Impaired monocyte activation in schizophrenia.

Abstract:
An inflammatory process is hypothesized in schizophrenia. Innate immunity, in particular the monocyte/macrophage system, has rarely been studied in this disorder, although alterations in microglia indicate a role for this system. Increased monocyte numbers have repeatedly been described. Toll-like receptors (TLRs) mediate the activation of monocytes. We studied the expression of the toll-like receptors TLR-2, TLR-3 and TLR-4 on CD14(+) monocytes in 31 schizophrenia patients and 31 sex- and age-matched healthy controls. Blood samples were taken and stimulated with either lipopolysaccharides (LPS), to mimic a bacterial infection, or polyI:C, to mimic a viral infection. Moreover, the intracellular concentration of interleukin-1ß (IL-1ß) in CD33(+) monocytes was estimated before and after stimulation. The intracellular concentrations of IL-1ß and the TLR surface markers were analyzed by flow cytometry. Receptor expression of TLR-3 and TLR-4, but not of TLR-2, was significantly higher in the schizophrenia patients. After stimulation, patients showed less increase in the expression of TLR-3 and TLR-4 than controls did. The IL-1ß concentration was significantly lower in patients both before and after stimulation with polyI:C, and there was a trend towards a lower concentration after LPS stimulation. The higher expression of TLR-3 and TLR-4 receptors might compensate for a
functional deficit, and the lower intracellular concentrations of IL-1ß might reflect the blunted monocytic function in schizophrenia. The immunological dysfunctions might be associated with a poor clearance of pathogens in schizophrenia, which in turn could lead to a low-grade inflammatory process.