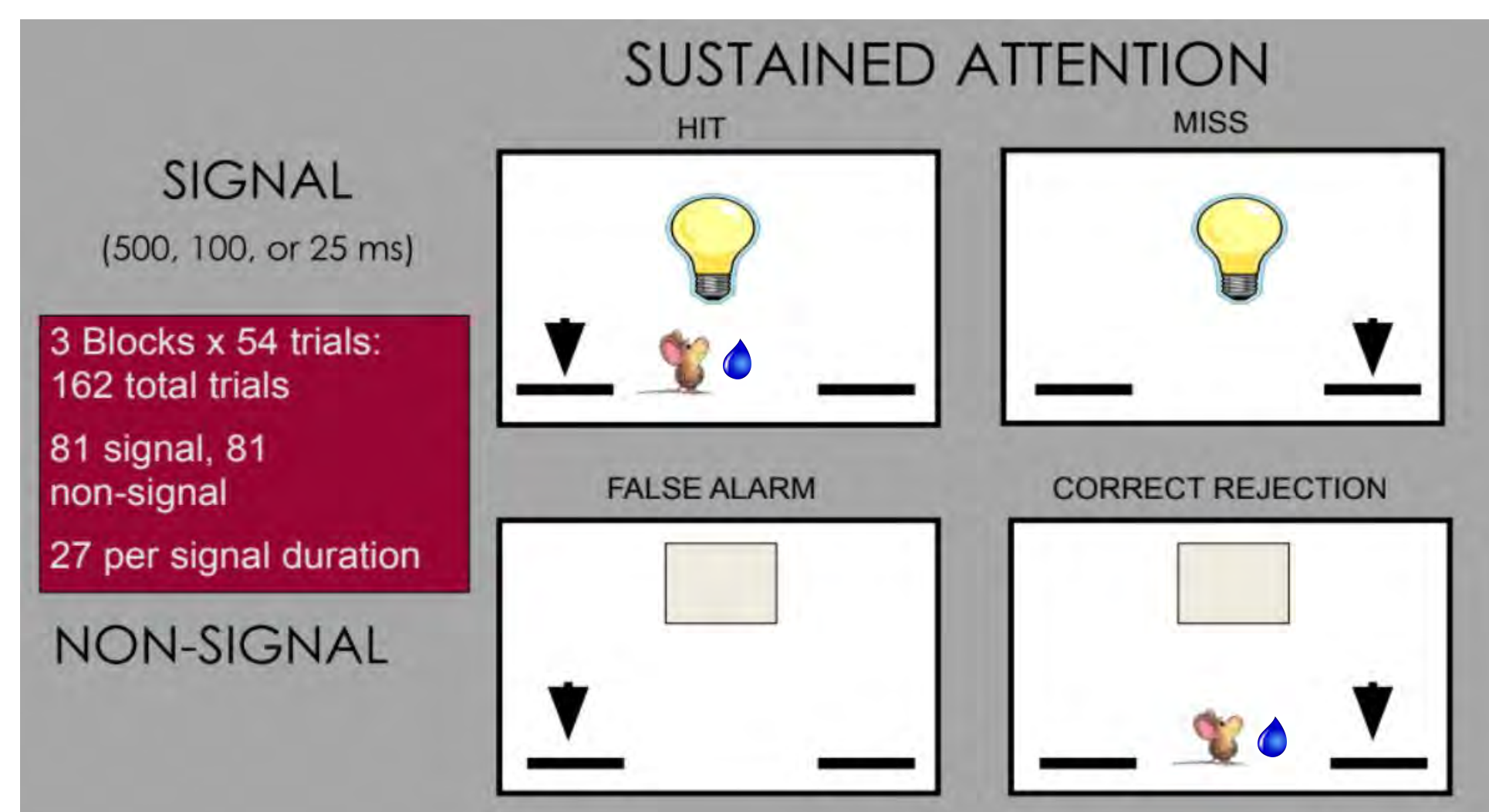
### SUBJECTS:

Male and female Long-Evans Rats (bred onsite at Vassar College, NY, pair-housed, males n=25, females n=27) were used in this study.

