PHARMACOLOGICAL CONTROL OF STRESS-INDUCED DYSFUNCTION OF NEUROTRANSMITTER RELEASE

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Chronic exposure to stressful events has been shown to precipitate or exacerbate many neuropsychiatric disorders, including depression, anxiety and schizophrenia. Cortical monoaminergic neurons are highly sensitive to the effects of acute stressful stimuli. Moreover, chronic stress increases the sensitivity of these neurons to an acute stressful stimulus. The stress-induced increase in cortical monoamines output is completely prevented by the acute administration of benzodiazepines.
We have shown that chronic, but not acute, treatment with antidepressant drugs with different mechanism of action (TCAs, NaSSA, NaSRI, NaRI) or with the atypical antipsychotic drugs olanzapine and clozapine, is able to reduce the increase in the extracellular concentration of catecholamines in the prefrontal cortex induced by stress or by the anxiogenic drug FG 7142 in freely moving rats.
Rats have been chronically treated (3 weeks, once a day) with the drugs and exposed to footshock stress (0.2 mA/500 msec per sec per 8 min) or received an acute administration of the anxiogenic benzodiazepine receptor ligand FG7142 (20 mg/kg, i.p.) and norepinephrine or dopamine release were measured in the prefrontal cortex by vertical microdialysis. As expected, in control rats footshock increased extracellular catecholamine concentrations (about +90%). Long term administration of antidepressants or atypical antipsychotics reduced (about +40%) the effect of stress and of the acute administration of FG7142 on basal monoaminergic output.
Our data are consistent with clinical and experimental evidences that have shown that treatment with antidepressant drugs or with atypical antipsychotics is associated with an effective reduction in the cluster of anxious and depressive symptoms.
The reduced sensitivity of cortical monoaminergic neurons to the action of stress and anxiogenic drugs elicited by treatment with antidepressants or atypical antipsychotics might represent a relevant neurochemical mechanism in the anxiolytic action of these drugs.