Structural plasticity changes in major depression

Lucassen PJ
Institute Neurobiology, SILS, University of Amsterdam, Amsterdam

Depression is a serious mental disorder with a relatively high incidence in the Western world. Although the etiology is poorly understood, chronic stress and/or stressful (early) life events are considered important risk factors for the development of depression in genetically vulnerable individuals. Indeed, clear indications for an enhanced hypothalamus-pituitary-adrenal (HPA) axis activity have been reported in a significant proportion of depressed patients.

Based on animal studies, such dysregulation of the HPA axis, may inflict cumulative hippocampal injury, which would be consistent with the hippocampal volume reductions frequently found in depressed patients using NMR imaging. However, although various histopathological investigations have revealed subtle structural changes in selected brain regions like the prefrontal cortex and amygdala e.g., the principal neuronal layers of the hippocampus failed to show massive loss, or obvious neuropathology, in depressed patients, stressed rodents or cortisol treated monkeys. This indicates that other (structural) parameters like glia or adult neurogenesis e.g., are involved in the hippocampal atrophy in these conditions.

Stress indeed induces prominent reductions in the numbers of adult-generated neurons (neurogenesis) in the hippocampus (Heine et al., 2004), an effect that is more profound when applied earlier in life, and that, over time, could contribute to hippocampal volume reductions. Although stress appears involved in depression, the underlying mechanism of action, or, notably, that of most antidepressant drugs used today, remain unclear. Recent evidence indicated that many antidepressant drugs influence neurogenesis and apoptosis in adult hippocampus (Lucassen et al., 2004).

In this session, speakers focus on stress-induced disruption of adult hippocampal turnover and/or structural neural plasticity in depression (models). Antidepressants may act by correcting this dysfunction.

Heine VM et al.(2004). Eur. J. Neurosci. 19: 131-144
Lucassen PJ et al. (2004) Biol. Psych. 55: 789–796

Paul J. Lucassen, Institute Neurobiology, SILS, University of Amsterdam, Amsterdam, t 020 5257631, e-mail lucassen@science.uva.nl

Speaker Session 30 Adult neurogenesis and depression, Thursday June 3rd