Abstract

Depression is a serious mental illness that unfortunately has limited effective treatments. Despite its prevalence, there is a striking lack of literature investigating the biological responses underlying depressive symptoms, particularly in females. This gap in research may contribute to low favorable pharmacological treatment outcomes. Despite the growing recognition of the involvement of inflammation in depression, the specific role of NF-κB, a major regulatory inflammation transcription factor, and microglia, the brain's macrophages, remains relatively understudied. While there is a growing body of literature implicating NF-κB activation and microglial dysfunction in depression, the specific mechanisms underlying their involvement in the pathogenesis of depressive symptoms, remain poorly understood. This study investigates the relationship between NF-κB and microglial activation following an LPS-induced depression-like inflammation paradigm in female rats. To further understand inflammatory cytokine signaling in depression pathogenesis, we focused on specific brain regions associated with serotonin signaling: the thalamus (TH), dentate gyrus (DG), and striatum (STr). Our findings indicate there is a potential connection between serotonin signaling and alternative NF-κB activation in female subjects. Specifically, NF-κB-microglia colocalization was found only to be significant in the thalamus, determined by analysis across regions, and against global population-adjusted means. In contrast to canonical pathway activation, microglia morphology was found to be nonsignificant only in the thalamus. This argues that serotonergic antidepressants may have broader effects than just neurotransmitter modulation, extending into inflammatory disease response. This serves as a basis for further research regarding female subjects and suggests NF-κB as a potential therapeutic target for depression.