S100B in psychiatric disorders

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Recent research has supported a potential role of immune pathology in the etiopathogenesis of schizophrenic and affective psychoses. For schizophrenia specific and unspecific evidence has been obtained. In the CNS various viruses (e.g. HERV, BDV) were identified in the brains of schizophrenic patients. Pro-inflammatory cytokines were found to be associated with the stage of disease. Microglial cells were reported to be activated in a subgroup of schizophrenic patients in post mortem as well as imaging studies. For affective disorders, especially depression, evidence has also emerged that there is an activation of the innate inflammatory immune response including alterations in the ability of immune cells to express proinflammatory cytokines. It has been shown that peripheral immune signals can lead to an exacerbation of sickness and the development of symptoms of depression in vulnerable individuals. This illustrates that inflammation is an important biological event that might increase the risk of major depression.

Until recently, astrocytes were regarded as mere supporters of neurons regulating the environmental milieu. New research, however, has demonstrated that astrocytes together with microglial cells are the major immunocompetent cells of the brain and play an important role in the regulation of neuronal proliferation and differentiation. Since neuronal remodelling appears to be a relevant pathogenic factor in various psychiatric disorders the role of astrocytes needs to be evaluated. S100B, a calcium binding astrocyte-specific cytokine, presents a marker of astrocytic activation.

Several independent studies showed increased S100B levels in medicated acutely psychotic patients with schizophrenia and drug naïve schizophrenics. A positive correlation between negative symptoms and S100B was described. In a longitudinal approach over 24 weeks a continuously increased S100B concentration was associated with continuity of negative symptoms and deceleration of therapeutic

response. Cognitive deficits are observed primarily in patients with persistently elevated concentrations of S100B. Increased S100B concentrations are associated with increased myo-inositol, another astrocytic marker measured by MRSpectroscopy.

In acute major depression S100B has been found to be significantly increased directing towards astrocyte activation. Obviously, this phenomenon is limited to the more biologically determined types of depression such as the melancholic subtype. In these patients a moderately elevated S100B concentration seems to be beneficial since patients with higher S100B showed better response and remission rates. Antidepressant treatment appears to normalize S100B concentrations. On a functional level it could be shown that depressed patients with increased S100B experience a better normalization of initially pathological evoked potential (ERP) patterns than patients with unchanged S100B. Even three months after psychopathological remission only those patients with primarily higher S100B showed normal ERP patterns while in patients with initially normal S100B the pathological patterns remained.

These findings suggest that the activation of astrocytes is an important pathogenic factor for the development of schizophrenia and depression. Astrocytic activation is associated with course of disease, treatment response, and functional outcome. This exemplarily illustrates the importance of immunological mechanisms in the etiopathogenesis of major psychiatric disorders.