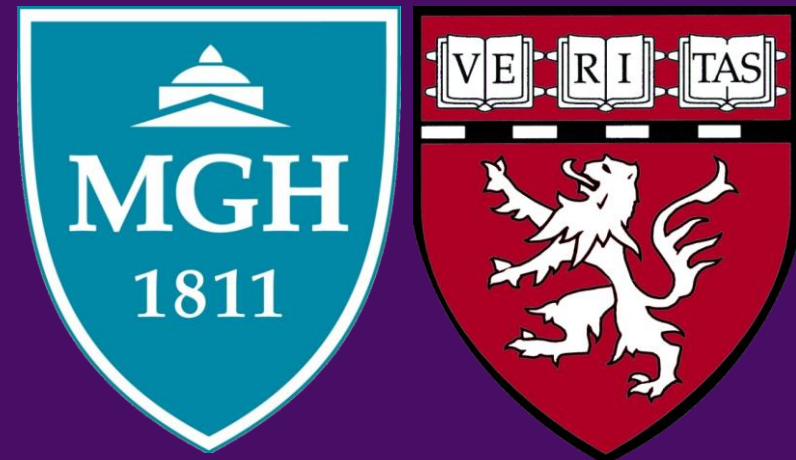


# Psychostimulants Accelerate Recovery of Attention Following General Anesthesia in the Tgf344-AD Rat Model of Alzheimer's Disease



P1-001

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## INTRODUCTION

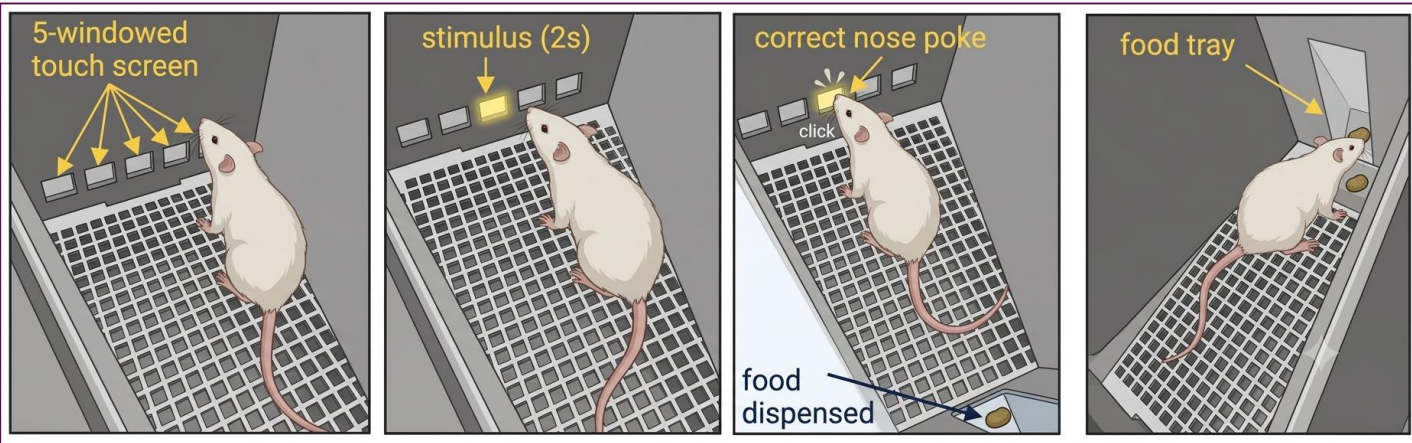
- **Postoperative delirium (POD)** is a serious complication characterized by a transient state of confusion and inattention following anesthetic emergence.
- Older adults and patients with Alzheimer’s disease (AD) are at elevated risk of POD and there are no treatments available.
- **General anesthetics** suppress **dopaminergic** and **noradrenergic** arousal systems, which are also impaired in AD.
- It is not known whether these shared catecholaminergic deficits underlie the propensity for POD in AD patients.

**Hypothesis:** psychostimulants, such as **methylphenidate (MPH)** and **d-amphetamine (DAMP)** which enhance prefrontal catecholamine signaling, will improve attentional recovery following general anesthesia.