### SUSTAINED ATTENTION TASK:

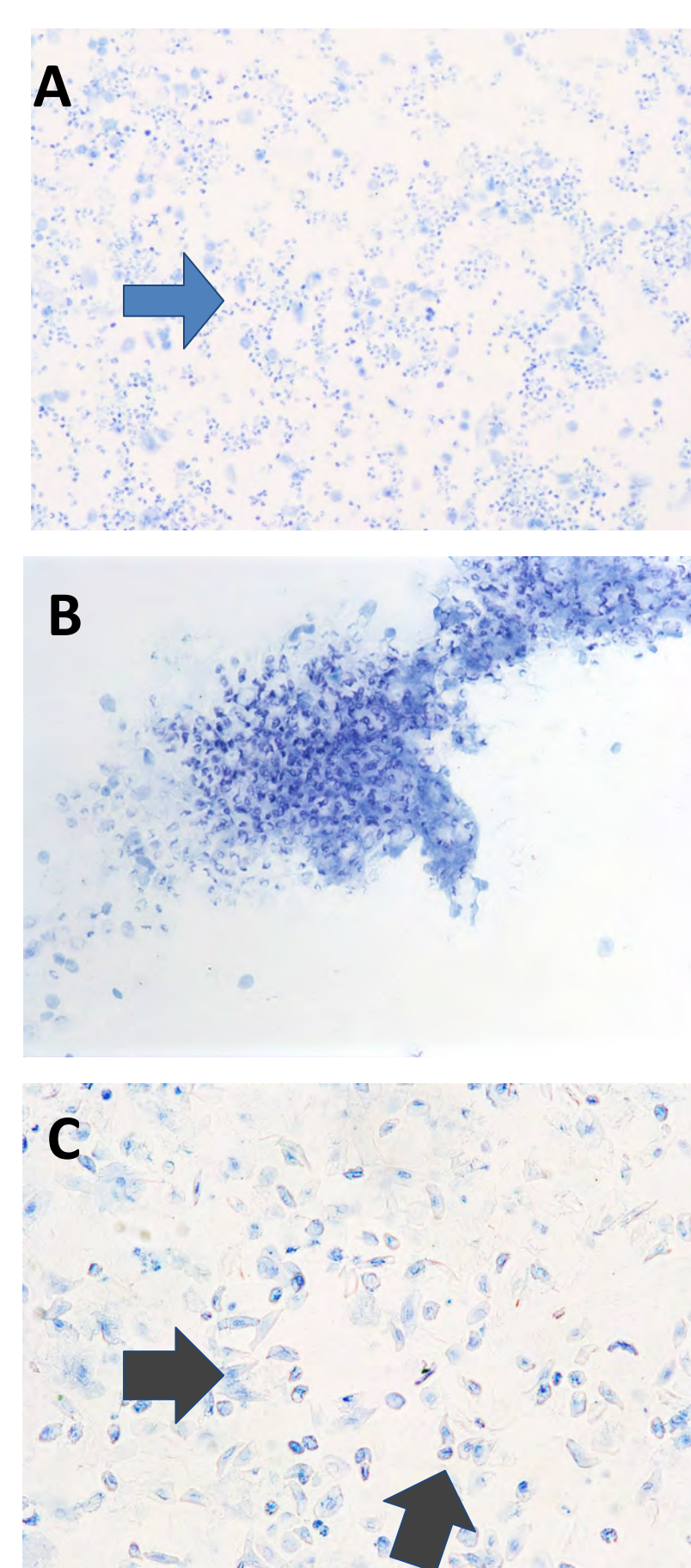
Subjects were trained on the sustained attention task, and then separated into an attending, unattending, and side bias groups based on their performance:

- Attending rats had at least above 70% correct during the 500 ms signal trials and nonsignal trials.
- Unattending rats averaged around chance performance (50%).
- Side bias rats achieved less than 40% on signals or non-signals suggesting they were pressing the same lever regardless of the signal/non-signal trials.



### VAGINAL SMEARS

Vaginal smears were taken before and after the sustained attention task. Smears were mounted onto microscope slides and stained with toluidine blue. Microscopy was used to obtain images of smears. The estrous cycle lasts 4-5 days, and can be classified by the cells that are present in a vaginal smear (Cora et al., 2015). Previous studies have indicated that performance on learning and memory tasks can be affected by the stage of the cycle the rat is in, with phases with higher estrogens improving spatial working memory (Korol, 2004). Images are at 200X magnification. **A** Diestrus, indicated by the large number of neutrophils present (arrow). **B** Proestrus, indicated by the clumps of small nucleated epithelial cells. **C** Estrus, indicated by the presence of large, anucleated epithelial cells (arrows).



