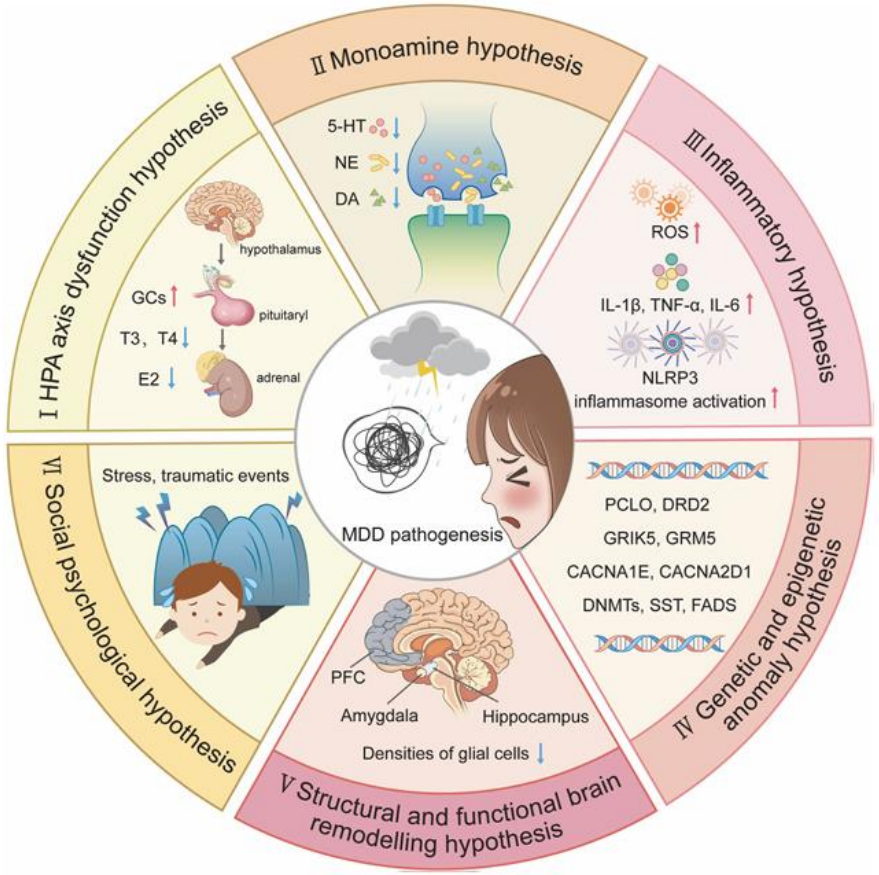
Chronic Unpredictable Mild Stress Model in Antidepressant Preclinical Drug Discovery

