

Modeling Sporadic Alzheimer's Disease Across Age: Behavioral Effects of ICV Streptozotocin in Female Rats



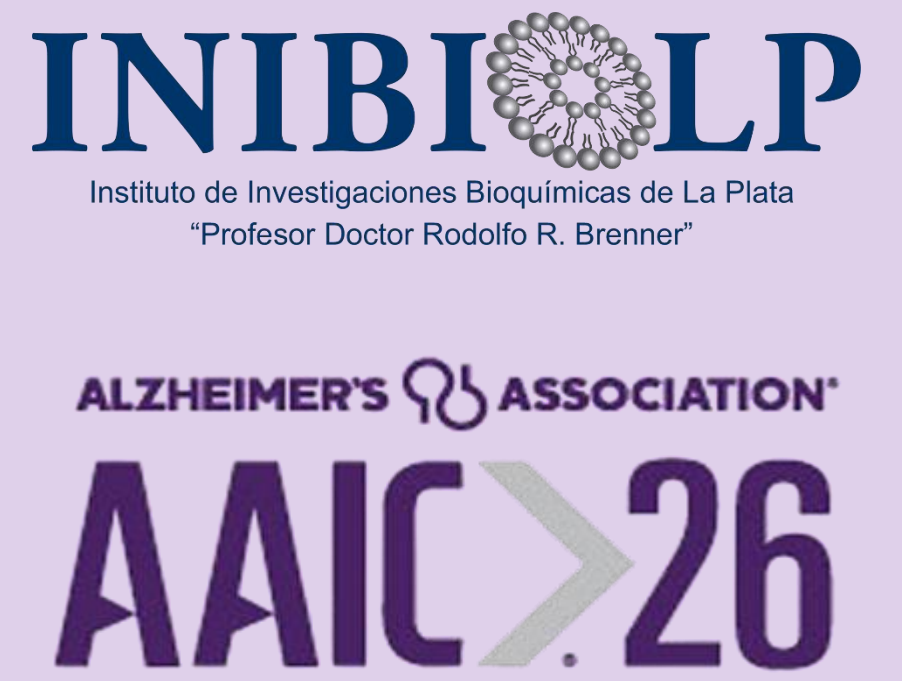
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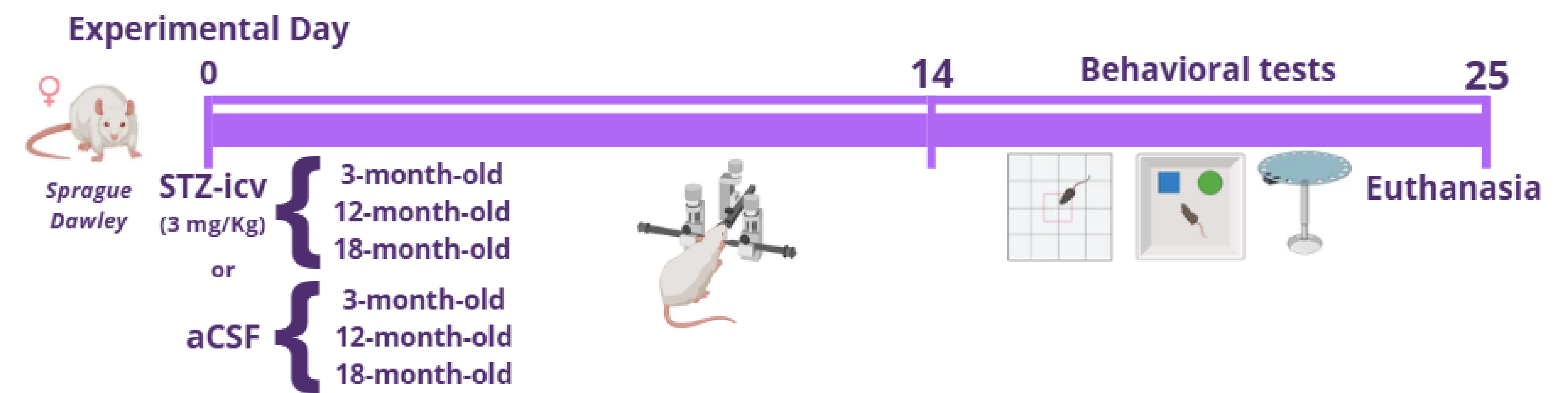
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Background

