

## The role of actual and early life Stress for inflammation and Major Depression

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The influence of inflammatory immune changes and several other environmental factors on the pathophysiology of depressive disorders is generally accepted. An imbalance between the pro- and anti-inflammatory side of the immune system with predominance on the proinflammatory side and increased production of proinflammatory cytokines has been described repeatedly in depressed patients. The cytokine changes are of crucial importance in the kynurenine pathway, which is part of the tryptophan catabolism. Tryptophan, the precursor of serotonin, is catabolized by the enzymes indoleamine 2,3-dioxygenase (IDO) and tryptophan 2,3-dioxygenase (TDO) into kynurenine, which releases several neuroactive (both neuroprotective and neurotoxic) metabolites in the further degradation. The ubiquitously present key enzymes IDO and TDO are stimulated and induced by proinflammatory cytokines and psychological stress.

44 patients fulfilling the diagnostic criteria for major depressive disorder according to the DSM IV and 44 age and gender matched healthy control subjects were included in the study. Besides the utilization of psychological questionnaires to detect the level of stress experienced recently (everyday stress and life threatening experiences) and formerly (childhood trauma) by the participants, several tryptophan pathway metabolites and pro- and anti-inflammatory cytokines were analyzed in the participants' venous blood plasma.

The results confirm the generally increased inflammatory state with significantly higher levels of proinflammatory cytokine interleukin 6 (IL-6) in the patient group. Besides, significantly higher levels of anti-inflammatory cytokine interleukin 10 (IL-10) were found in the patient group, which is in disaccord with the neurodegeneration hypotheses of depression.

Higher levels of acute and chronic stress and a deficiency in an adequate immunological response to stress could be demonstrated in the patient group. The inducing effect of stress and proinflammatory cytokines on the kynurenine pathway enzymes was demonstrated by a significantly higher ratio of 3-hydroxykynurenine/kynurenine and lower levels of tryptophan in depressed patients.

This study supports the importance of psychological stress and vitamin deficiency and childhood trauma to an increased immune activation in the pathophysiology of depression. Furthermore it provides new approaches for future research projects with focus on anti-inflammatory treatment in major depressive disorder. This will be discussed in the light of the actual literature.

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