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Sex-dependent 5-HT₆R_s effects on hippocampal synaptic activity

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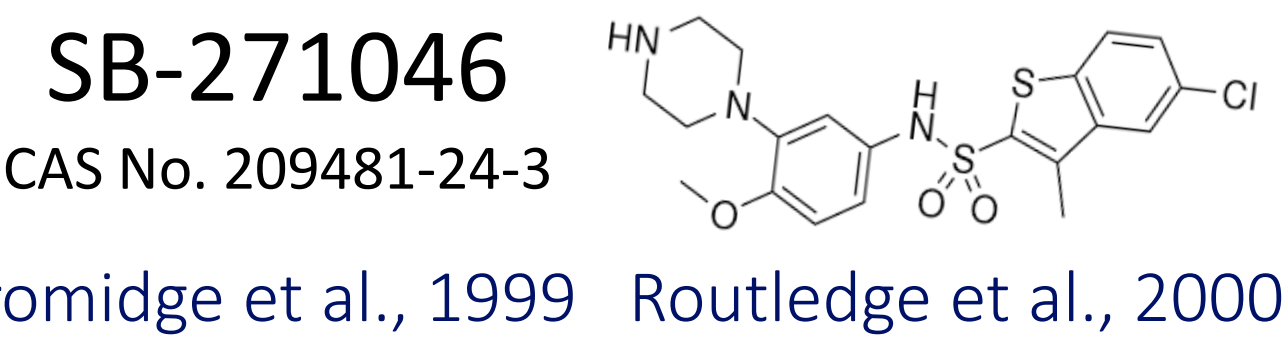
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Introduction

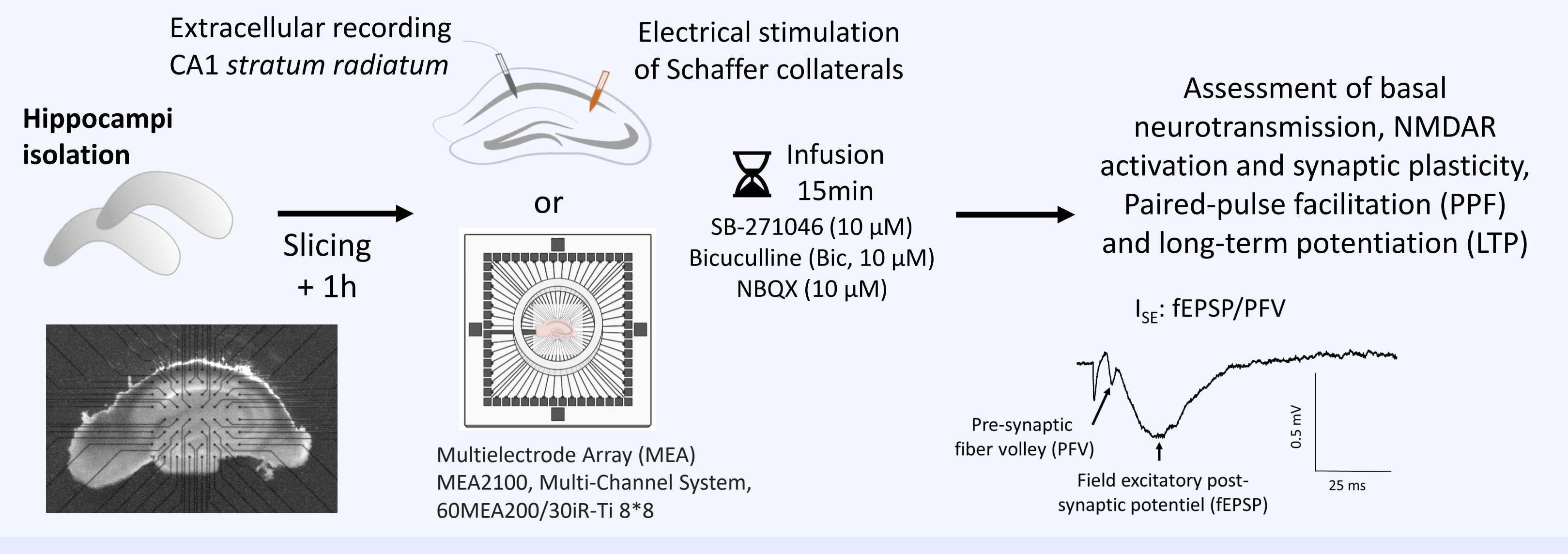
- Memory impairments belong to symptoms of schizophrenia which are not alleviated by antipsychotic drugs
 - N-methyl-D-aspartate subtype of glutamate receptors (NMDARs):**
 - Key regulators of memory processes
 - Crucial role in the physiopathology of schizophrenia
 - Serotonergic subtype 6 receptors (5-HT6Rs):**
 - Interesting target to improve current treatment
 - Mainly expressed in brain regions involved in memory processes (Ruat et al., 1993)
 - Blockade of 5-HT6Rs (SB-271046) improve short- and long-term memory in rodents (Da Silva Costa-Aze et al., 2011, 2012)**
- underlying functional mechanisms still need to be established