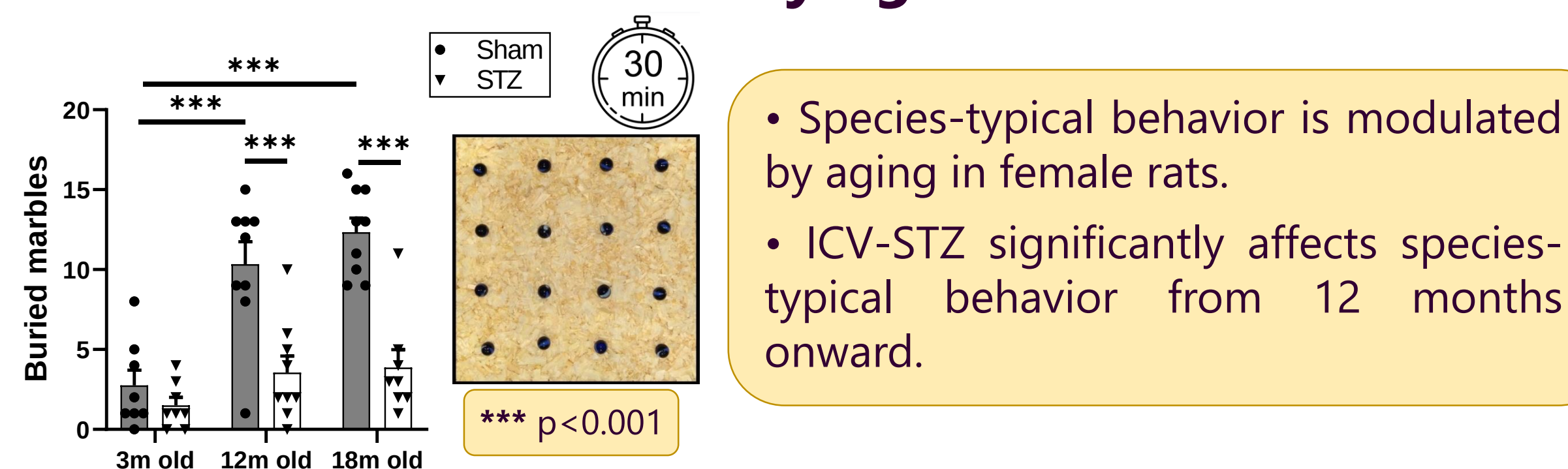
Alzheimer's disease (AD) is the most common cause of dementia and affects women disproportionately, yet female animals remain underrepresented in preclinical studies. The intracerebroventricular streptozotocin (ICV-STZ) model is widely used to mimic sporadic AD-like alterations, although its characterization has focused mainly on male. Whether the behavioral impact of STZ in females is modulated by age across the lifespan remains unclear. This study aimed to assess age-related differences in STZ-induced behavioral alterations in female rats, considering young, middle age, and advanced age.

