Investigating microglial activation in schizophrenia: post-mortem or in vivo?

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Abstract

Background: Ensuing from the psychoneuroimmunology hypothesis, neuroinflammatory activation of microglial cells is explored as a hallmark of neurodegenerative and neurodevelopmental aberrations in schizophrenia. Because extrapolation of preclinical research results to the human brain - particularly in pathological conditions - is limited, investigation of microglial activation in schizophrenia is preferably done using immunohistochemistry on post-mortem brain tissue or with in vivo TSPO PET-CT nuclear imaging.

Objective: To compare immunohistochemistry and nuclear imaging methods for the study of microglial activation in schizophrenia.

Methods: We reviewed existing literature on microglial immunostaining and TSPO nuclear imaging in schizophrenia on PubMed.

Results: The scarcity of post-mortem tissue with sufficient clinical information, required for the careful selection of cases to minimize heterogeneity due to confounding variables such as cause of death, means few studies have examined microglial activation on post-mortem tissue in schizophrenia. In immunohistochemistry, the specificity of different microglial markers represents both a challenge and an asset, but currently only HLA-DP/DQ/DR and CD68 markers have been used in schizophrenia tissue. Also for TSPO nuclear imaging, different markers have been developed. Newer TSPO markers offer higher specificity but require genotyping of subjects for rs6971 polymorphism. Three studies have investigated microglial activation in schizophrenia patients with nuclear imaging.

Conclusion: Both immunohistochemistry with specific microglial phenotypic markers and TSPO PET imaging involve specific advantages and challenges, and the combination of both techniques offers the optimal chance to determine the role of microglial activation in the pathophysiology of schizophrenia.

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