NEUROSTEROIDS, BRAIN PLASTICITY, AND MENOPAUSE

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Menopause, the cessation of menstruation induced by the decline of ovarian hormone production, is frequently accompanied by a variety of secondary physiological and behavioural changes. Depression, anxiety and insomnia are among the most cited psychological symptoms that are observed in post-menopausal women and can be of considerable consequence for the individuals and families in question and contribute to lowered quality of life. There is now clinical evidence for a possible role of neurosteroids in neuropsychiatric disorders including anxiety and depression: neurosteroid concentrations are decreased during depression and normalize after successful treatment. Neurosteroids are steroid derivatives that are synthesized *de novo* in the brain from cholesterol or from precursors derived from peripheral sources. Among them allopregnanolone and alloterahydrocorticosterone (THDOC), exert a rapid, non genomic, inhibitory effect on excitability of neurons through a direct modulation of the activity of type A receptor of γ-aminobutyric acid (GABA). Thus, the administration of allopregnanolone and THDOC elicit anxiolytic, anticonvulsant, sedative-hypnotic and neuroendocrine effects similar to those produced by benzodiazepines. Moreover, fluctuations in the brain and plasma physiological concentrations of these steroids derivatives associated with pregnancy, postpartum and estrus cycle elicit in animals selective changes in $GABA_A$ receptor subunit expression and function and consequently in the associated emotional and affective behaviours regulated by these receptors.
Exposure of neonatal female rats to estrogen, has been proposed as an early animal model of reproductive senescence. Data on brain and plasma concentration of neurosteroids, changes in specific $GABA_A$ receptor subunit expression and sensitivity to neurosteroids, benzodiazepines and antidepressants in this animal model will be presented.