

Local Effect of Allopregnanolone in Rat Ovarian Steroidogenesis, Follicular and Corpora Lutea Development

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ABSTRACT

Allopregnanolone (ALLO) is a known neurosteroid and a progesterone metabolite synthesized in the ovary, central nervous system, peripheral nervous system, adrenals and placenta. Its role in the neuroendocrine control of ovarian physiology has been studied, but its *in situ* ovarian effects are still largely unknown. The aims of this work were to characterize the effects of ALLO intrabursal administration on different ovarian parameters, and the probable mechanism of action. ALLO administration increased serum progesterone concentration ($p=0.0010$, $n=5$) and ovarian 3β -HSD ($p=0.0451$, $n=4$) while decreasing 20α -HSD mRNA expression ($p=0.0137$, $n=4$). ALLO increased the number of atretic follicles ($p=0.0077$, $n=4$), and the number of positive TUNEL granulosa and theca cells (theca: $p=0.0019$ and granulosa: $p<0.0001$, 16 sections/ovary, 5 ovaries/group), while decreasing positive PCNA immunostaining (theca: $p=0.0312$ and granulosa: $p<0.0003$). Meanwhile, the diameter of *corpora lutea* ($p<0.0001$, $n=300$ CL) and the PCNA immunostaining increased ($p<0.0001$, 16 sections/ovary, 5 ovaries/group), while decreasing TUNEL positive cells ($p<0.0001$, 16 sections/ovary, 5 ovaries/group). Ovarian angiogenesis (α -actin $p=0.0005$; Von Willebrand $p=0.0058$) and the GABA_A receptor immunohistochemical expression also increased after ALLO treatment. To evaluate if the ovarian GABA_A receptor was involved in these effects, we

conducted a functional experiment with a specific antagonist, bicuculline. The administration of bicuculline returned the number of atretic follicles ($p=0.0002$, $n=5$ animals/group) and the diameter of corpora lutea ($p<0.0001$, $n=5$ animals/group, 51 CL/group) to normal values. These results show ALLO actions on the ovarian physiology of the female rat during the follicular phase, some of them through the $GABA_A$ R. Intrabursal ALLO administration alters several processes of the ovarian morphology of the female rat, related to fertility and oocyte quality.

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