

## COGNITIVE PERFORMANCE IN DEPRESSION: PATHOPHYSIOLOGICAL AND THERAPEUTIC CONSIDERATIONS

Norbert Müller

Klinik für Psychiatrie und Psychotherapie der Ludwig-Maximilians-Universität München

Since cognitive deterioration is one of the core symptoms of depression and the immune system, particularly an inflammatory process is increasingly discussed to be involved in the pathophysiology of depression, a role of the immune system in cognition came into the focus of research. Interestingly, several studies show in the meanwhile a strong involvement of the immune system in cognition. In inflammation, proinflammatory cytokines as part of the immune system are activated. An overactivation of proinflammatory cytokines, such as IL-6, IL-1 and TNF- $\alpha$  plays a role in depression. The term 'inflammaging' reflects the increasing pro-inflammatory immune state during aging, but it has also been shown that the blood-concentration of proinflammatory proteins such as Interleukin-6 (IL-6) and haptoglobin predict the cognitive performance three and six years later in aged people.

In an animal model, the intact T-cell response was shown to be the pre-condition for a better cognitive performance. The recently published Whitehall II study showed that the concentrations of C-reactive protein and IL-6 were predictive for cognitive symptoms of depression after 12 years.

Accordingly, anti-inflammatory or immunomodulatory therapy would be expected to enhance cognitive performance. Up to now there are only few data focussing on the influence of those compounds to cognition. In Alzheimer's disease, there have been studies with disappointing results. An own study using the cyclo-oxygenase-2 (COX-2) inhibitor celecoxib showed therapeutic effects on cognitive symptoms in patients with schizophrenia. COX-2 inhibition reduces the levels of proinflammatory cytokines. The results and consequences of these data will be discussed.