Immune Disorders in Nondeficit and Deficit Schizophrenia

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In 1995, Smith and Maes launched the monocyte-T lymphocyte theory of schizophrenia, which considered that activated immune-inflammatory pathways account for the increased neurodevelopmental etiopathology linked with gestational infections through the detrimental effects of peripheral immune activation and oxidative and nitrosative stress, activated microglia, cytokine-induced activation of the tryptophan catabolite (TRYCAT) pathway and modulation of the N-methyl D-aspartate receptor (NMDAR).

Here we review our findings (1993-2017) suggesting that schizophrenia and deficit schizophrenia are two separate immune disorders. Schizophrenia patients and patients with drug-naïve first episode psychoses (FEP) show multiple signs of activated immune-inflammatory pathways, oxidative stress and lowered antioxidant defenses. The combination of immune biomarkers allows to predict schizophrenia and chronic schizophrenia with high predictive value. In FEP, increased levels of pro-inflammatory cytokines may dysregulate genes involved in microRNA machinery, while increased IL-10 may have neuroprotective properties, by elevating NDEL1, DISC1, and MBP expression. The negative symptoms and neurocognitive deficits of schizophrenia are strongly associated with immune biomarkers and with a specific TRYCAT profile indicating increased inflammatory, oxidative, cytotoxic, neurotoxic, excitotoxic and neuroppressive properties. Deficit and undifferentiated schizophrenia are two different disorders, the former being characterized by increased deficits in episodic memory and false memory creation, which are associated with a specific TRYCAT profile and by specific defects in IgM-mediated natural autoimmune responses. Multiple episode schizophrenia is additionally accompanied by deficits in semantic memory as compared with single episodes. The neurocognitive impairments in deficit schizophrenia are significantly greater than in elderly patients with mild cognitive impairment. MRI measurements, including gray matter and cortex volume, cerebro-spinal fluid and lateral ventricle volume are strongly associated with immune-
inflammatory and oxidative stress biomarkers. Negative symptoms of schizophrenia are associated with decreased gray matter and cortex volumes, and increased lateral ventricle volumes and inflammatory signaling. A new neuro-immune and neuro-oxidative model of undifferentiated schizophrenia and deficit schizophrenia is presented.