

EFFECT OF UNCONTINGENT AND SUBCHRONIC ADMINISTRATION OF ADDICTIVE DRUGS ON NEURONAL PLASTICITY IN THE RAT NUCLEUS ACCUMBENS

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The administration of drugs with addictive potential stimulates dopamine transmission, as determined by in vivo brain microdialysis, preferentially in the shell of the nucleus accumbens compared to the core. Subchronic, intermittent administration of morphine, nicotine and cocaine has been shown to result in sensitized behavioural responses upon administration of a challenge that also reverts the shell/core ratio of stimulation of dopamine transmission with respect to acute administration (1, 2, 3). The aim of the present study was to determine whether uncontingent, subchronic and intermittent administration of morphine, nicotine and cocaine would also result in changes of synaptic plasticity in the nucleus accumbens. To this end we administered morphine twice daily for 3 days at increasing doses (10, 20, 40 mg/kg), nicotine once a day for 5 days (0.4 mg/kg) and cocaine twice daily for 14 days (10 mg/kg) according with the schedule that was previously reported to elicit behavioural sensitization and to revert the shell/core ratio, upon challenge after, respectively, 30, 1 and 10 days (1, 2, 3). Changes in synaptic plasticity were determined by evaluating the consequences of the above treatments on spines' density of second order dendrites of medium size spiny neurons of the nucleus accumbens shell and core following Golgi-Cox staining. Our results indicate that after subchronic morphine spine's density was significantly reduced in the shell but unaffected in the core of the nucleus accumbens with respect to controls. In contrast, following nicotine and cocaine we found that their subchronic administration significantly increased spine's density of second order dendrites both in the shell and in the core. Overall these results confirm and extend previous findings (4) by systematically investigating the changes in spine's density in the shell and core of the nucleus accumbens following subchronic, intermittent and uncontingent administration of morphine, nicotine and cocaine and provide original information on the rearrangement of synaptic connectivity in the nucleus accumbens. These results may, finally, provide the basis for the study of the synaptic changes following repeated, intermittent contingent administration of these drugs in the self-administration paradigm.

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- 2) Cadoni C. and Di Chiara G.(2000); *Eur J Pharmacol.* 387(3):R23-5
- 3) Cadoni C. et al. (2002); *Psychopharmacol (Berl)*. 158(3):259-66.
- 4) Robinson T.E. and Kolb B. (2004); *Neuropharmacol.*47 Suppl 1:33-46