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Sex-related impairment of synaptic plasticity in the hippocampus of hypergravity-exposed mice: new insights for cognition in space

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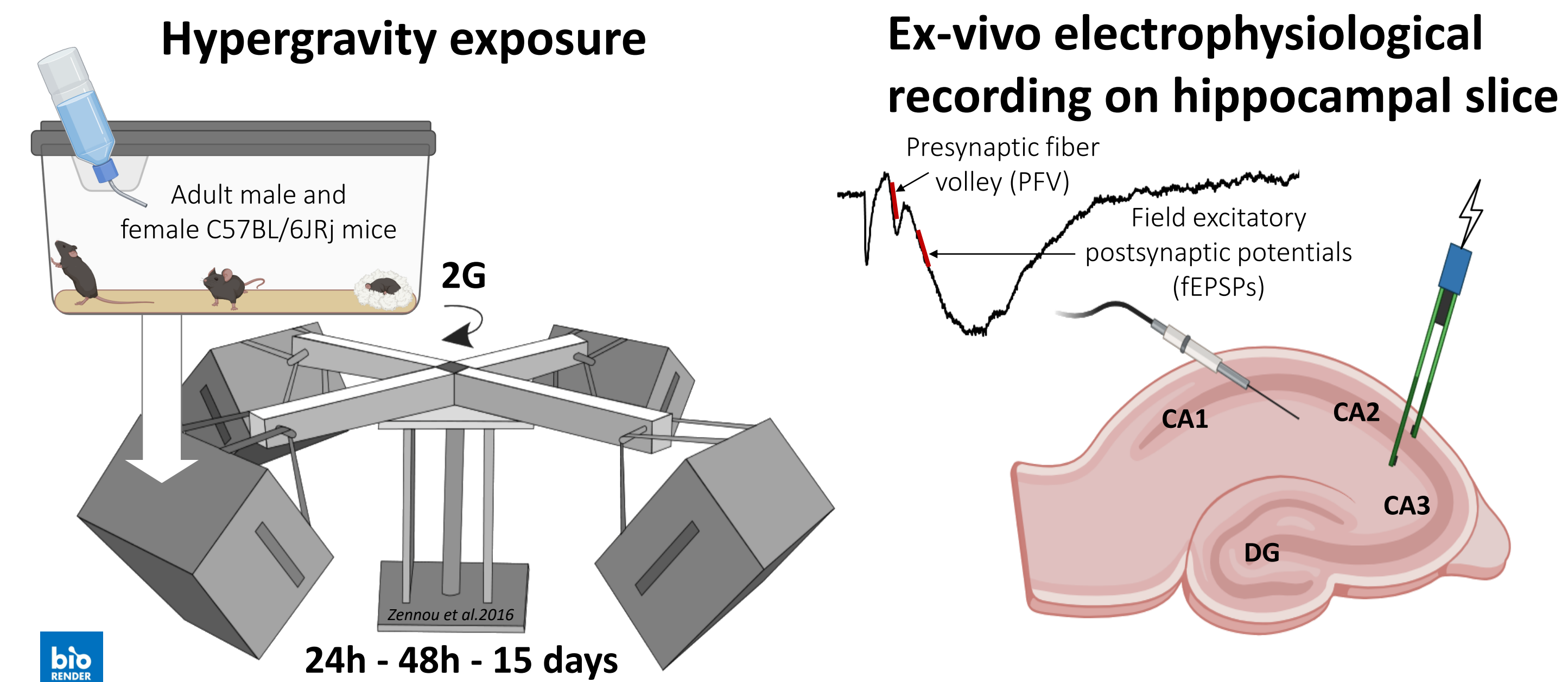
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Introduction

One of the difficulties for space human missions is the exposure to repeated gravitational fluctuations during flight, which particularly affect the vestibular system. Given the **vestibulo-hippocampal connections** (Hitier, et al. 2014), hippocampal activity could be altered and would affect **cognitive performances** of the crew (Clement, et al. 2013).

This preclinical study aimed to investigate functional synaptic changes in hippocampal neuronal networks after **2G hypergravity** (HG) for different durations.

