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Poster presentation

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Fear state induced by diazepam withdrawal may be due to the sensitization of the neural substrates of aversion in the dPAG

Manoel Jorge Nobre* and Jana Batista De Ross

Address: Department of Psychology and Education, FFCLRP, Laboratory of Neuropsychopharmacology, University of Sao Paulo, Sao Paulo, Brazil
* Corresponding author

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Background

In this study, we evaluated the effects of diazepam withdrawal [1] on the aversion promoted by the electrical stimulation of the dPAG [2], the influence of withdrawal on motor and attentional processes of withdrawn-rats - through the startle and prepulse inhibition tests, and the importance of the dPAG glutamate neurons in the modulation of this response [3].

Materials and methods

Wistar rats, 100-110 g, were used. Animals were submitted daily to 14 hours of water deprivation. At the end of this period diazepam was separately dissolved (10 mg/ml of saline plus propilenoglycol 5%) and offered to the animals, once daily during eighteen days, in a volume of 1ml/kg diluted in a solution of 2 ml of tap water added to sucrose (5%) plus propilenoglycol (5%). Surgeries were performed on day 15 and a cannula made by stainless steel needle (24G) was directed to the dPAG. Animals were tested at the last day or 48 hours after the last diazepam ingestion.

Results

Forty-hours of diazepam withdrawal elicit high levels of aversion in rats as revealed by the decrease on aversive thresholds and the enhance of the startle response. These aversive effects were blocked through antagonism of the NMDA glutamate receptors in the dPAG.

Conclusions

It is suggested that an enhanced neural activation of neural substrates of fear in the midbrain tectum, that involves glutamate, may underlie the aversive state elicited in diazepam-withdrawn rats.

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