Article: EPA-0759
Topic: EPW12 - Neurobiology

MULTI-IMMUNOSTAINING FOR MICROGLIAL ACTIVATION IN SCHIZOPHRENIA

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Background Activation of microglial cells is currently explored in schizophrenia pathophysiology. Post-mortem immunohistochemistry remains the most accurate method to investigate microglial morphology and function, since high microglial plasticity limits extrapolation of in vitro and animal research results to the human brain.

Method To investigate microglial morphology and activation patterns, we performed immunohistochemistry with specific microglial markers: Iba1 (marker of resting and activated microglia), CD68 (marker of microglial lysosomes, indicative of phagocytic microglia) and CD64 (FcγRI, binds IgG) on formalin fixed paraffin embedded brain tissue from the Corsellis Collection (BRAIN UK), in 15 schizophrenia cases and 15 non-neurological controls. Immunostaining was quantified by image capture and analysis (Image J, NIH, US) to provide a measure of protein load. We also reviewed existing literature on microglial immunostaining in schizophrenia using Pubmed.

Results Few studies have examined post-mortem microglia in schizophrenia, mostly with HLA-DP/DQ/DR markers. Although frequently studied in neurological disorders Iba1, but also CD64 were never previously investigated in schizophrenia patients. Two studies explored CD68, but results were misinterpreted for resting state tissue macrophages. Our pilot study shows Iba1, CD68 and CD64 can detect microglial cells in schizophrenia brain tissue, but considerable heterogeneity exists both in patients and controls, probably due to confounding by clinical variables, e.g. age and cause of death.

Conclusion Future research needs careful selection of cases and controls to minimize heterogeneity due to confounding clinical variables. Highly specific microglial markers such as Iba1, CD64 and CD68 are very useful and ought to be introduced into schizophrenia research.

https://doi.org/10.1016/S0924-9338(14)78106-4 Published online by Cambridge University Press