Materials & methods

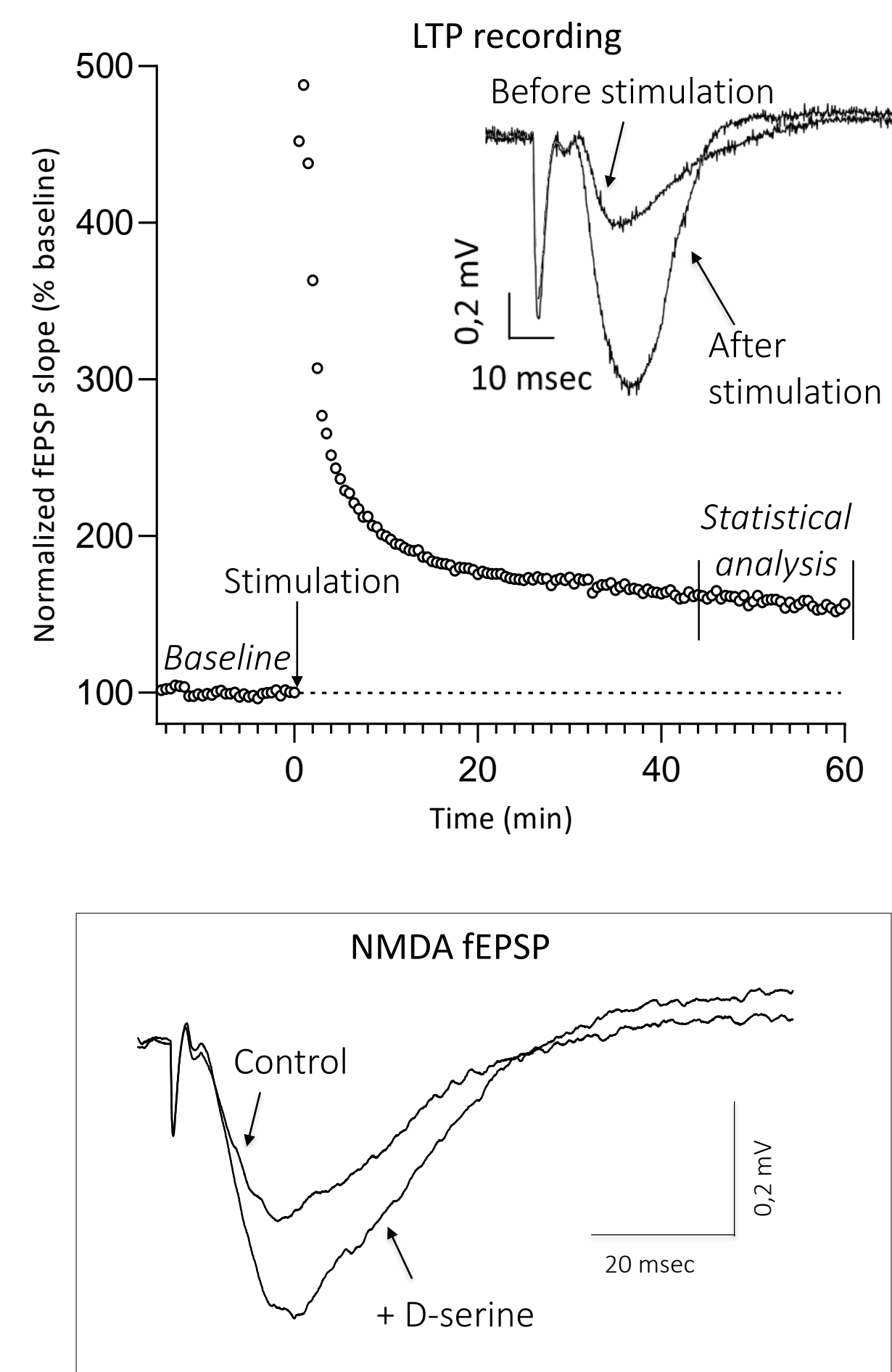


Functional assessments

1. Long Term Potentiation (LTP) of synaptic strength was induced by high-frequency stimulation (HFS) and theta burst stimulation (TBS). LTP magnitude was measured over the last 15min relative to baseline.

