

Enduring attenuation of norepinephrine synaptic availability and augmentation of the pharmacological and behavioral effects of desipramine

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Abstract

Here we provide evidence that repeated immobilization stress (RIS) in rats induces a persistent increase in noradrenergic activity in the anterior aspects of the anterolateral bed nucleus of the stria terminalis (alBNST). This increase in noradrenergic activity results from both enhanced synthesis and reuptake of norepinephrine (NE). It leads to a decrease in the synaptic availability of NE, which elicits an augmented noradrenergic response to the inhibitors of NE reuptake (NRIs), such as desipramine (DMI), an antidepressant. The enduring depression-like behavior and the augmentation of the climbing behavior seen in repeatedly stressed rats following subchronic administration of DMI in the forced swimming test (FST) might be explained by a dysregulation of noradrenergic transmission observed in alBNST. Taken together, we propose that dysregulation of noradrenergic transmission such as the one described in the present work may represent a mechanism underlying major depressive disorders (MDD) with melancholic features in humans..

Keywords

Depression, Anxiety, Microdialysis, Norepinephrine release, Bed nucleus of the stria terminalis, Forced swimming test.