

## NEUROSTEROIDS, NEURODEVELOPMENT AND BEHAVIOR

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Our research line focuses on the role that neurosteroids such as allopregnanolone (AlloP) play during brain maturation and the effects that the alterations of neonatal neurosteroids levels have on adolescent and adult behavior, and on hippocampal inhibitory mechanisms. We can resume our recent work in three main lines:

1.-Alterations in neonatal AlloP levels affect adolescent and adult behavior, and this effect is related to neonatal stress: We have reported disruptions in prepulse inhibition (PPI), increases in novelty-directed locomotion measured in the open field test and decreases in anxiety-like responses in the elevated plus maze test. Some of the deleterious effects of neonatal stress (by means of early maternal separation -EMS-) can be prevented by previous neonatal AlloP administration.

2.-Role of the hippocampus and the hippocampal inhibitory mechanisms: (a) Behavioral effects of intrahippocampal AlloP infusions in adult age (decrease in anxiety and locomotion or increase in PPI) are not present in those subjects in whom neonatal AlloP levels were altered. (b) Neonatal alteration of AlloP levels alters the expression of type A gamma-aminobutyric-acid receptors (GABA<sub>A</sub>) containing  $\alpha 4$  and  $\delta$  subunits, molecular alterations that can persist into adult age and that can explain, in part, the reported behavioral disturbances.

3.-Vulnerability to drug abuse: Sensation seeking patterns of behavior, impulsivity and novelty preference can increase the vulnerability to drug abuse in humans and animals. Given the anxiolytic-like profile and the increase in novel environments exploration caused by neonatal AlloP administration, we hypothesize that neonatal AlloP levels manipulations can alter the vulnerability to drug abuse. At present, we are investigating the effects of neonatal AlloP levels alteration alone or in combination with environmental stress (by EMS) on alcohol abuse throughout the study of voluntary alcohol intake, ethanol motor stimulant effects, dopamine levels in the nucleus accumbens, and monoamine levels in ventral striatum.