MODULATION OF NEUROPEPTIDE Y AND Y1 RECEPTOR EXPRESSION IN THE AMYGDALA BY FLUCTUATIONS IN THE BRAIN CONTENT OF NEUROACTIVE STEROIDS DURING ETHANOL WITHDRAWAL IN MICE

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Increases in the brain content of neuroactive steroids induced by physiological or pharmacological conditions have been shown to result in increased expression of the gene encoding the Y1 receptor (Y1R) for neuropeptide Y (NPY) in the medial amygdala of mice. With the use of Y1R/LacZ transgenic mice, which harbor the murine Y1R gene promoter linked to a lacZ reporter gene, we have now investigated the functional relations between fluctuations in the brain content of neuroactive steroids induced by chronic voluntary ethanol consumption or ethanol withdrawal and both the level of NPY immunoreactivity and Y1R/LacZ transgene expression in the amygdala. The voluntary consumption of consecutive solutions of 3, 6, 10, and 20% (v/v) ethanol over 4 weeks increased the cerebrocortical concentration ofthe progesterone metabolite 3α-hydroxy-5α-pregnan-20-one (3α, 5α - TH PROG), with this effect being no longer apparent 48 h after ethanol withdrawal. Ethanol withdrawal resulted in a significant decrease in the level of NPY immunoreactivity and a concomitant increase in Y1R/LacZ transgene expression in both the medial and central amygdala, whereas chronic ethanol intake had no effect on these parameters. Treatment with the 5α –reductase inhibitor finasteride during the last week of ethanol consumption, which prevented the increase in the cerebrocortical concentration of 3α, 5α - TH PROG normally apparent after 4 weeks of ethanol intake, also prevented the changes in NPY immunoreactivity and transgene expression induced by ethanol withdrawal. These data suggest that 3α, 5α - TH PROG may play an important role in the changes in NPY-Y1R signaling in the amygdala during ethanol withdrawal.