## METHODS

**Animals:** Aged Tgf344-AD rats (N=13, 7 females, 6 males; 19-20 months)

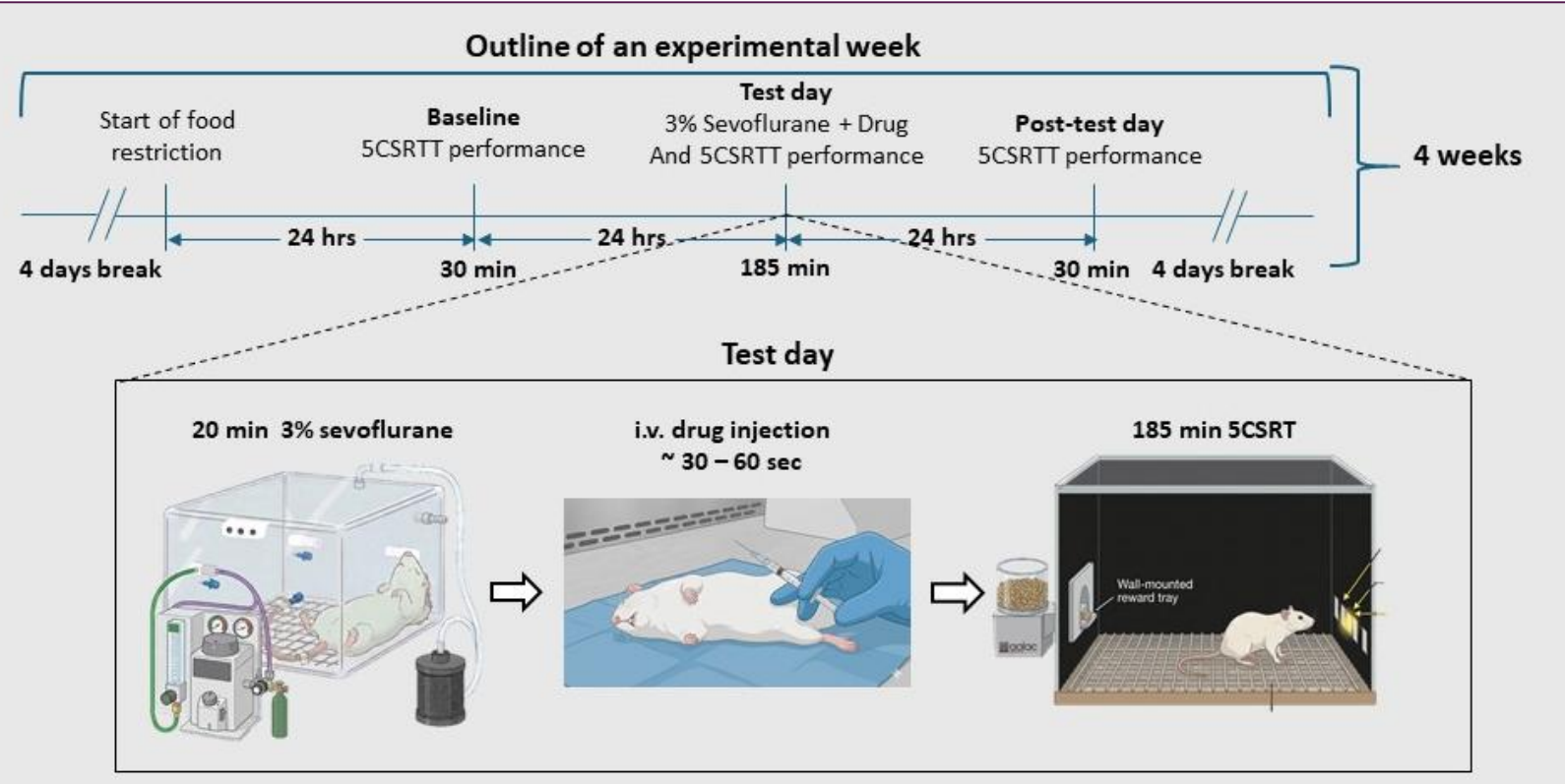
**Task:** Touchscreen-based 5-choice serial reaction time task (5-CSRTT), a sustained attention task.