2026.01

Depression and Stress

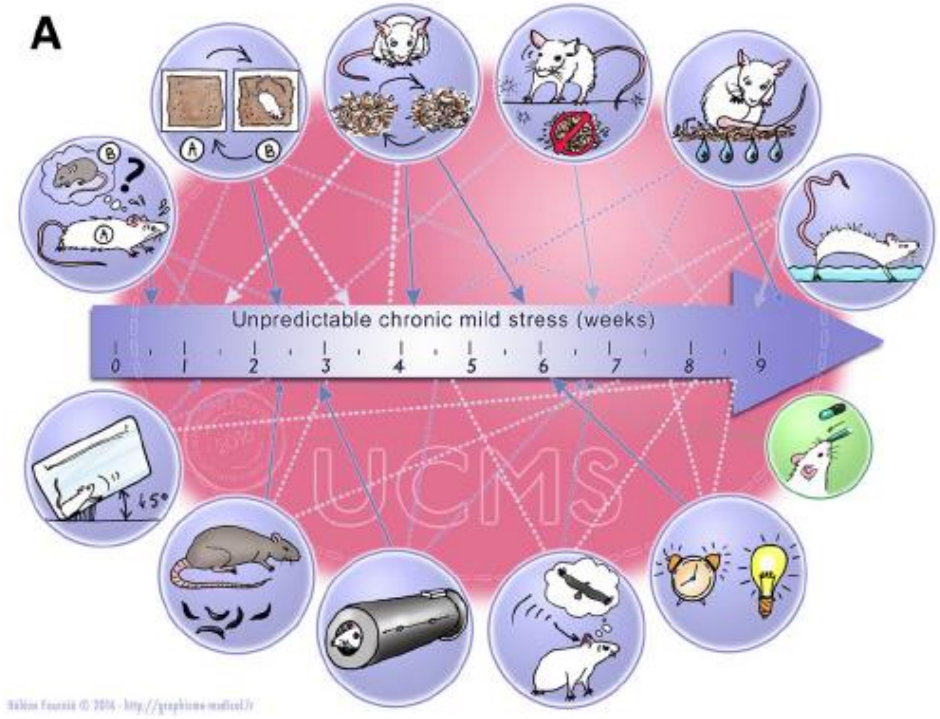


Lulu Cui et al., 2024

- Stress is a core environmental factor that triggers depressive episodes, inducing classic symptoms such as anhedonia, cognitive bias, and social withdrawal through mechanisms including hyperactivity of the HPA axis, inflammation, and impaired neuroplasticity[1].
- Rodent stress models - CUMS, CSDS, and LH reproduce key features of human depression across behavioral, molecular, and physiological levels, and exhibit repeatable, quantifiable responses to antidepressant treatments[2].
- In addition to verifying existing medications, these models also facilitate the clinical transformation of rapid, effective, and personalized antidepressant treatments by enabling target identification, efficacy stratification, and biomarker validation, thereby acting as a crucial link connecting foundational research with the needs of patients[2].

1. Kunying Zhao et al.2025, Front Cell Neurosci
2.XiaoXue Lu et al. 2025, World journal of psychiatry

Etiology Related Model | Chronic Unpredictable Mild Stress Model



Planchez et al., 2019

- A rodent behavioral model centered on repeated exposure to a variety of mild, unpredictable socio-environmental stressors over several weeks, to induce anhedonia and depressive-like states;
- Good face validity showing chronic stress–related depression symptoms mimicking despair, anhedonia, sleep disturbance and body weight loss;
- Good construct validity including HPA axis dysfunction, neuroinflammation, neurotrophins and synaptic plasticity alternation, and neurotransmitter alternation;
- Good predict validity showing response to chronic antidepressant and to ketamine and psilocybin.

- **Predict Validity:** Ketamine, Psilocybin (Acute); Psilocybin, Fluoxetine, Paroxetine (Chronic)
- **Species Availability:** Mouse; Rat
- **Behavioral Endpoints:** SPT, TST, FST, OFT, EPM, SIT
- **Throughput:** 100 animals/batch

SPT: sucrose preference test
TST: tail suspension test
FST: forced swim test
OFT: open field test
EPM: elevated plus maze
SIT: social interaction test