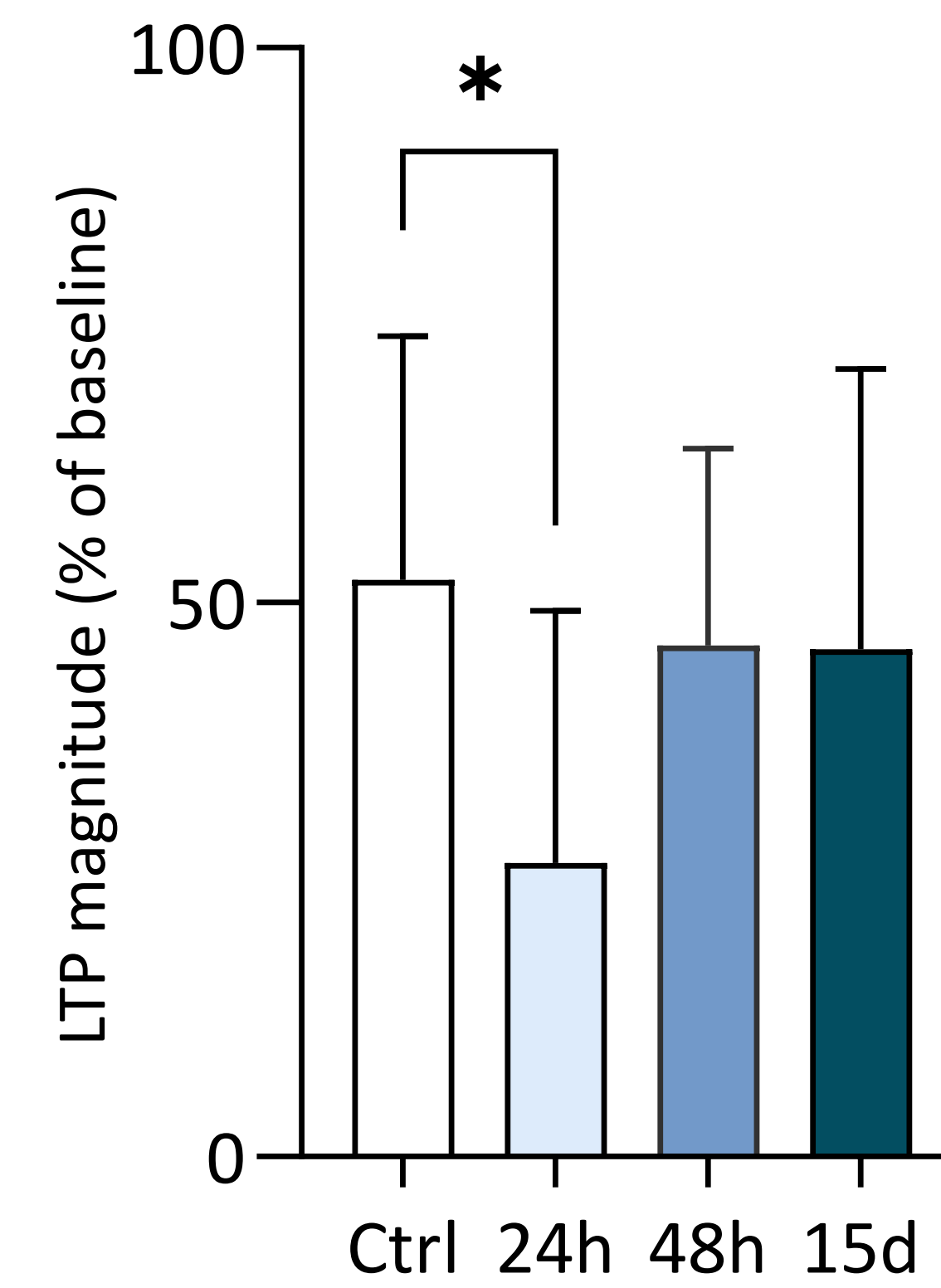
2. Activation of NMDA receptors is essential for LTP. fEPSP/PFV ratio of **isolated NMDA-mediated fEPSPs** were constructed in a low magnesium medium supplemented with the non-NMDAR antagonist NBQX (10μM).