**5-CSRT task:** Rats initiate trials via a nose-poke into the food magazine. Following a 2s stimulus in one of five windows, rats have 5s to respond for a reward. Performance is measured by accuracy (correct responses/(correct + incorrect responses)) and omission rate (missed responses/total trials).

## METHODS

### Experimental Design



**Drug Conditions:** Saline, Methylphenidate 2 & 5 mg/kg, d-Amphetamine 1 mg/kg (i.v. administered after anesthesia).

### Outcome Measures:

- **Recovery of Working Memory:** latency to attain  $\geq 4$  correct out of 5 consecutive responses ( $\geq 80\%$  windowed accuracy)
- **Recovery of Sustained Attention:** latency to achieve  $\leq 1$  omission out of 5 consecutive trials ( $\leq 20\%$  windowed omissions)
- **Motor Activity:** total number of beam breaks and median correct response latency.
- **Motivation:** total number of trials initiated and median food reward collection latency.

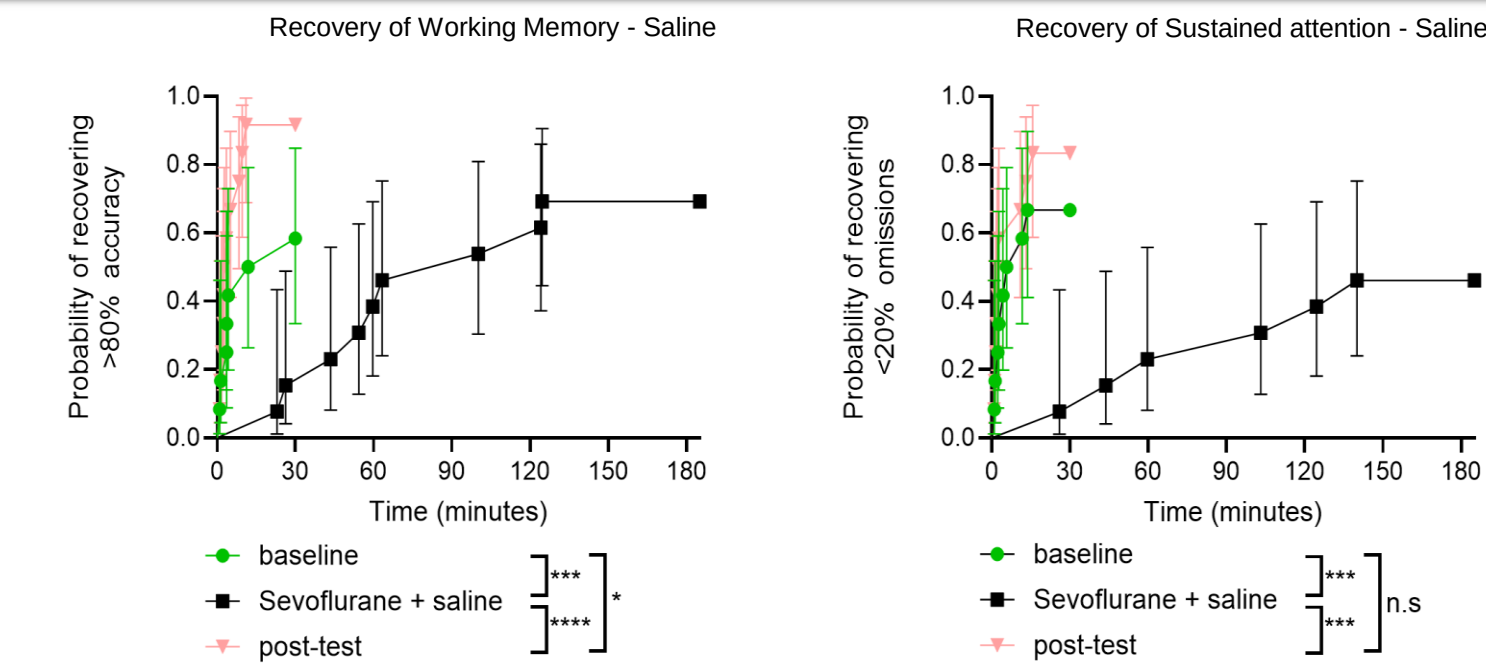
### Statistics:

- The latencies to recover cognitive function post-sevoflurane across drug conditions are analyzed by Kaplan–Meier curves with log-rank tests.
- Overall performance metrics are analyzed by repeated one-way ANOVAs.