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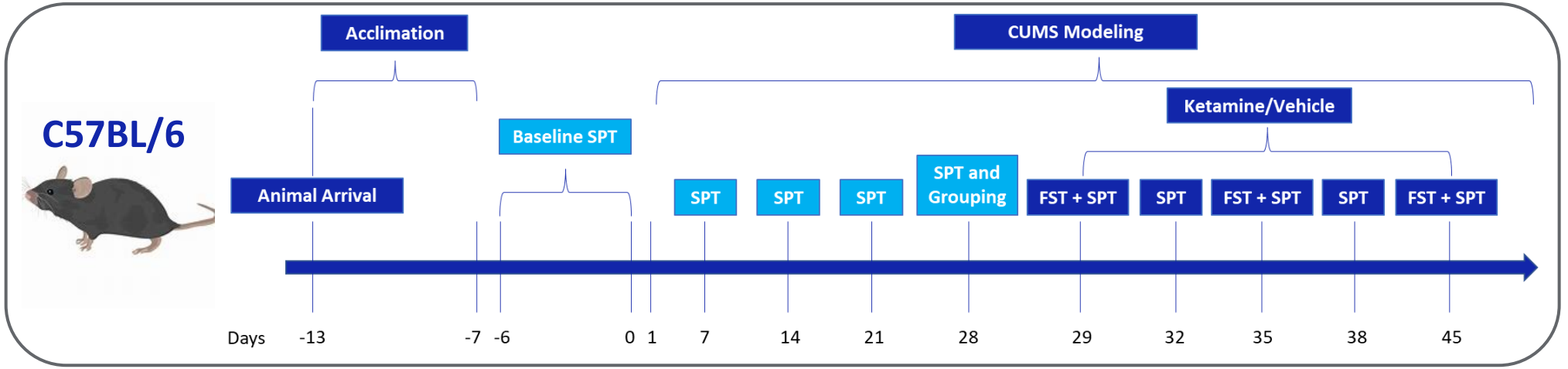
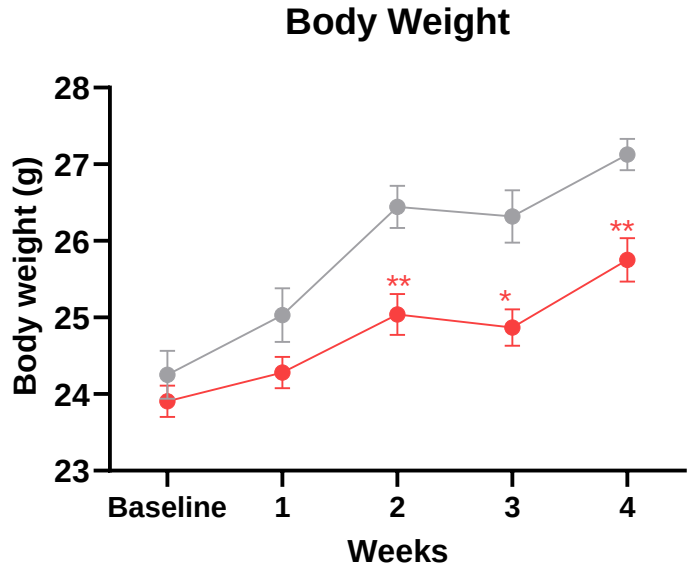
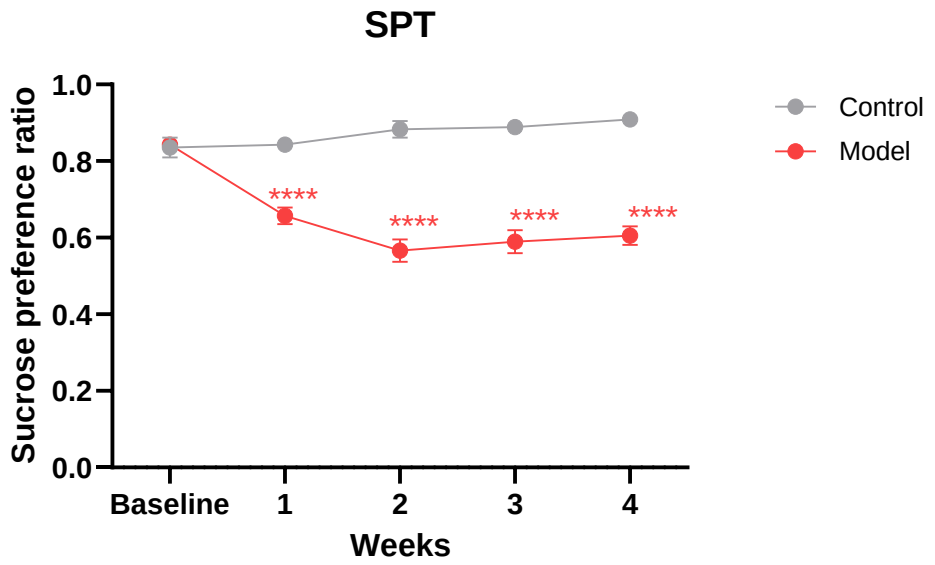


Endpoints During Modeling





Data are mean ± SEM. Repeated measures two way ANOVA with Sidak post-hoc analysis: *P<0.05 ,**P<0.01, ****P<0.0001 vs Control. n=12 for Control group, n=24 for Model group.