3. LTP impairment and altered NMDAR activation were pharmacologically characterized with **exogenous D-serine** (100μM) to assess the role of the NMDA glycine binding site.



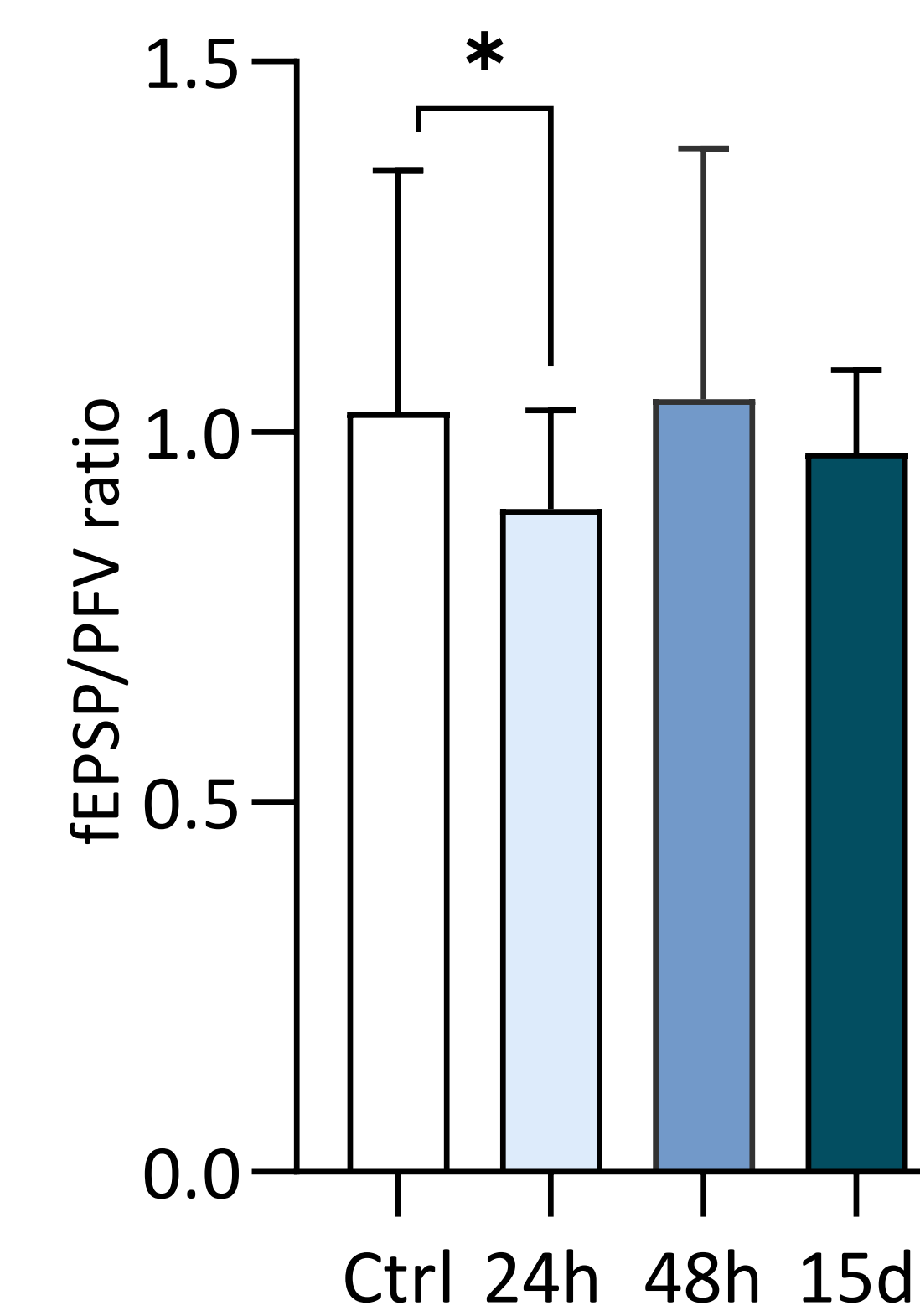
Recordings in males

1. LTP HFS



