

### Inflammation in schizophrenia.

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#### **1. Abstract**

Although there is no doubt that the dopaminergic neurotransmission is strongly involved in the pathophysiology of schizophrenia, the exact mechanism leading to dopaminergic dysfunction is still unclear. A disbalance in the immune response associated with a slight inflammatory process of the central nervous system (CNS) has been postulated. Such a mechanism is the basis for the "mild encephalitis" concept. A dysfunction in the activation of the type-1 immune response seems to be associated with decreased activity of the key enzyme of the tryptophan/kynurenine metabolism, indoleamine 2,3-dioxygenase (IDO). Theoretically, a decreased activity of IDO results in the increased production of kynurenic acid, an N-methyl-D-aspartate antagonist in the CNS, and a reduced glutamatergic neurotransmission in schizophrenia. Accordingly, in animal models of schizophrenia, increased levels of kynurenic acid in critical regions of the CNS were described, although studies of peripheral blood levels of kynurenic acid in schizophrenic patients showed controversial results. The immunological effects of a lot of existing antipsychotics, however, rebalance in part the immune imbalance and the overweight of the production of kynurenic acid. The inflammatory state in schizophrenia is associated with increased prostaglandin E(2) production and increased cyclooxygenase-2 (COX-2) expression. Growing evidence from clinical studies with COX-2 inhibitors points to favorable effects of anti-inflammatory therapy in schizophrenia, in particular in an early stage of the disorder. Further options for immunomodulating therapies in schizophrenia will be discussed.