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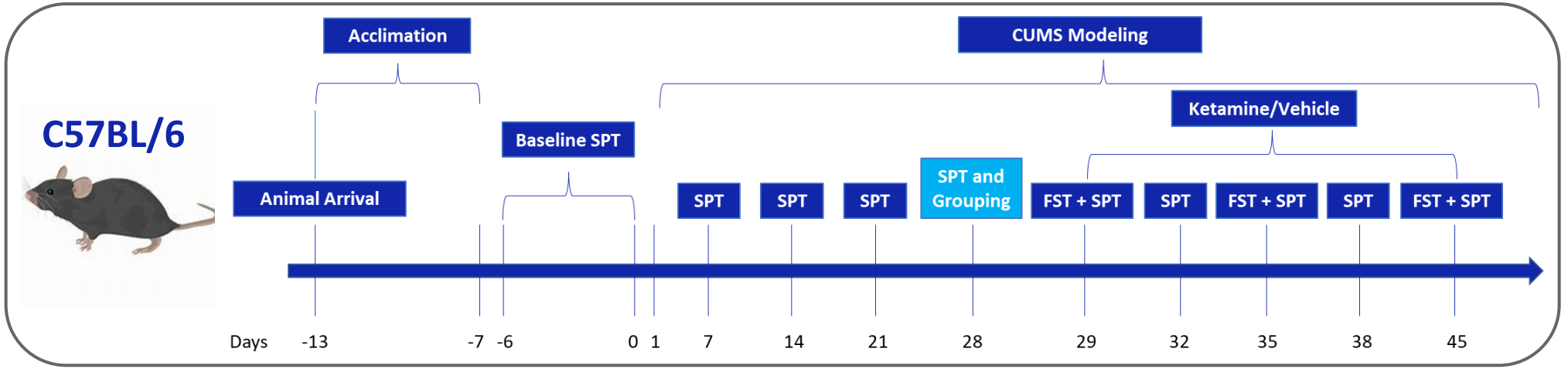
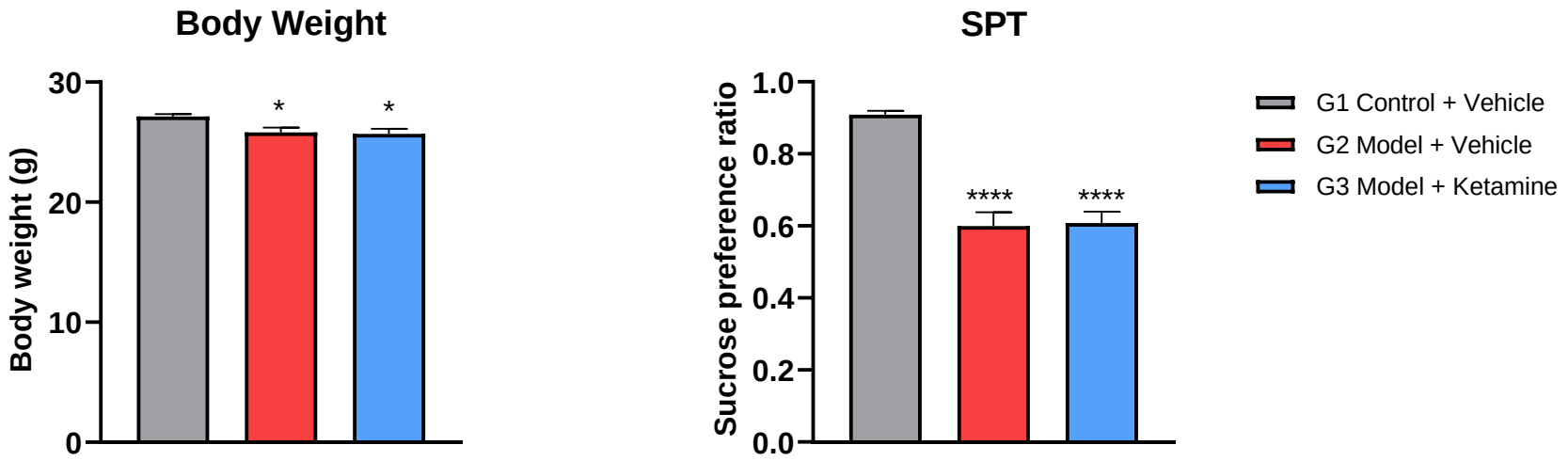


Animal Grouping After Modeling



Data are expressed as mean + SEM. One way ANOVA with Tukey's post-hoc analysis: *p<0.05, **p<0.01, , ****P<0.0001 vs Control + Vehicle group;