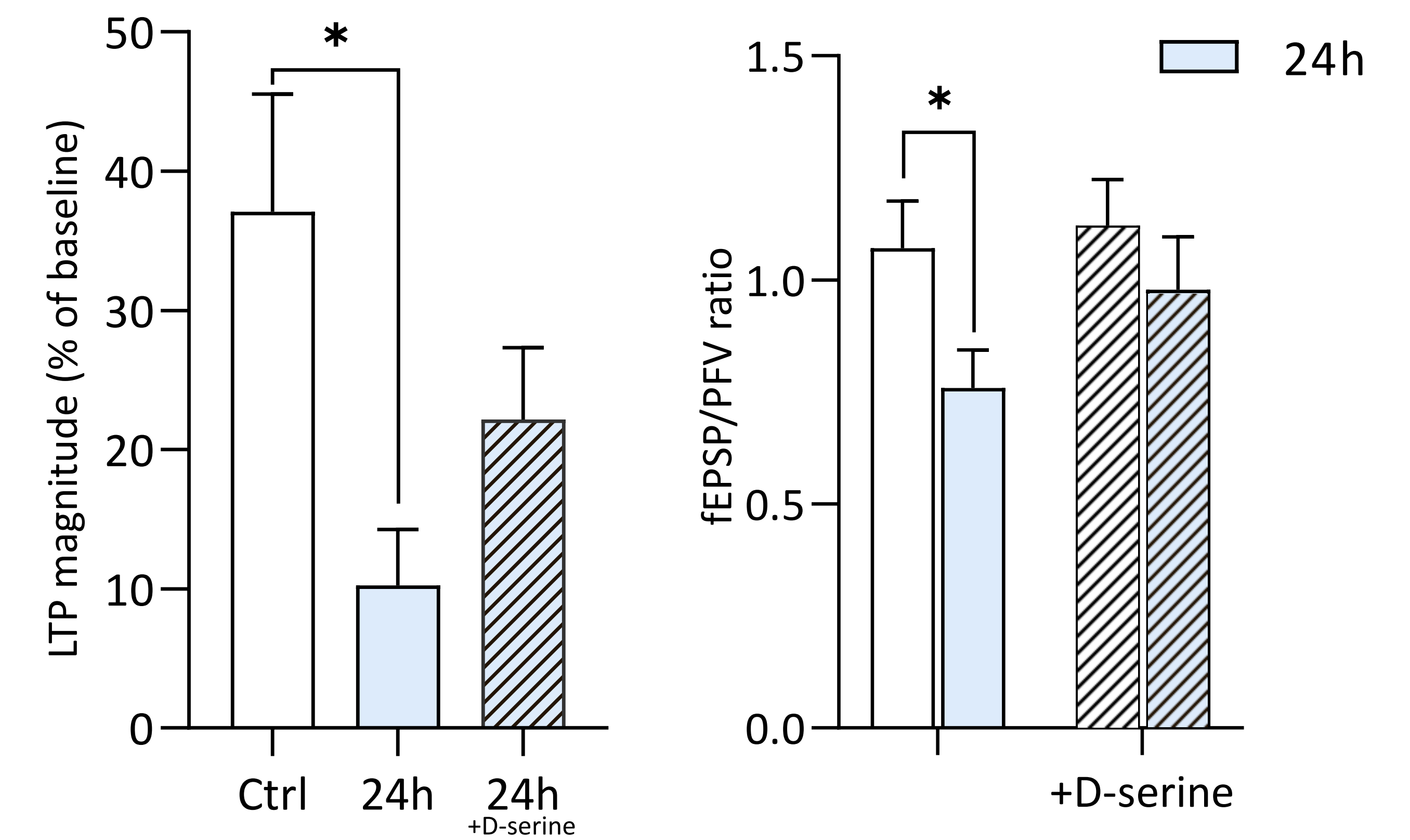
HFS-induced LTP magnitude was depressed in mice exposed to **24h** of HG. No impairment was found for TBS-LTP.

2. NMDAR activation



As for LTP, NMDAR activation was depressed in **24h** exposed mice.