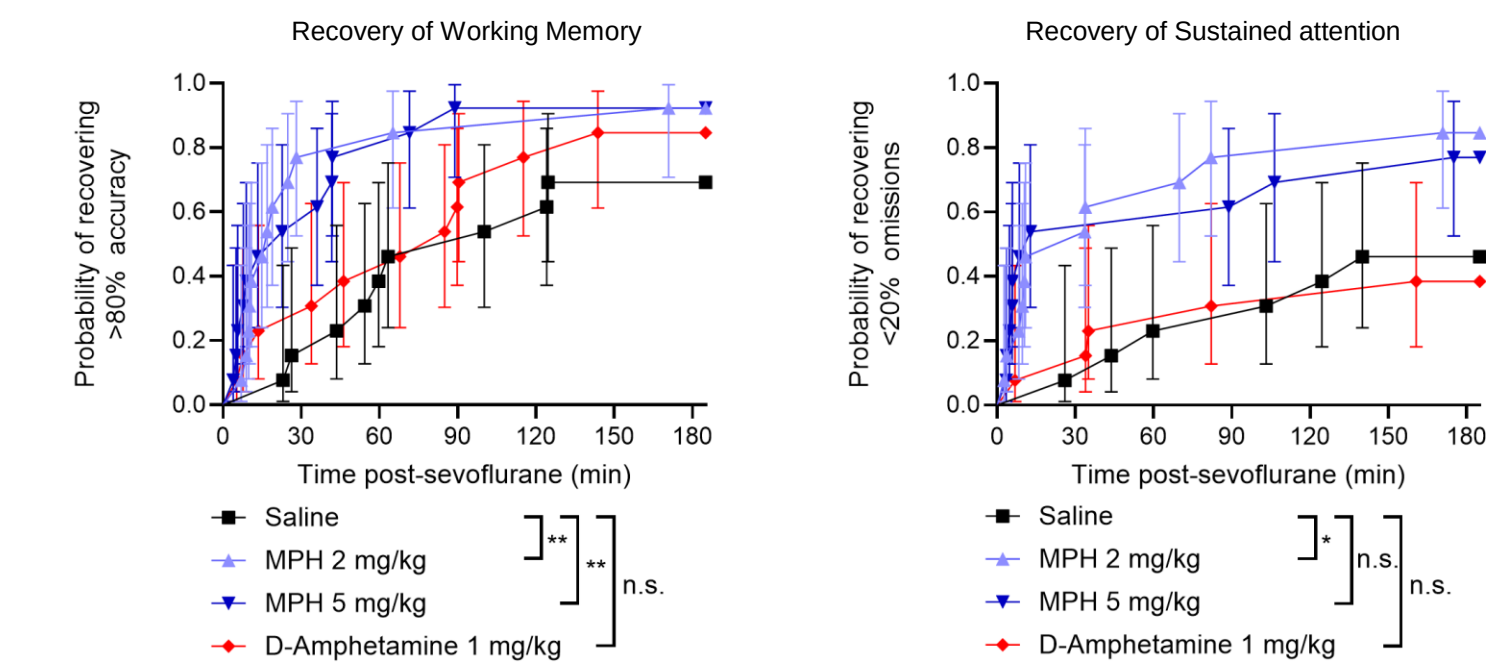
**Note:** Paired scatters (trials, beam breaks, latencies) each point = one rat; gray = baseline. bar = group mean.

