



Editorial: Neuroglia Molecular Mechanisms in Psychiatric Disorders

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Editorial on the Research Topic

Neuroglia Molecular Mechanisms in Psychiatric Disorders

Neuroglia are an extended class of cells of ectodermal (astroglia, oligodendroglia, and peripheral glial cells) and mesodermal (microglia) origin, which provide extensive homeostatic support, protection, and defense of nervous tissue (Kettenmann and Ransom, 2013; Verkhratsky and Butt, 2013; Verkhratsky and Nedergaard, 2018). Pathological potential of glial cells has been recognized since their discovery (Virchow, 1858; Andriezen, 1893; Nissl, 1899; Alzheimer, 1910), while recent decade highlighted the fundamental role of neuroglia in the progression of all types of neurological diseases (Giaume et al., 2007; Verkhratsky et al., 2013, 2014, 2016, 2017; Burda and Sofroniew, 2014; Sofroniew, 2014; Zeidan-Chulia et al., 2014; Burda et al., 2016; Pekny et al., 2016; Verkhratsky and Parpura, 2016; Ferrer, 2018). The neurogliopathology is complex and is represented by glial reactivity (activation of microglia, astrogliosis) or glial degeneration, atrophy, and loss of functions. In particular glial cells undergo prominent changes in the context of neuropsychiatric diseases; these changes are generally represented by loss and asthenia of astroglia and oligodendroglia in conjunction with microglial activation (Rajkowska and Stockmeier, 2013; Verkhratsky et al., 2015; Cobb et al., 2016; Rajkowska et al., 2018). In this research topic we addressed the contribution of neuroglia to major neuropsychiatric conditions including major depression, schizophrenia, and alcohol use disorders.

The gliocentric theory of major depression has been overviewed by Czéh and Nagy who presented recent findings on glial structural and functional abnormalities at molecular and cellular levels. Subsequently they focused on clinical studies and summarized neuroimaging as well as post-mortem molecular and histopathological evidence supporting leading role of glia in the progression of depression and related mood disorders. Notably, the depression is associated with substantial loss of macroglial cells with loss of their function, in conjunction with microglial activation, which summarily affect neuronal networks and brain function. Structural and molecular alterations of astrocytes and oligodendrocytes also lie at the core of alcohol use disorders (Miguel-Hidalgo). In particular alcohol exposure, as well as alcohol withdrawal affects glial transporters, glutamate (GABA) glutamine shuttle and gap junctions, which connect glial syncytia. The association of endothelial cells, blood-brain barrier and neurovascular unit with neuropsychiatric diseases has been discussed by Malik and Di Benedetto, who presented evidence supporting pathophysiological role of disrupted erythropoietin-producing-hepatocellular carcinoma receptors (EphR)/Ephrin signaling cascades.

Pathophysiological changes in microglia in context of environmental stress associated with neurodevelopmental and neuropsychiatric disorders are overviewed by Tay et al. In particular, they discuss the role of microglia in Nasu-Hakola disease, hereditary diffuse

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leukoencephaly with spheroids, Rett syndrome, autism spectrum disorders, obsessive-compulsive disorder and major psychiatric pathologies such as addiction, major depressive disorder, bipolar disorder, schizophrenia, eating disorders, and sleep disorders. Studies on humans have demonstrated neuroinflammation and microglial reactivity in patients with schizophrenia as well as in animal models. In the latter, the gender differences have been also described (Hui et al.); and it turned out that in males prominent differences in microglial distribution, morphology, and microglial activation may account for higher incidence of schizophrenia. Up-regulation of microglia associated genes following administration of IgG-Saporin has been demonstrated to alter a memory-associated behavior (Dobryakova et al.). The role of microglial activation and phagocytosis in Parkinson's disease and therapeutic potential of targeting microglia were reviewed by Janda et al. Of note both asphyxia and cesarean section are associated with the expression of Schizophrenia risk genes (Paparelli et al.). The link between

neuregulin and β -secretase with schizophrenia is shown by Zhang et al.

Glial cells can be targets for specific therapy. Effects of electro-acupuncture on hippocampal neuroinflammation in rat depressed model (induced by unpredictable stress-induced depressive- and anxiety-like behavior) are presented by Yue et al. They showed that treatment with acupuncture reduce behavioral abnormalities and abrogate neuroinflammation. Quercetin neuroprotection was discussed by Gao et al.

All in all, the papers assembled in this Research Topic provide a wide picture of the importance of neuroglia in the pathogenesis of neuropsychiatric diseases and discuss possible therapeutic strategies aimed at glial cells.

AUTHOR CONTRIBUTIONS

CS, MN, and AV wrote the editorial. All authors read and approved the submitted version.

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