3. D-serine pharmacological supplementation



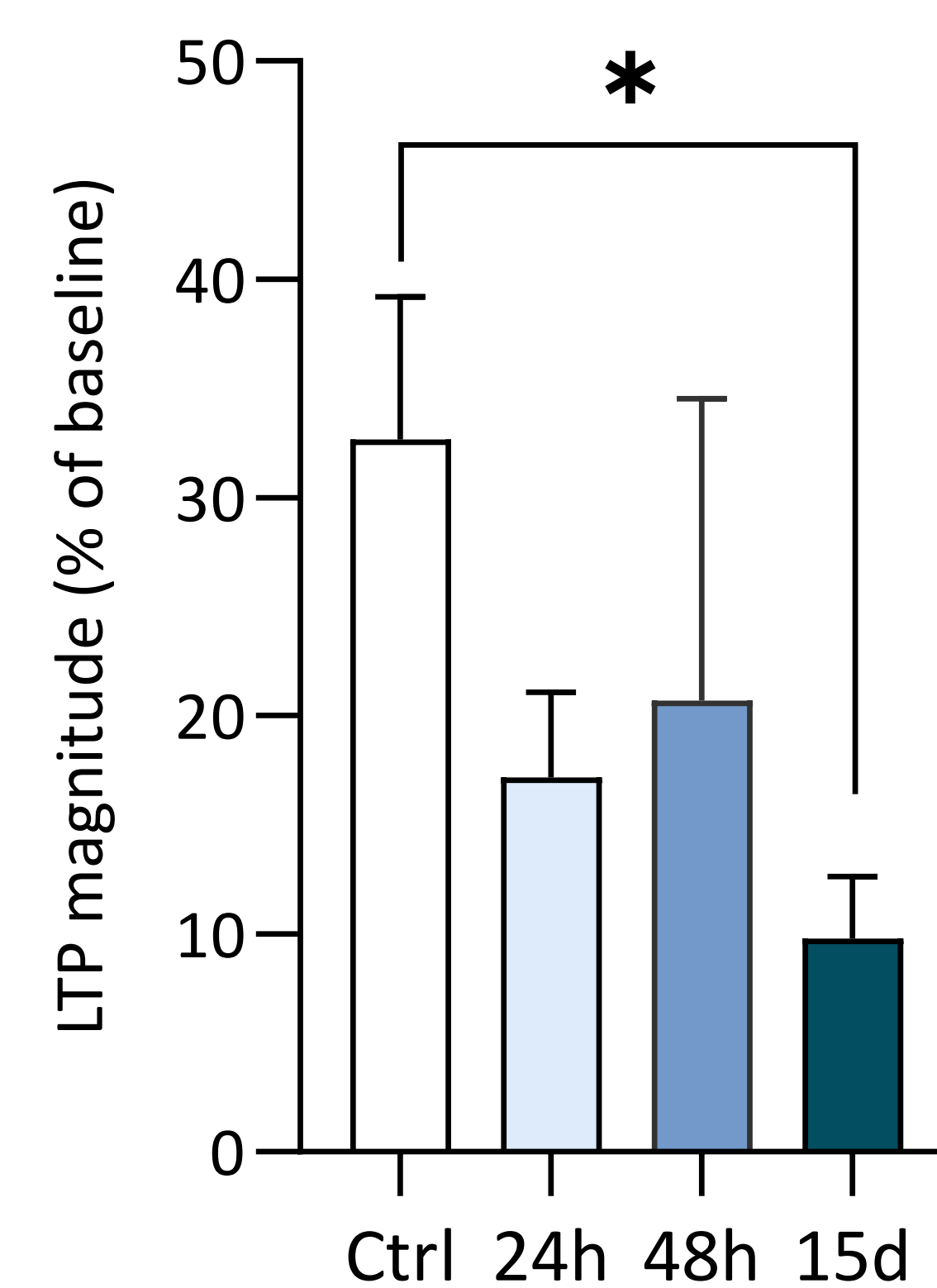
Exogenous D-serine partially **reversed LTP deficit** exhibited by **24h** exposed mice.

Exogenous D-serine **reversed NMDAR activation deficit** in **24h** exposed mice.