## RESULTS

### 1. Methylphenidate accelerates post-sevoflurane cognitive recovery

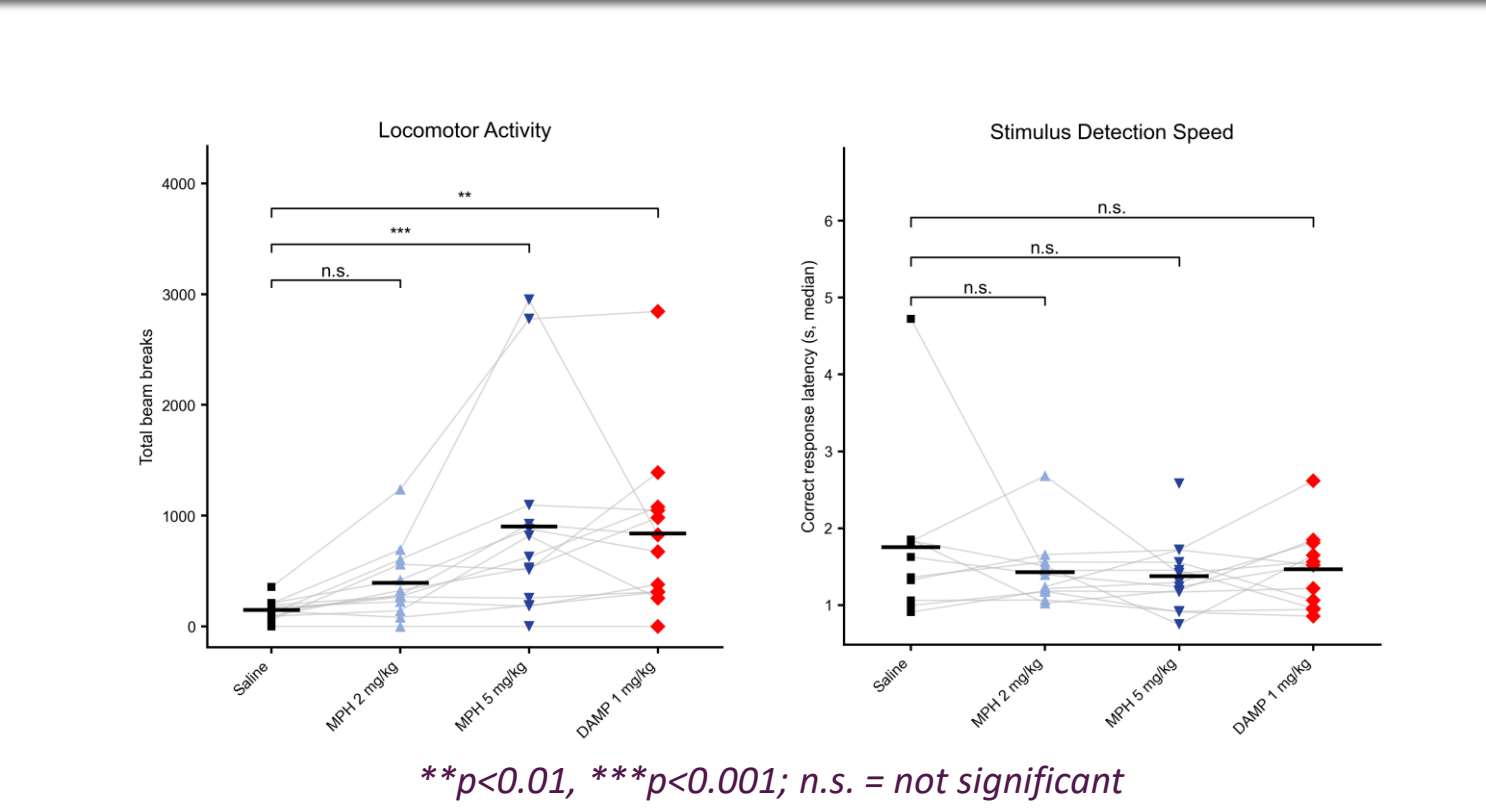


Sevoflurane anesthesia significantly delays cognitive recovery in aged Tgf344-AD rats. Performance largely recovers within 24 hours.



Methylphenidate facilitates recovery of working memory and sustained attention in Tgf344-AD rats.

