SP081

Immunometabolic function in depression: From etiology to treatment

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Abstract: Background: Major depressive disorder is a common, disabling mental disorder characterized by extensive etiological and phenotypic heterogeneity. This heterogeneity makes treatment approaches imprecise and often ineffective. Insight into the underlying biological mechanisms underpinning depression and its subtypes may enable more personalized treatments.
Methods: A review of the literature as well as data analyses from 2981 individuals from the Netherlands Study of Depression and Anxiety (NESDA), of whom ˜1900 persons have or lifetime or current Major Depressive Disorder and 650 were healthy controls.
Results: Significant immuno-metabolic dysregulations are present in about 20-30% of people with depression. Such immuno-metabolic depression is characterized by the clustering of 1) atypical, energy-related depressive symptoms such as hypersomnia, fatigue, hyperphagia, and possibly anhedonia, 2) systemic low-grade inflammation with elevated levels of e.g. C-reactive protein, cytokines and glycoprotein acetyls, and 3) metabolic abnormalities involving e.g. obesity, dyslipidaemia, insulin and leptin resistance. Evidence for such clustering is confirmed in large-scale proteomic, metabolomic, gene expression as well as genome-wide data analyses. Persons with immuno-metabolic depression are at a higher risk for cardiometabolic diseases and – from pooled analyses of 4 RCTs in over 1000 individuals - seem to respond less well to standard antidepressant treatment.
Discussion: Interventions targeting inflammation, metabolism or lifestyle may be more effective treatment options for individuals with immuno-metabolic depression, in line with principles of precision psychiatry.

Disclosure of Interest: None Declared

SP082

Advancing Biomarker Research in Depression: The role of neuroprotective and inflammatory markers

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Abstract: The search for biomarkers to diagnose depression is an endeavor being pursued in psychiatric research since the 1980s, but hasn't resulted in clinical application. This remains challenging since the symptomatology of depression is very heterogeneous and because there is no diagnostic gold standard that focuses on an underlying biological mechanism. Despite knowing about the metabolic, endocrine, inflammatory as well as autonomous dysregulation that has been observed in depressed patients, none of these are broadly used to stratify patients. A novel area of research involves the insulin-like growth factor (IGF) system, which plays a vital role in brain development, neurogenesis, and neuroprotection. The insulin-like growth factor (IGF) system, encompassing IGF-I, IGF-II, IGFBPs (1-6), and their receptors, is critical for brain development, neurogenesis, neuroplasticity, and neuroprotection. Insulin-like growth factor binding protein-2 (IGFBP-2), the predominant IGFBP in the central nervous system, regulates IGF-I and IGF-II bioavailability, half-life, localization, and receptor interactions. Serum levels of IGFBP-2 inversely correlate with DTI-derived myelin integrity measures, especially in anterior brain regions.
In a data-driven clustering analysis of a depressed cohort, elevated IGFBP-2 levels delineated a healthier subgroup within a hospitalized cohort of patients with unipolar depression. Additionally we discovered, that patients with higher IGFBP2 levels at inclusion were more likely to remit faster concerning their depressive symptoms, in contrast to an inflammatory marker-defined subgroup. These findings suggest IGFBP-2 as a biomarker for stratifying patients and tailoring interventions in depression. Future research should explore IGFBP-2 and inflammatory markers to better stratify patients and develop targeted therapies, advancing precision medicine for depression and related disorders.

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SP083

State- versus trait- dependent immune alterations in major depression: Exploring CRP, numerical and functional changes in neutrophils and monocytes

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Abstract: Background: Inflammatory processes and innate immune system activation have been implicated in psychiatric disorders. While our prior research highlighted elevated neutrophils, monocytes, and C-reactive protein (CRP) associated with symptom severity in schizophrenia, this study investigates whether similar immune alterations characterize major depression (MD).
Methods: Differential blood counts, CRP levels, depression severity (HAMD-21), and psychosocial functioning (GAF) were assessed in controls (n = 129) and patients with first-episode (FEMD: n = 82) or recurrent (RMD: n = 47) MD at hospital admission (T0) and after 6 weeks of treatment (T6). Functional immune parameters, including the phagocytic activity of neutrophils and monocytes, were also measured in a subset of patients with MD (n = 16) and healthy controls (n = 27).
Results: At T0, both FEMD and RMD patients exhibited increased neutrophils ($p = 0.034$) and CRP levels (FEMD: $p < 0.001$, RMD: $p = 0.021$) and decreased eosinophils (FEMD: $p = 0.005$, RMD: $p = 0.004$) compared with controls, adjusted for covariates (smoking, BMI, gender). Baseline lymphocyte counts were elevated in RMD ($p = 0.003$) but not FEMD. Functional analyses revealed significantly increased phagocytic activity of neutrophils in MDD

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