Aim

To study how the blockade of 5-HTRs (SB-271046) affects synaptic activity and plasticity of CA3/CA1 synapses of hippocampus in ♂ and ♀ mice



Materials and methods

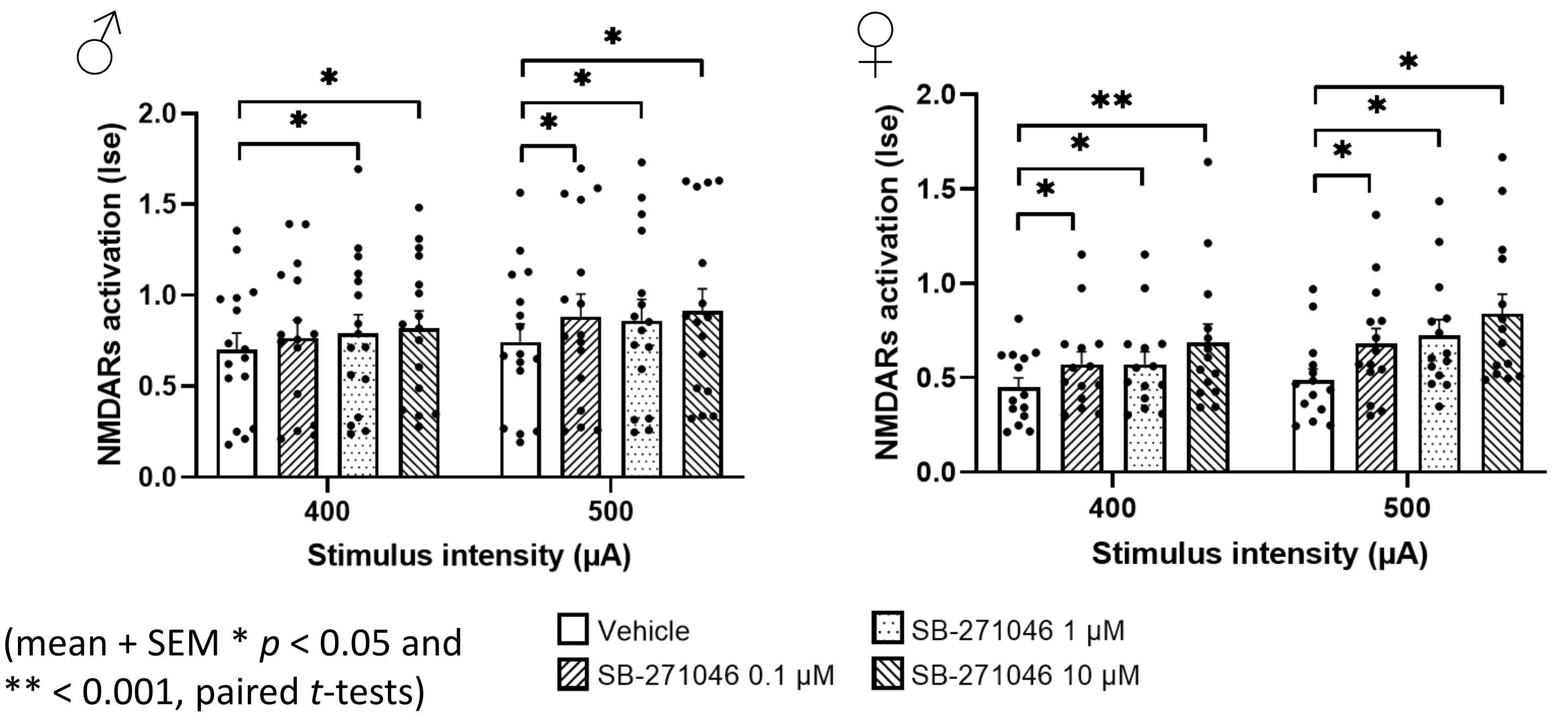


Take home message

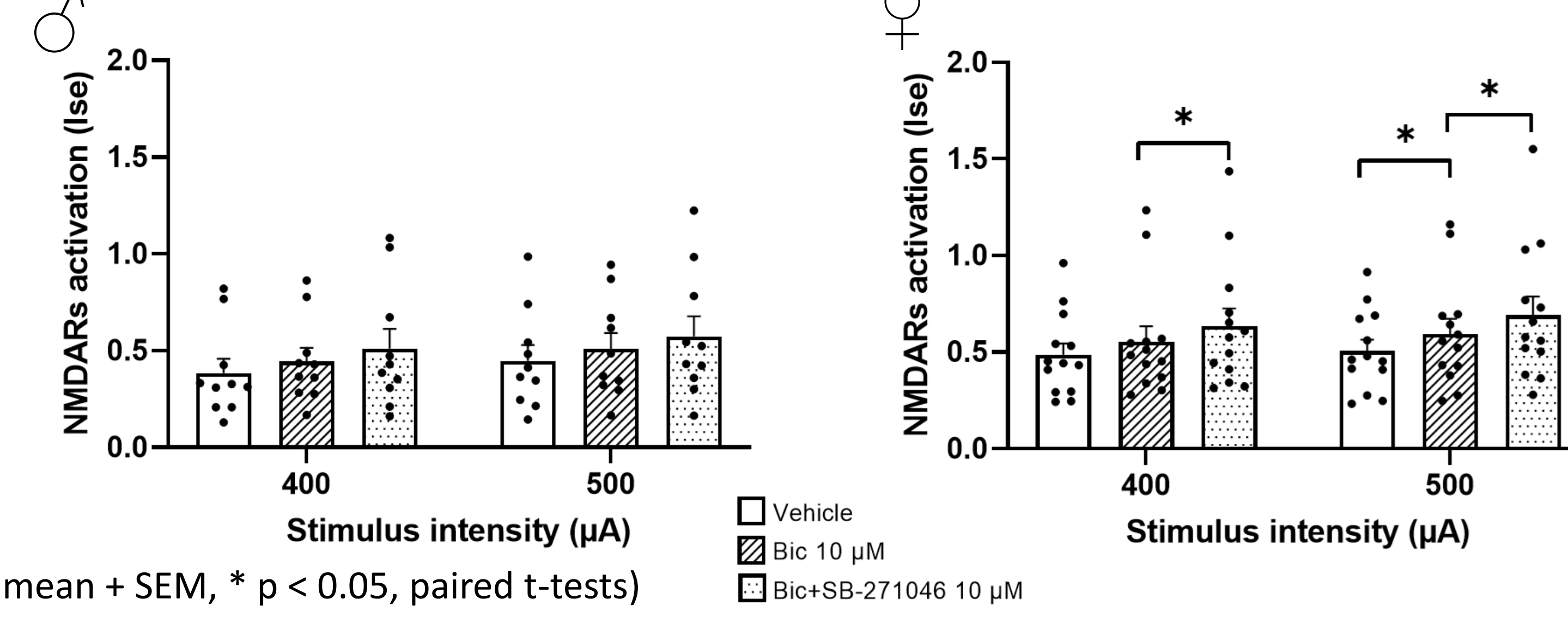
In ♂: 5-HT6Rs indirectly control glutamate transmission through the modulation of the inhibitory tone
 In ♀: 5-HT6Rs directly act on pyramidal cells through changes in membrane excitability
 These data could help in initiating new pharmacological strategies to treat sex-dependent cognitive impairments associated those with schizophrenia.

Bromidge et al. *J. Med. Chem.* 1999, 42, 202–205, doi:10.1021/jm980532e.
 Da Silva Costa-Aze, V.; et al. *Psychopharmacology (Berl)*. 2012, 222, 99–115, doi:10.1007/s00213-011-2627-3.
 Da Silva Costa-Aze, V. et al. *Behav. Brain Res.* 2011, 222, 134–140, doi:10.1016/j.bbr.2011.03.046.
 Routledge, C. et al. *Br. J. Pharmacol.* 2000, 130, 1606–1612, doi:10.1038/sj.bjp.0703457.
 Ruat, M. et al. *Biochem. Biophys. Res. Commun.* 1993, 193, 268–276.

