FUNCTIONAL ANTAGONISM BETWEEN NOCICEPTIN/ORPHANIN FQ (N/OFQ) AND CRF IN THE RAT BRAIN: EVIDENCE FOR INVOLVEMENT OF THE BED NUCLEUS OF THE STRIA TERMINALIS

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Rationale: Nociceptin/orphanin FQ has been proposed to be a functional antagonist of corticotropin releasing factor (CRF) in relation to its anti-stress action (1,2) and for its property to antagonize the anorectic effect of CRF in rats without exhibiting affinity for CRF receptors (3). The bed nucleus of the stria terminalis (BNST) is highly sensitive to the inhibitory effect of N/OFQ on CRF-induced anorexia (4). Objective: The present study was aimed at further evaluating the role of the BNST in the functional antagonism between N/OFQ and CRF by examining it at molecular level and in the context of CRF-induced anxiety in the rat. Materials and methods: First, in situ hybridization experiments investigated the expression of the pro-N/OFQ and NOP receptor mRNA in several brain areas 6 h after the injection of CRF (0.2 and 1 μg/rat) into the lateral cerebroventricle (LV). Second, the elevated plus maze test was also used to evaluate whether N/OFQ, injected into the BNST (0.05 and 0.5 μg/rat) or into the LV (0.5, 1.8 and 2.4 μg /rat), inhibits the anxiogenic-like effect evoked by LV injection of CRF (1 μg /rat) in rats. Results: The in situ ibridization study showed that LV injection of CRF 1 μg /rat increases NOP receptor mRNA expression in the BNST and in the locus coeruleus (LC) while no changes of the N/OFQ precursor were observed. On the other hand, N/OFQ injection into the BNST blocks the anxiogenic effect of CRF at doses lower that those required by LV injection (0.5 vs 1.8 μg, respectively). Conclusion: These data provide further support for the hypothesis that N/OFQ may behave as functional antagonist of CRF and suggest that this antagonism may occur within the BNST.

References:

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