EFFECT OF ETHANOL IN SOCIALLY ISOLATED RATS: INFLUENCE OF GENDER

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Social isolation of rats immediately after weaning reduces the cerebrocortical and plasma concentrations of 3α,5α-TH PROG (Serra et al., 2000). Moreover, the steroidogenic effect of acute administration of ethanol was more pronounced in socially isolated than in group-housed rats (Serra et al., 2003). The ethanol-induced increase in the abundance of 3α,5α-TH PROG is also more pronounced in the brain than in the plasma of isolated rats. In agreement with this result, we have recently shown that ethanol stimulate steroidogenesis independently from peripheral sources (Sanna et al., 2004). Several studies demonstrated a gender difference in the sensitivity to ethanol: to evaluate how different basal levels of neurosteroids can influence the steroidogenic effect of ethanol, we study 1) the effect of this drug in female and male rats and 2) how subchronic treatment with progesterone could modify ethanol sensitivity in males.

Animals and social isolation: Male and female Sprague-Dawley CD (Charles River, Como, Italy) rats at 25 days of age, immediately after weaning, were housed for 30 days, either in groups of six per cage (group-housed) or individually in smaller cages (isolated). The stage of estrus cycle was determined by post-mortem vaginal smears. All animals were tested between 10:00 a.m. and 13:00 a.m. Thirty days after isolation, rats were injected intraperitoneally with ethanol (1g/kg , 20% v/v) 40 min before killing. Control rats received an equal volume of saline.

Progesterone treatment: Male rats received progesterone (dissolved in olive oil by sonication for 4 h) at a dose of 5 mg/kg i.p. once a day for 5 days; animals were sacrified 29 h after the last administration of progesterone and 40 min after acute ethanol (1g/kg , 20% v/v) administration. Control animals received an identical volume of saline.

Results: Social isolation increased the brain sensitivity to the steroidogenic effect of ethanol both in male and female rats, in spite of their different basal levels of 3α,5α-TH PROG.

However, we found a gender difference in the effect of ethanol in socially isolated rats: in fact, social isolation induced an increase sensitivity in plasma of males but not in females.

Moreover, changes in the levels of 3α,5α-TH PROG, following progesterone treatment, modulate the effect of ethanol on steroid levels: infact, progesterone-treated male rats, like grouped-housed females, are less sensitive than vehicle-treated males to the steroidogenic effect of ethanol. Taken together, these data demonstrated that 3α,5α-TH PROG levels play a crucial role in the sensitivity to the steroidogenic effect of ethanol and this may be correlated to changes in the $GABA_A$-receptor gene expression induced by the different levels of brain progesterone metabolites.