Curr Pharm Biotechnol. 2012 Jun;13(8):1606-13.

Immunological treatment options for schizophrenia.

Müller N, Myint AM, Schwarz MJ.

Department of Psychiatry and Psychotherapy, Ludwig-Maximilian University, Nussbaumstr. 7, 80336 Munich, Germany. Norbert.Mueller@med.uni-muenchen.de

1. Abstract

The exact pathophysiological mechanism leading to dopaminergic dysfunction in schizophrenia is still unclear, but inflammation is postulated to be a key player: a dysfunction in the activation of the type 1 immune response seems to be associated with decreased activity of the key enzyme in tryptophan/kynurenine metabolism, indoleamine 2,3- dioxygenase (IDO), resulting in increased production of kynurenic acid - a N-methyl-D-aspartate (NMDA) antagonist in the central nervous system (CNS) - and reduced glutamatergic neurotransmission. The differential activation of microglia cells and astrocytes as functional carriers in the immune system in the CNS may also contribute to this imbalance. Existing antipsychotics, which predominantly act as dopamine D2 receptor antagonists, have several shortcomings. The immunological effects of many existing antipsychotics, however, rebalance in part the immune imbalance and the overproduction of kynurenic acid. The immunological imbalance results in an inflammatory state with increased prostaglandin E2 (PGE2) production and increased cyclo-oxygenase-2 (COX-2) expression. Growing evidence from clinical studies with COX-2 inhibitors points to favourable 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.