## BEHAVIORAL RESULTS

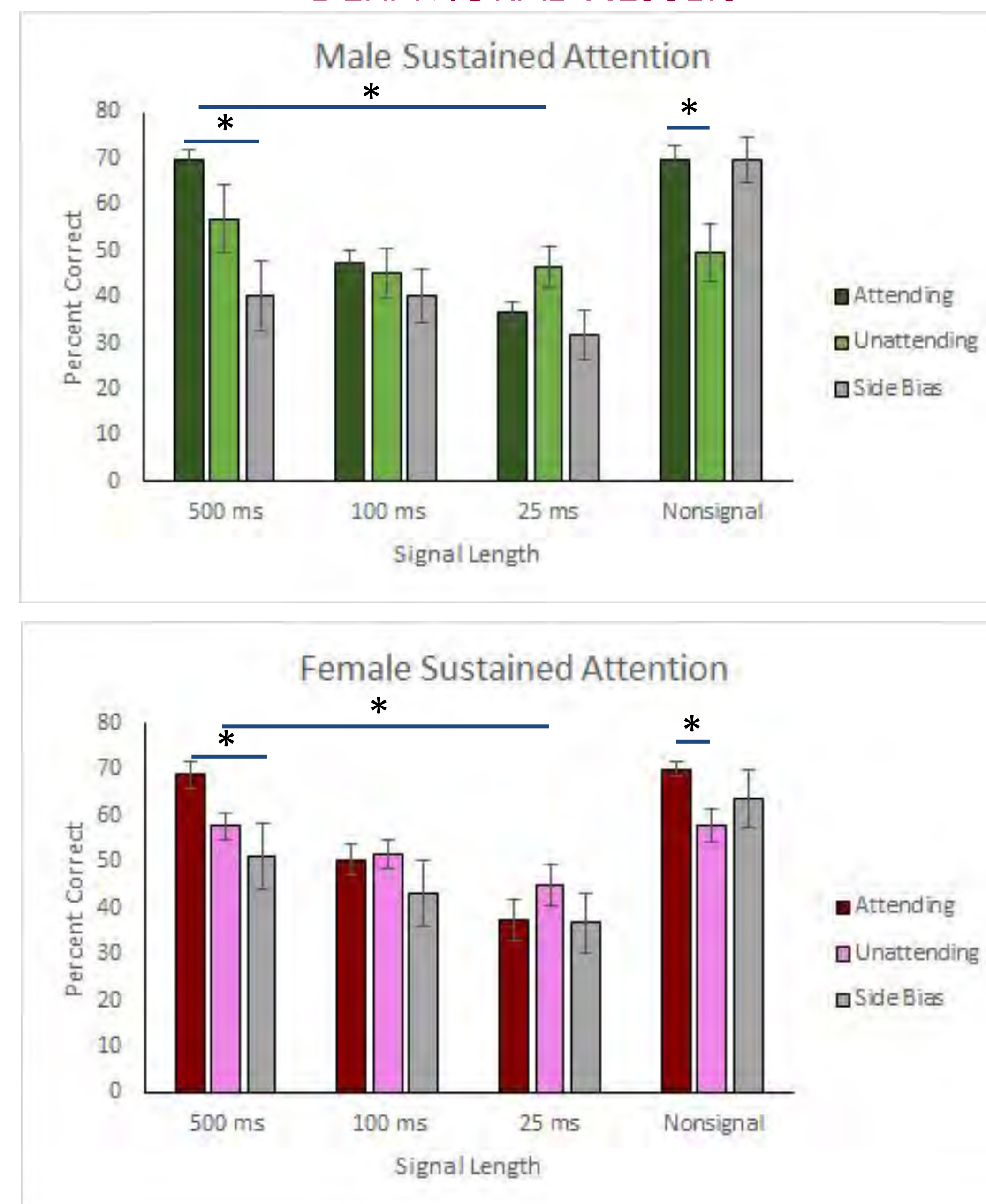


FIGURE 1:

There was no significant sex difference between male and female accuracy on the sustained attention task ( $p > 0.3$ ). There was a significant effect of signal length on percent correct with longer signal lengths correlating with better performance ( $F_{2,92} = 79.85, p < 0.001$ ) and this significantly interacted with attention level ( $F_{4,92} = 13.30, p < 0.001$ ) such that attending animals were significantly better at detecting the 500 ms signal compared to animals with a side bias ( $p < 0.001$ ). There was a significant effect of attention level, with attending animals performing significantly better than side bias animals on signals ( $F_{2,46} = 3.31, p = 0.046$ ) and unattending animals on nonsignals ( $F_{2,46} = 5.91, p = 0.005$ ).

