

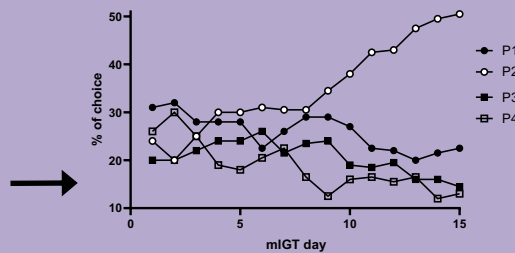
# Common doses of LSD lack acute effects in mouse Iowa Gambling Task

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**Background** While the interest towards psychedelic drugs has emerged during the last decades, the general understanding of the effects of these drugs on the executive functions and goal-directed behaviours remains deficient, both in humans and in commonly used animal models.

**Objectives** To explore the effects of acute doses of psychedelic lysergic acid diethylamide (LSD) on reward-driven decision-making using the mouse version of Iowa Gambling Task (mIGT).

## Methods



- 15 C57/B6 male mice
- Touchscreen operant chamber
- Four panels, different contingencies of reward (1 to 4 pumps of 20% sucrose solution) and time-out punishment.
- Mice learned to optimize the choice (P2 = best).

P1:	P2:	P3:	P4:
p=0.9	p=0.8	p=0.5	p=0.4
T.O= 5 s, p=0.1	T.O= 10 s, p=0.2	T.O= 30 s, p=0.5	T.O= 40 s, p=0.6
R:259	R:327	R:153	R:120

p = probability of reward  
T.O. = timeout length and probability  
R = theoretical maximum reward



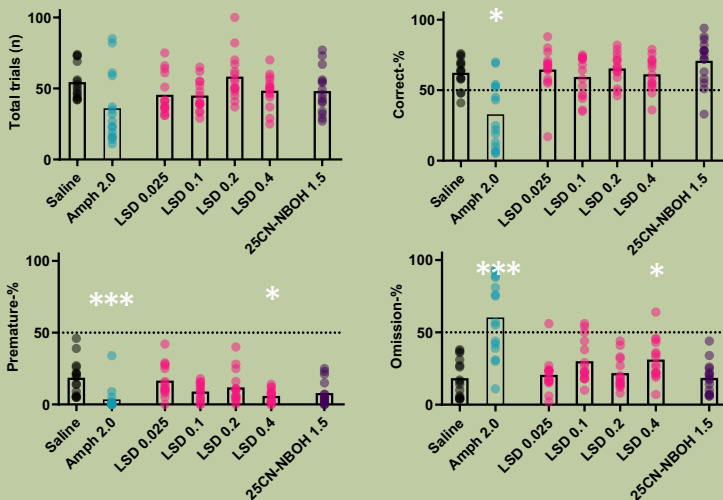
### Acute drug treatments:

- Saline (negative control)
- d-amphetamine (2.0 mg/kg; positive control)
- LSD (0.025, 0.1, 0.2, 0.4 mg/kg)
- 25CN-NBOH (1.5 mg/kg; 5-HT<sub>2A</sub> selective agonist)

### Statistics:

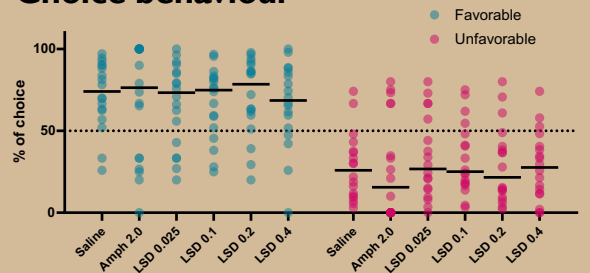
Friedman's repeated measures ANOVA + Dunn's pairwise comparison with Bonferroni correction.

## Action execution



- Amphetamine significantly decreased the correct responses and premature responding while increasing the omission rate (\* p<0.05; \*\*\* p<0.001) similar to van Enkhuizen et al. 2013, Psychopharmacology, 225(3), 661-674.
- 25CN-NBOH and the three lowest doses of LSD showed no statistically significant changes in the general functioning.
- The highest dose, 0.4 mg/kg, of LSD significantly decreased the premature responding and increased the omission-percentage (\* p<0.05).

## Choice behaviour



None of the used treatments affected the choice behaviour in a significant way in comparison to saline.

## Conclusions

- Mice continue to perform learned, decision-making tasks uninterrupted while under the acute influence of LSD at the commonly used dose-range.
- Lack of observable effects on the choice behaviour is in line with human data with acute LSD and Cambridge Gambling Task (Pokorny et al. 2019, Psychological medicine, 1-10.)
- Increased deliberation time, also shown in humans with Cambridge Gambling Task, could in part explain the changes seen after 0.4 mg/kg LSD, but further research would be needed to conclude.