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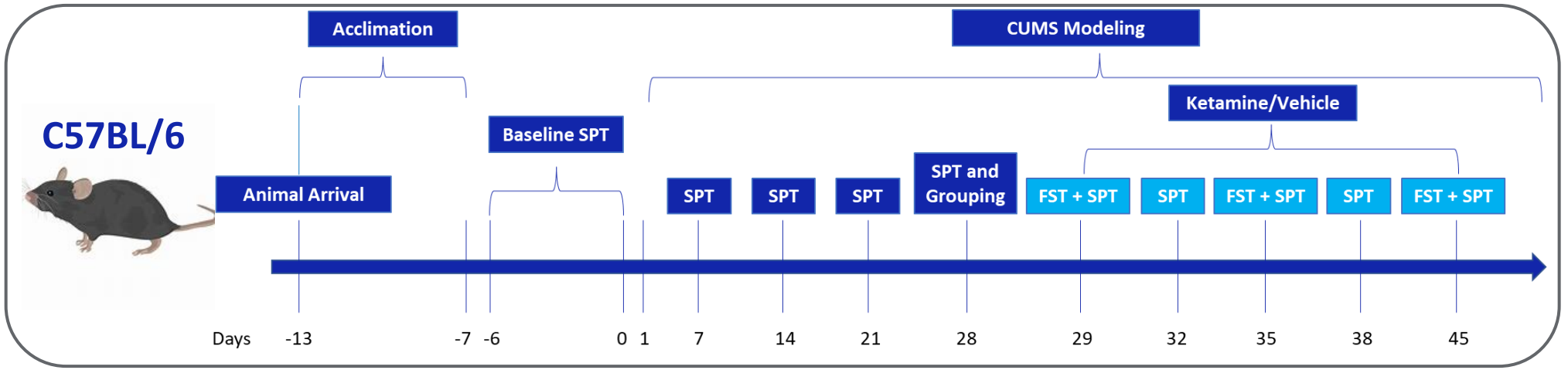
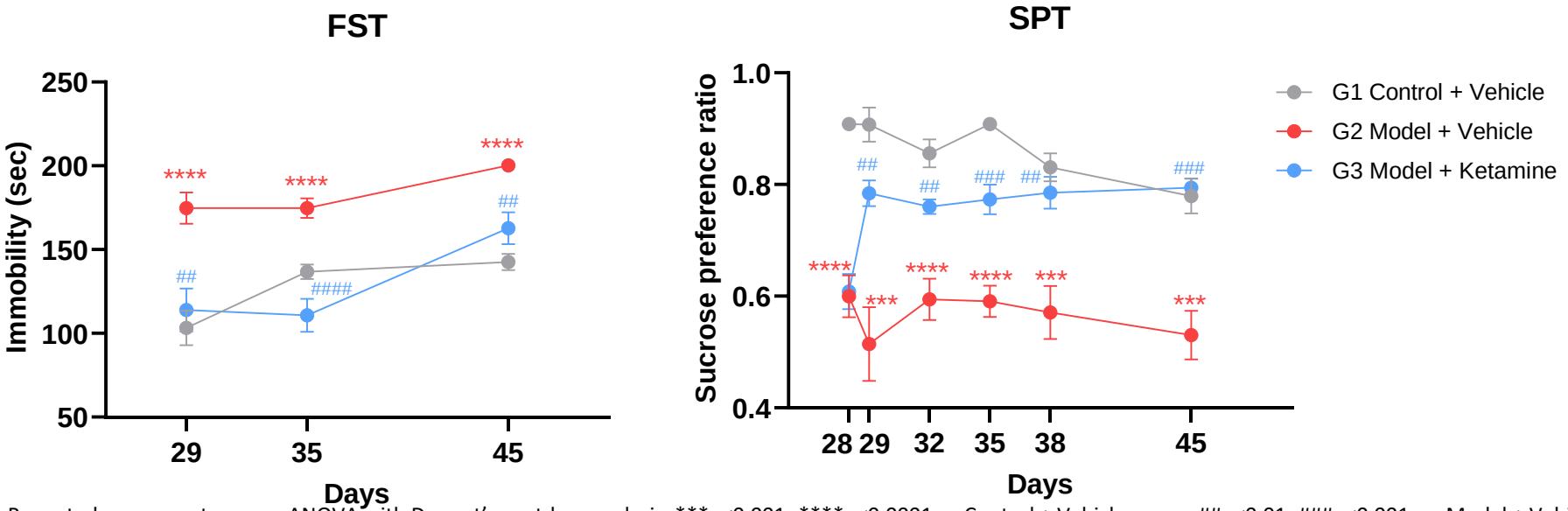


Effects of Ketamine on FST and SPT After Treatment



Data are expressed as mean + SEM. Repeated measures two-way ANOVA with Dunnet's post-hoc analysis: ***p<0.001, ****p<0.0001 vs Control + Vehicle group; ##p<0.01. ###p<0.001 vs Model + Vehicle group. n=12/group

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