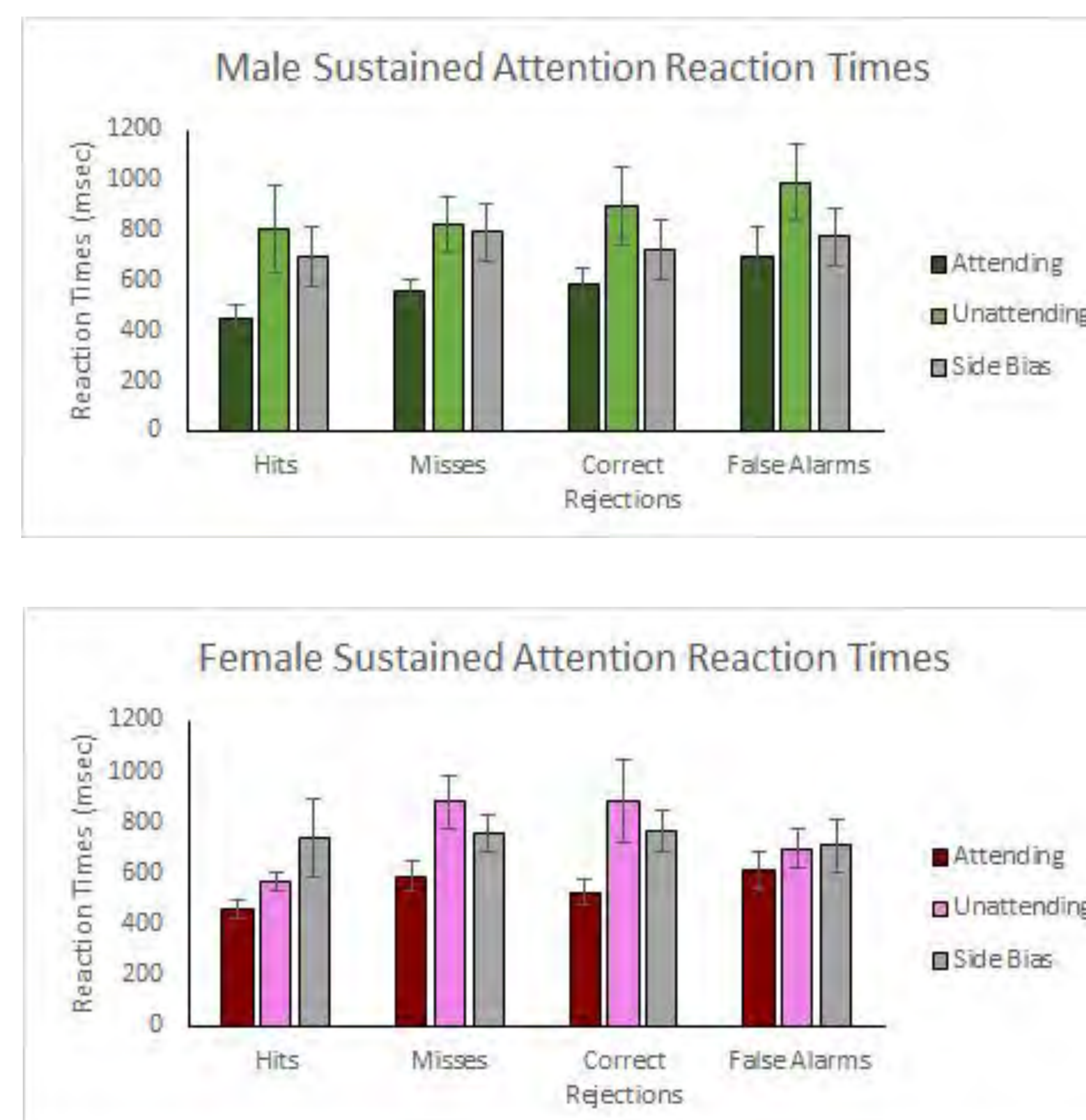


FIGURE 2:

Correct responses were significantly faster than incorrect responses ( $F_{1,45} = 8.71, p = 0.005$ ). There was a significant difference between signal trials and nonsignal trials with signal trials being significantly faster than nonsignal trials ( $F_{1,45} = 10.34, p = 0.002$ ). There is a significant effect of attending levels on reaction time with attending animals having significantly faster reaction times than side bias and unattending animals ( $F_{2,45} = 5.34, p = 0.008$ , attending vs. unattending:  $p = 0.013$ ).

## RESULTS CONTINUED

### GLUTAMINE SYNTHETASE (GS) IMMUNOHISTOCHEMISTRY

Brains were sectioned using a cryostat (40  $\mu$ m) and stained for glutamine synthetase (GS) by immunohistochemistry. GS levels were quantified using Fiji software.