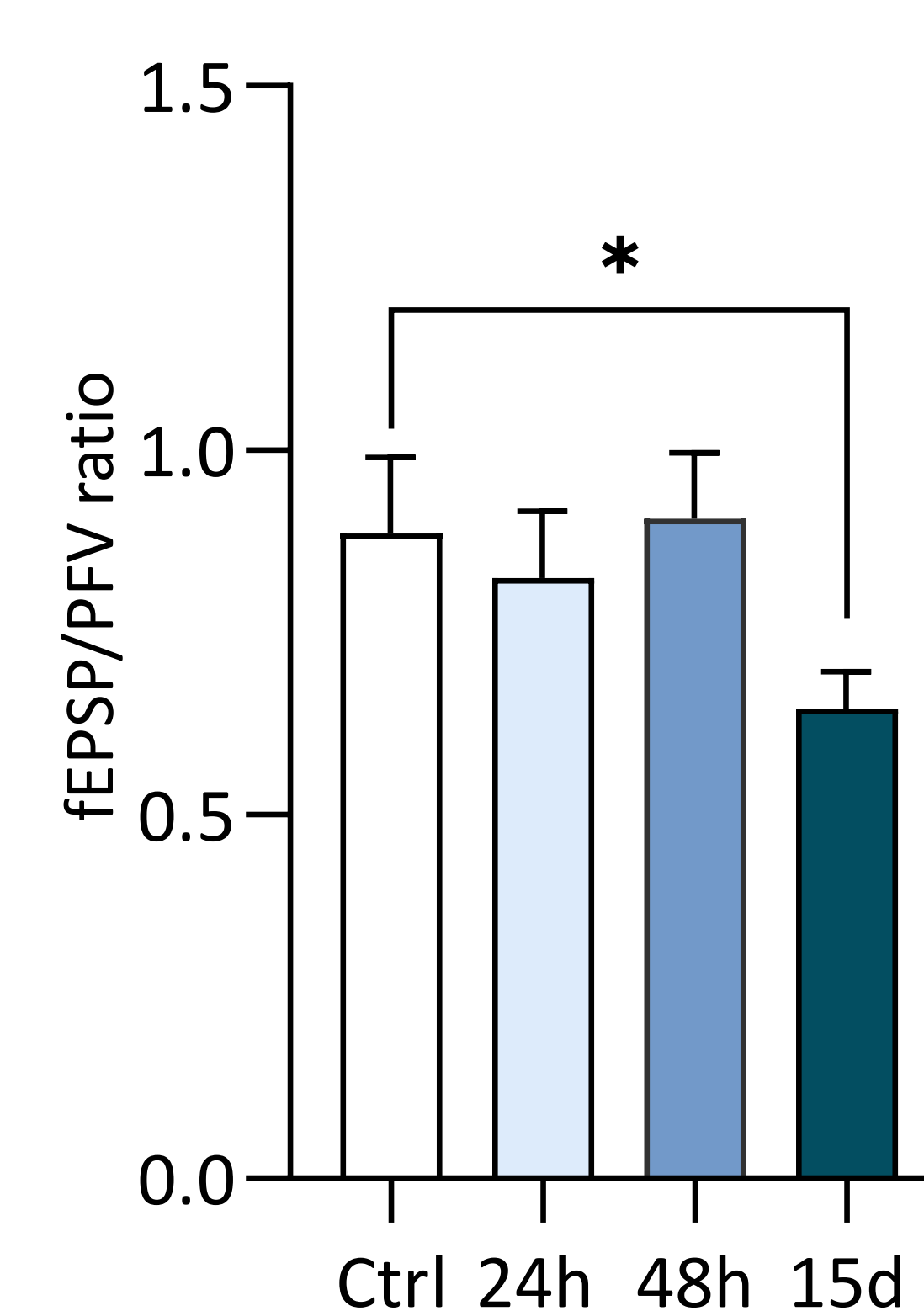
Recordings in females

1. LTP TBS



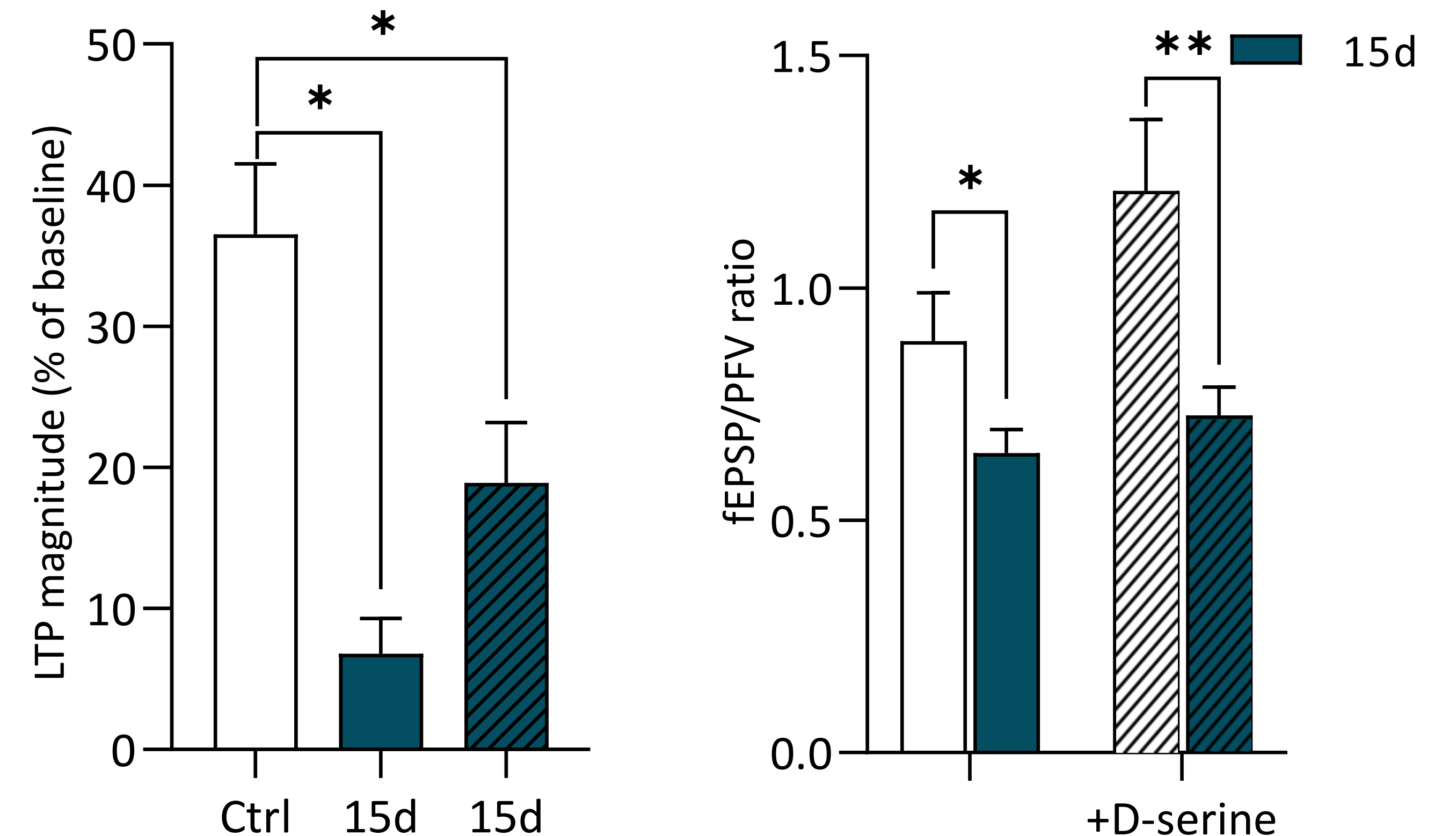
TBS-induced LTP was depressed in **15d** exposed mice. In contrast to males, HFS-induced LTP was not affected.

2. NMDAR activation



As for LTP, NMDAR activation was depressed in **15d** exposed mice.

3. D-serine pharmacological supplementation



Exogenous D-serine **did not reverse LTP deficit** exhibited by **15d** exposed mice.

Exogenous D-serine **did not reverse NMDAR activation deficit** in **15d** exposed mice.

This study reveals changes in hippocampus functional plasticity of mice exposed to hypergravity. Evidence is provided for sex differences that rely not only on HG duration but also on the type of functional plasticity and on the underlying synaptic mechanisms. Whether these changes in functionality may trigger significant cognitive deficits is currently under investigation.