Metodology

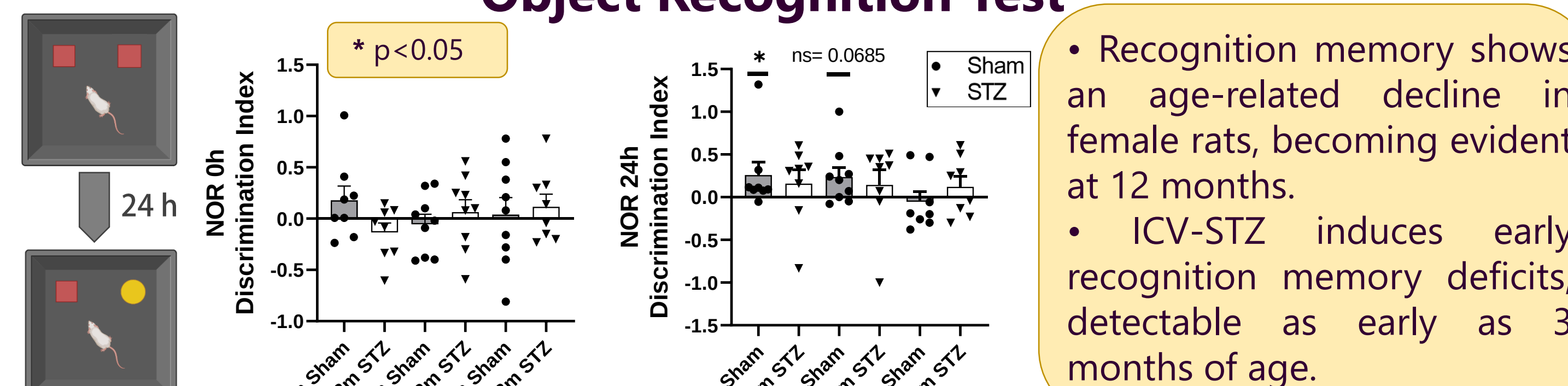


Results

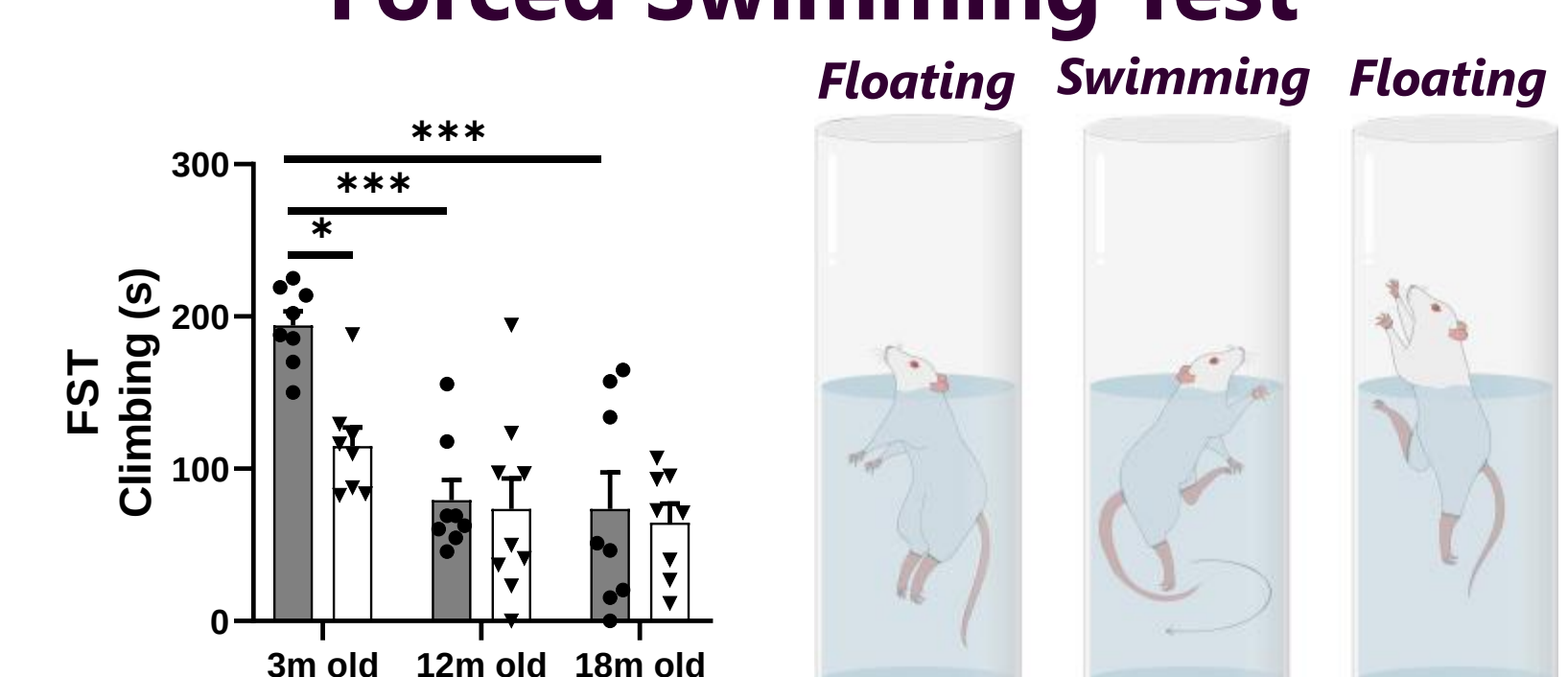
Marble Burying Test



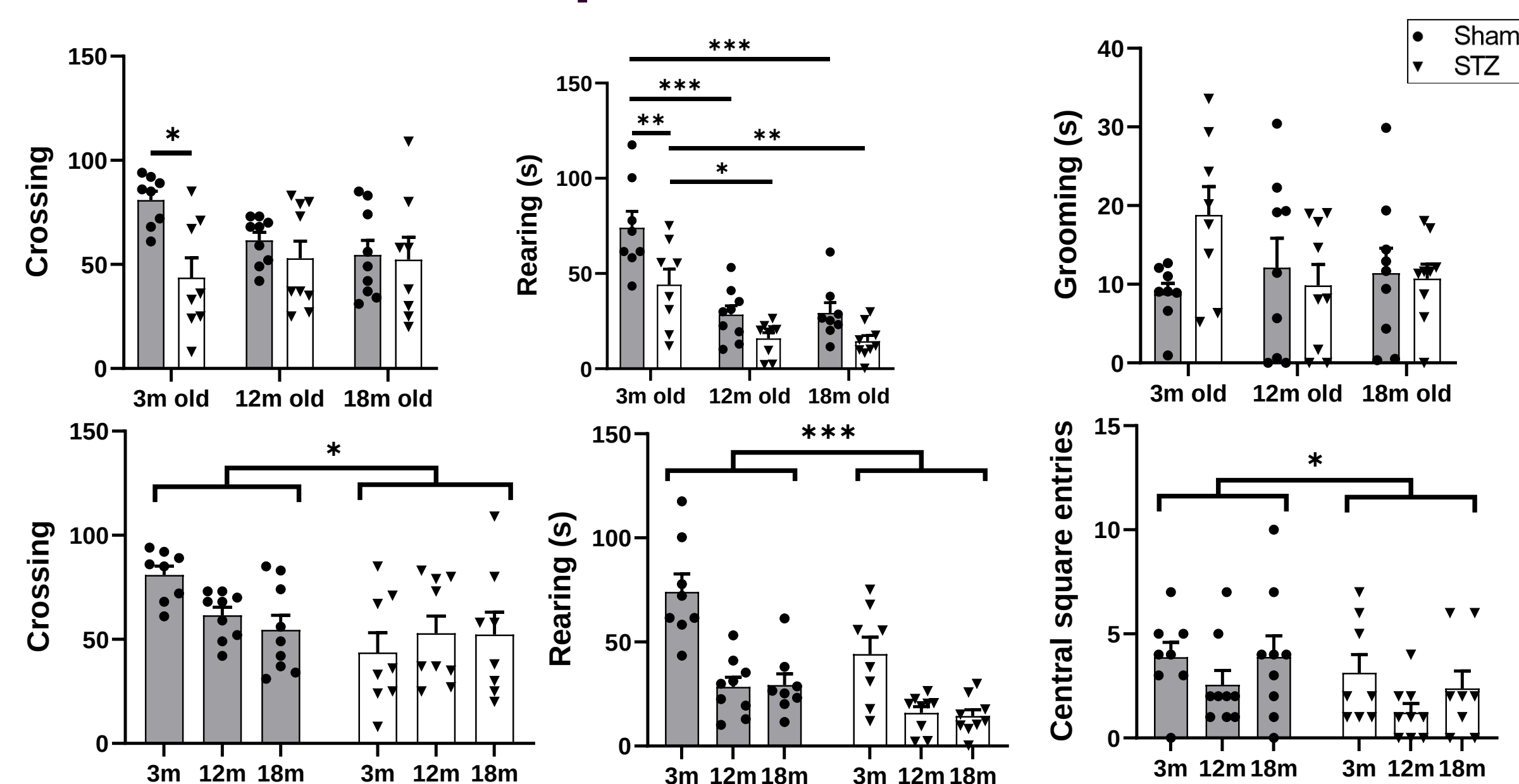
Object Recognition Test



Forced Swimming Test



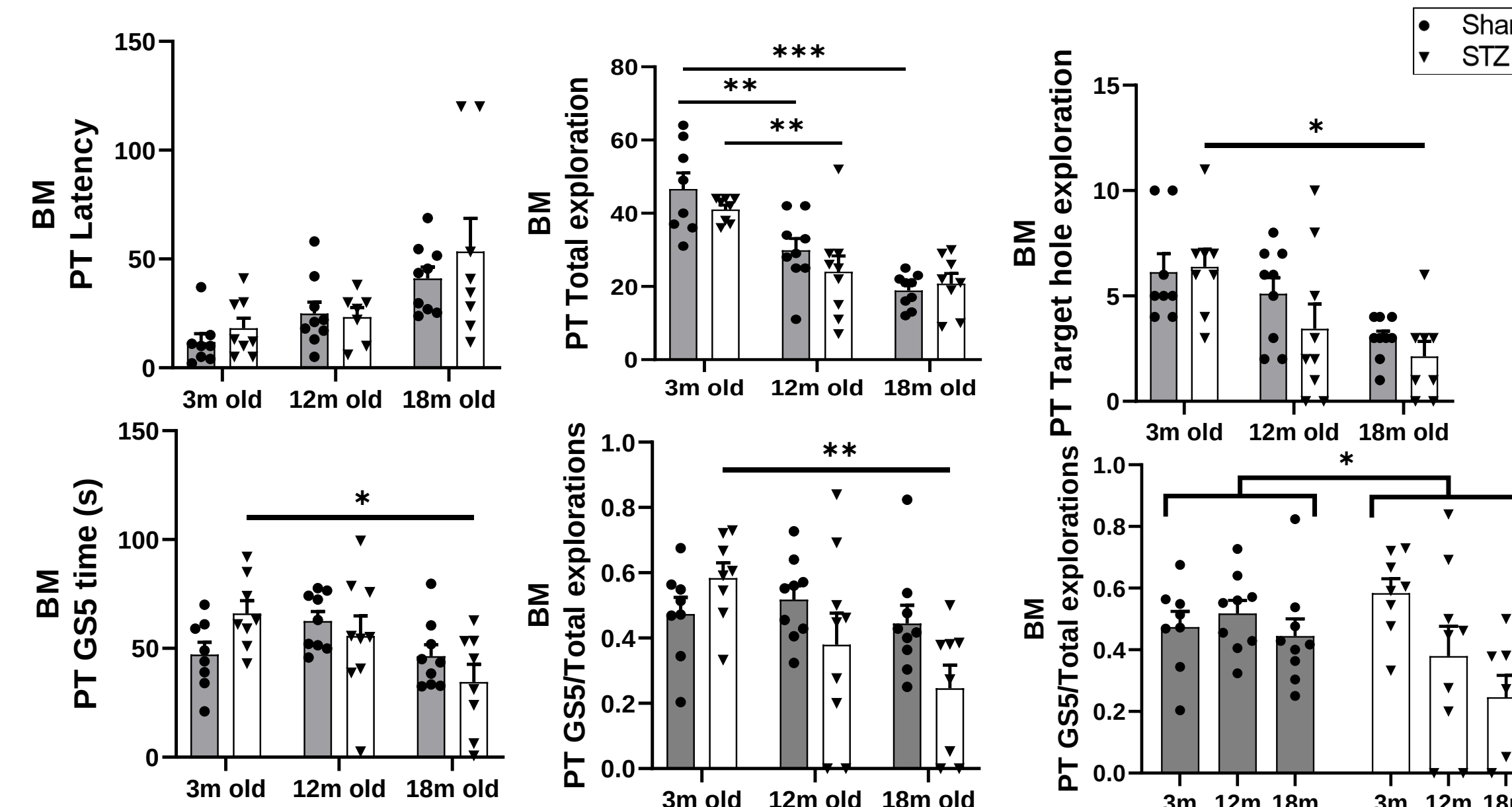
Open Field Test



- Aging reduces exploration without affecting anxiety.
- STZ reduces exploration and increases anxiety, regardless of age.

*p<0.05
**p<0.01
***p<0.001

Barnes Maze



- An age-related decline in spatial memory is observed in female rats
- ICV-STZ impairs specific spatial memory parameters across all age groups.

*p<0.05
**p<0.01
***p<0.001

- An age-related increase in depression-like behavior is observed at 12 months, evidenced by reduced climbing and increased floating.
- ICV-STZ enhances depression-like behavior only in young female rats.

Behavioral performance



*p<0.05
**p<0.01
***p<0.001

Future Perspectives

- Neuropathological characterization of STZ-induced alterations across age.
- Assessment of neuroinflammation and oxidative stress.
- Evaluation of insulin signaling and cerebral glucose metabolism alterations.
- Correlation of molecular changes with behavioral outcomes.
- Identification of age-dependent vulnerability factors in female AD models.

Conclusions

These findings indicate that the behavioral effects of ICV-STZ in female rats are modulated by age, with distinct profiles in young, middle-aged and aged animals. Incorporating multiple age ranges is essential to capture the heterogeneity of AD-related behavioral alterations and to improve the translational relevance of preclinical models in females.