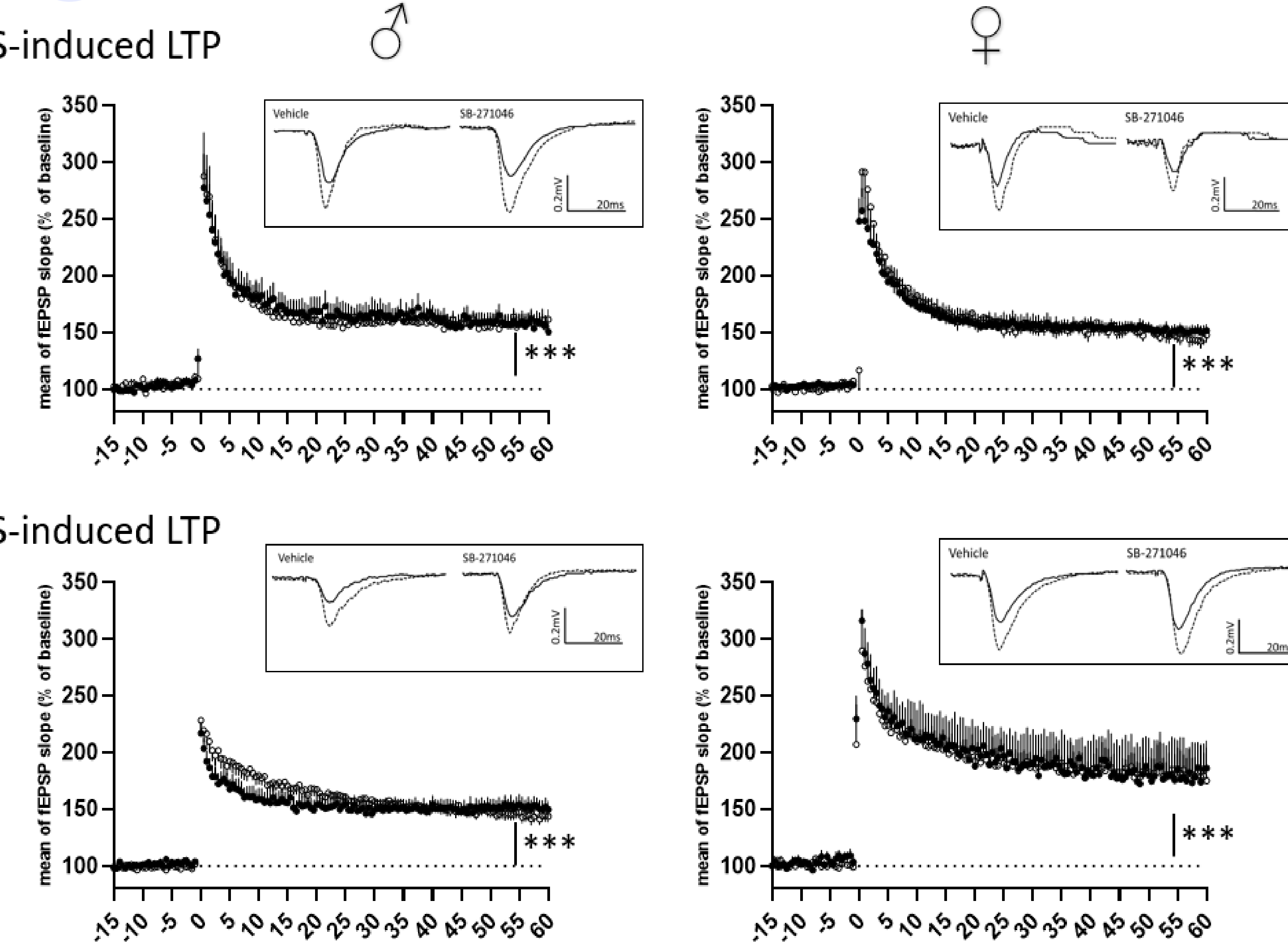
1 SB-271046 increases NMDARs activation in CA1 hippocampal networks in males and females



2 In male but not female mice, the potentiating effect of SB-271046 on NMDARs' activation involves GABAergic transmission



4 Long-term potentiation is not altered by SB-271046



3 SB-271046 increases basal transmission without affecting mechanisms underlying presynaptic release of glutamate