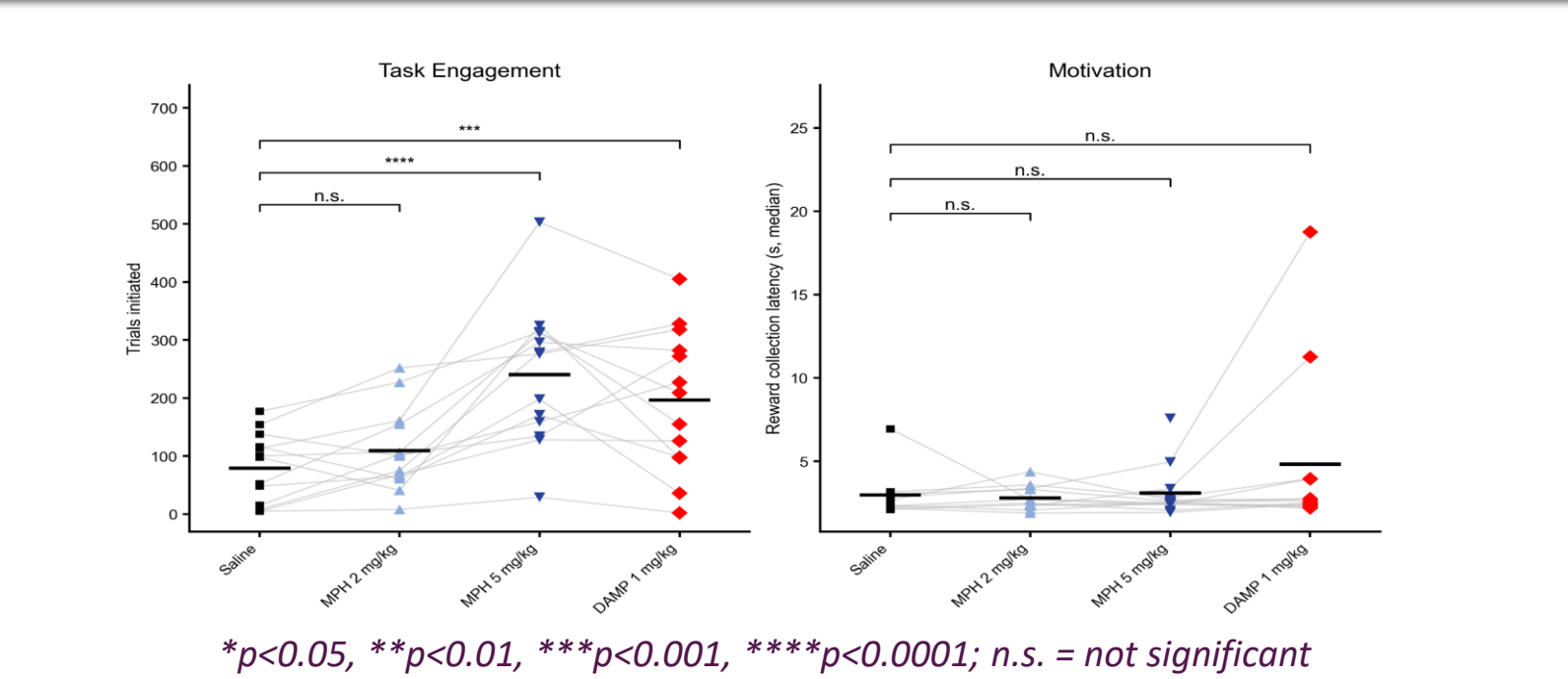
### 2. Elevated locomotion does not translate into faster stimulus detection



