NOCICEPTIN/ORPHANIN FQ RECEPTORS IN THE SUBSTANTIA NIGRA RETICULATA MODULATE MOTOR FUNCTION AND MOTOR CORTEX EXCITABILITY IN THE RAT

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Nociceptin/orphanin FQ (N/OFQ) is an opioid-like neuropeptide which activates a G-protein coupled receptor, the NOP receptor. N/OFQ and its receptor are widely expressed in cerebral areas involved in the control of motor function. In this study we investigated how exogenous and endogenous N/OFQ is able to influence motor activity and primary motor cortex (M1) excitability in adult rats. Ten nmol N/OFQ and 10 nmol UFP-101, a potent and selective NOP receptor peptide antagonist, were injected in the lateral cerebral ventricle (LCV), in the Substantia Nigra pars reticulata (SNr) and in the M1. Behavioural analysis: rats were tested on the fixed-speed rotarod, and rotarod performance calculated 10 and 60 min after drug injection. Electrophysiological analysis: movements evoked by intracortical microstimulation (ICMS) of M1 were mapped in each animal under ketamine anaesthesia, starting from 10 min after injection. The ICMS (30ms trains of 0.25ms cathodal pulses at 300Hz, stimulation current ≤60μA) was delivered at a depth of 1.5mm from the pial surface using glass-insulated tungsten microelectrodes (impedance: 0.6-1.2MΩ). After LCV injection, N/OFQ abolished (~95%) motor activity on the rotarod and increased the mean threshold to evoke vibrissa and forelimb movement (~55% and ~47%, respectively). UFP-101 facilitated motor performance (~75%) and decreased (~33%) the mean threshold to evoke forelimb movement. UFP-101 was ineffective in modulating vibrissa threshold. On the contrary, when injected in M1, N/OFQ and UFP-101 did not change rotarod performance and M1 excitability. SNr injections of N/OFQ and UFP-10 qualitatively reproduced the LCV pattern, although mean threshold to evoke forelimb movement by UFP-101 was decreased (~50%) more than after LCV injection. The present results show that activation of SNr NOP receptors impairs motor function and reduces M1 excitability, while blockade of NOP receptors exerts opposite effects. These data also suggest that endogenous N/OFQ in the SNr drives a tonic inhibitory control on motor behaviour probably by decreasing M1 excitability.