Stress-induced structural alterations in the hippocampus: reversal by antidepressants?

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Structural neuroimaging and *post mortem* histopathological studies of the brain have revealed morphological changes in cortical and subcortical regions in individuals diagnosed with depression. These findings suggest that morphological changes might be involved in the pathophysiology of depression, and implies that antidepressants may be able to regulate or reverse the detected structural abnormalities. Since stressful life events are one of the major predispositions for developing depression, we investigated structural changes in the hippocampus of tree shrews exposed to chronic psychosocial stress. Furthermore, we addressed whether antidepressant treatment can reverse the stress-related structural changes. Using this animal model of depression, some of the large-scale anatomical changes were also observed in the tree shrew brain. After 1 month of stress, we observed a substantial decrease of dentate cytogenesis and a minor reduction of hippocampal volume. Even though, long-lasting stress does not lead to a loss of principal hippocampal cells, we observed a regional specific change in the incidence of apoptotic cells. Notably, we could demonstrate that many of the stress- induced effects on structural plasticity could be counteracted by treatment with different antidepressants such as fluoxetine, clomipramine, tianeptine, and two NK1 receptor antagonists (compounds with potential antidepressant efficacy). These data provide experimental evidence for recent concepts of pharmacological modification of neuronal viability and neuronal remodeling in the treatment of mood disorders. Although these concepts are still in their infancy they have increasingly attracted research efforts which may result in new treatment strategies of neural resilience responsible for the etiopathophysiology of psychiatric disorders, such as major depression.

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