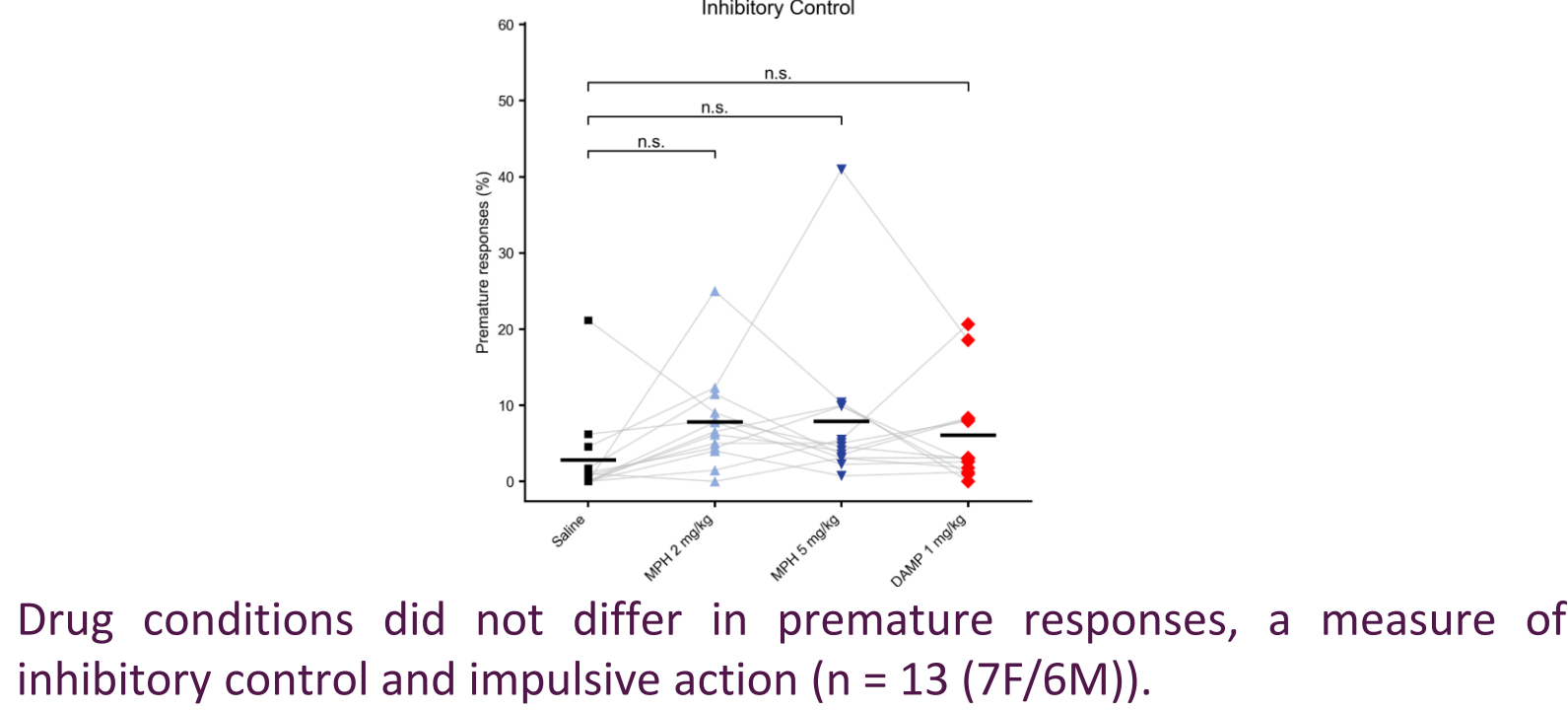
Both methylphenidate and d-amphetamine increase mobility post-sevoflurane; however, correct response latencies were not different across conditions.

## RESULTS

### 3. High-dose stimulants drive trial initiation without shifting motivation or impulsivity



High-dose MPH and DAMP significantly increase trial initiation. Latency to reward collection was unchanged across drugs conditions (n = 13 (7F/6M)).



Drug conditions did not differ in premature responses, a measure of inhibitory control and impulsive action (n = 13 (7F/6M)).

## CONCLUSIONS

- MPH (2 & 5 mg/kg), not DAMP, speeds cognitive recovery following general anesthesia in aged Tgf344-AD rats.
- The cognitive benefit is dissociable from locomotor stimulation: DAMP raised locomotion comparably to MPH 5 yet did not speed recovery and slowed reward collection.
- These data suggest that MPH, a widely prescribed stimulant, may provide therapeutic benefit for AD-associated POD.

## CONTACT & REFERENCES

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