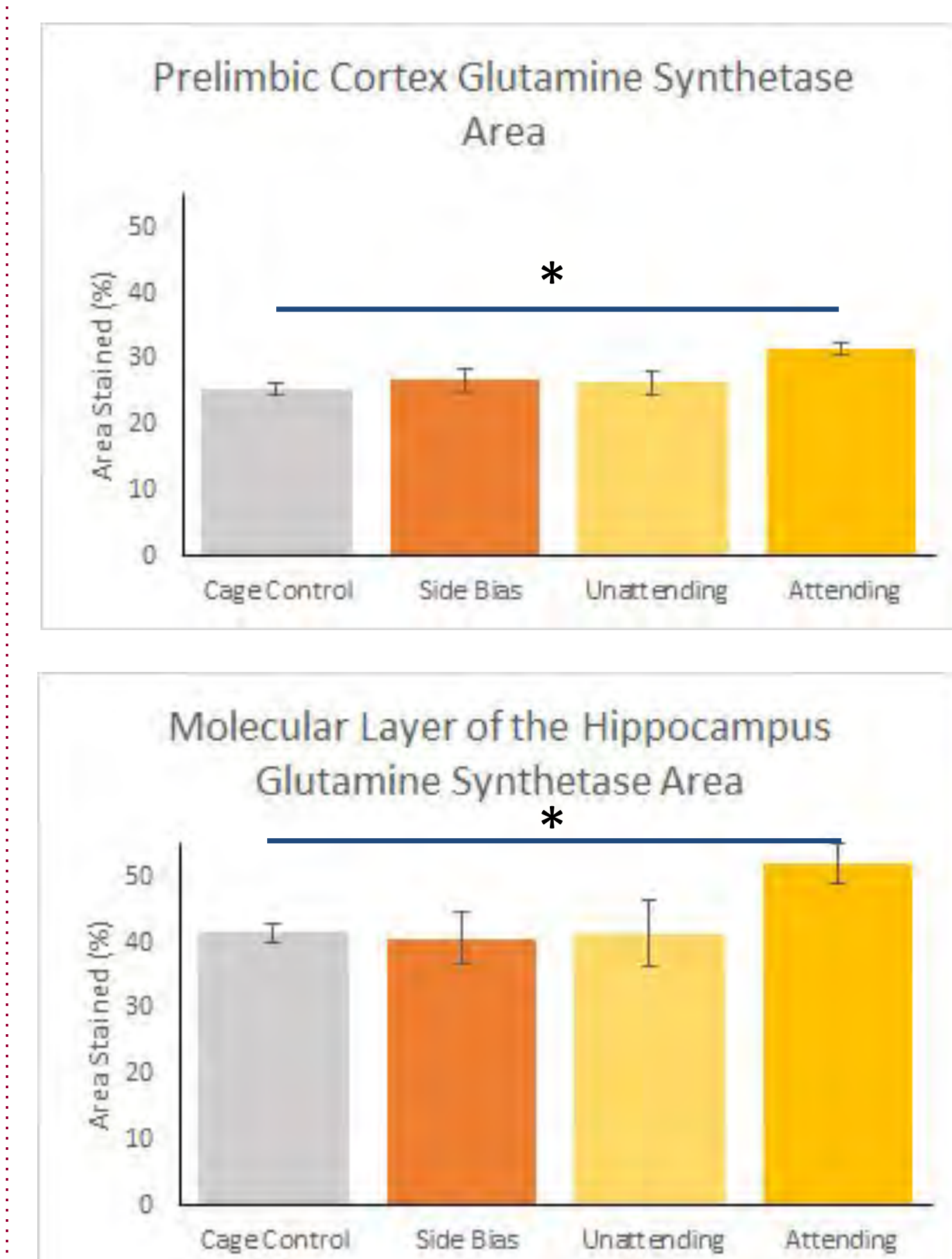


FIGURE 3:

In the prelimbic cortex and the molecular layer of the hippocampus, attending animals had significantly increased percent area stained compared to the cage control (prelimbic cortex:  $F_{3,34} = 5.92, p = 0.002$ , molecular layer:  $F_{3,34} = 3.21, p = 0.035$ ).

## CONCLUSIONS

- Attending animals are more accurate, particularly on the 500 ms signal, and have significantly faster responses.
- Attending animals demonstrated higher levels of glutamine synthetase within the prelimbic cortex and hippocampus, which are involved in attention and learning.
- No significant sex differences were seen in behavior, and further analysis is needed to assess sex differences in glutamine synthetase.
- Rats are faster to respond correctly than incorrectly, and responses to signal trials are faster than nonsignal trials. This may suggest that when the signal is presented the animal is already orienting to the signal lever.

## FUTURE PLANS

- We will continue to quantify glutamine synthetase levels.
- We will continue to examine female rat vaginal smears to see if there is a correlation between estrous levels and cognitive performance.

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