# Pregnenolone sulphate improves memory processing in early-handled female rats

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Early life experiences lead to sex-specific behavioural and neurochemical changes in adulthood. Indeed, early handling enhances learning and memory in male rats (Cannizzaro et al., 2005), whereas it impairs learning performance in female adult rats, a finding that has been correlated to decreased nitric oxide (NO) production in the hippocampus (Noschang et al., 2010). Pregnenolone sulfate (PREGS) is considered as one of the most potent memory-enhancing neurosteroids, since its activity as a potent positive modulator of N-methyl-d-aspartate receptors (NMDARs) and a negative modulator of gamma-aminobutyric acid(A) receptors (GABA(A)Rs) (Vallée et al., 2001). Given these premises, this study aims at characterizing the effect of PREGS on cognitive processes in adult female rats, subject to early handling protocol, by using an object-place association learning task, the "Can test", a motivated, non-aversive, spatial/object discrimination test (Popovic´ et al., 2001).
Female Wistar rats underwent daily, brief, maternal separation from postnatal day 2 until 21. Once in adulthood, the effect of PREGS administration (10 mg/kg, s.c.) on correct responses, reference memory and working memory was assessed.
Results show that PREGS was able to significantly increase the number of correct responses, and consistently, to decrease reference and working memory errors, compared with vehicle. No statistically significant effect of PREGS administration was observed in non-handled, control group.
These findings sustain the impact of neurosteroids in learning and memory processing, and suggest a particular role for PREGS in reversing conditions of altered functionality, likely due to the modulation of the glutamate-NO-cGMP pathway (Cauli et al., 2011), and thus neurobiological mechanisms underlying learning and memory. As a consequence, PREGS may represent an important therapeutic tool as memory-enhancer, in order to tackle cognitive deficit caused by stress in early life.

**References**

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