Cytokine-serotonin interaction through IDO: a neurodegeneration hypothesis of depression

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Summary There are different theories and hypotheses related to the aetiology of depression. The interaction between brain 5-HT level and the activity of its autoreceptors plays a role in mood changes and depression. In major depression, activation of the inflammatory response system (IRS) and increased concentrations of proinflammatory cytokines, prostaglandin E2 and negative immuno-regulatory cytokines in peripheral blood have been reported. Recently, pro-inflammatory cytokines have been found to have profound effects on the metabolism of brain serotonin through the enzyme indoleamine-2,3-dioxygenase (IDO) that metabolizes the tryptophan, the precursor of 5-HT to neurodegenerative quinolinate and neuroprotective kynurenate. The cytokine-serotonin interaction that leads to the challenge between quinolinate and kynurenic acid in the brain explains the neurodegeneration hypothesis of depression.

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