Neuronal and synaptic plasticity in subregions of rat hippocampus after antidepressant treatment

Fenghua Chen, MD, MS

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Official opponents: Karsten Nielsen, Andreas Reif, Germany, and Connie Sanchez, USA.

Tutors: Jens R. Nyengaard, Torsten M. Madsen, and Gregers Wegener.

Correspondence: Fenghua Chen, Stereology and Electron Microscopy Research Laboratory and MIND Center, Building 1185, Aarhus University, 8000 Aarhus C, Denmark.

E-mail: fenghua.chen@ki.au.dk

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ABSTRACT

Neuronal plasticity in the hippocampal formation is thought to play an important role in the pathophysiology of depression and effects of antidepressant therapy. Depression may result from an impairment of neurons in the hippocampus which makes it impossible to make appropriate adaptations and/or synaptic connections. Chronic antidepressant therapy increases levels of neurotrophic factors, promotes cell proliferation and neurogenesis, and regenerates synaptogenesis in the hippocampus.

The PhD dissertation includes three projects, which are aimed at investigating the underlying effect of antidepressants (imipramine in study I and III and repeated seizures in study II) on the neuronal plasticity in subregions of the hippocampus in normal rats (study I and II) and in an animal model of depression (study III). Design-based stereological methods were used to quantify regional volumes and the number of neurons and synapses.

In study I, we found that the number and percentage of spine synapses increased significantly and, conversely, the percentage of asymmetric shaft synapses significantly decreased following 14 days of imipramine treatment.

In study II, the results showed that volumes of dentate gyrus (DG) and hilus of the hippocampus were significantly larger in the ECS treatment group. The neuron number in DG, synapse number (including total synapses, spine synapses, and both perforated and nonperforated spine synapse subtypes) in CA1 were significantly increased in the ECS treatment group.

In study III, we found that regional volume, neuron number, and spine synapse number were significantly smaller in the FSL rats, and were related to decreased immobility in the forced swim test. The neuron numbers in the DG was significantly increased in the imipramine treated FSL rats, furthermore, the neuron numbers in the DG and hilus showed no differences in the treated FSL rats compared with the FRL rats. The spine synapse numbers increased significantly following imipramine treatment and, conversely, the shaft synapse numbers significantly decreased in the imipramine treated FSL rats.

Our findings provide experimental evidence for supporting the recent theories that major depression may be related to impairments of structural plasticity and neural cellular resilience, and that antidepressants counteract the structural impairments.