

brain microstructure, contributing to plasticity and synaptic formation, and responses to environmental challenges.^[48] So, it is possible that neuroglial activation and precisely aberrant neuroglial function, may be responsible for some neuronal miswiring that is consistent with some psychotic symptoms that are frequently observed in bipolar disorder.

Summarizing, the evidence for the existence of neuroinflammation in bipolar disorder is more yes than no. However, the hypothesis of a preexisting peripheral inflammation passing in the brain and establishing a disease mode function, thus maintaining the disorder, is a mere supposition that is not based on evidence. Whereas neuroinflammation might lead to bipolar symptoms, it is not always true that neuroinflammation causes bipolar disorder, and it might be that only rarely is so. It is more likely that stress interacts with the personal constitution and epigenetic factors to cause both neuroimmune dysreactivity and bipolar disorder in susceptible individuals. As de Baumont *et al.*^[36] stated, schizophrenia and bipolar disorder may “arise from shared genetic factors, but that the resulting clinical phenotype is modulated by additional alterations mediated by microglia, possibly caused by interference of environmental factors at different times during neurodevelopment and early life, and/or epistatic interactions among groups of genes and environment.” All this should be borne in mind when projecting investigations to explore the relationship between neuroinflammation and bipolar disorder.

CONCLUSION

This review attempted to answer the question of whether neuroinflammation plays a role in the pathophysiology of bipolar disorder. Direct and indirect evidence points to some degree of possibility that this is the case, but studies heretofore are much heterogeneous in their methodology and conclusions, thus suggesting caution. It appears that the topic of neuroinflammation in bipolar disorder is a much under-investigated but over debated and highly reviewed issue. Finally, PubMed should be trusted, but alternative search engines should be used, lest precious articles are lost.

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Conflicts of interest

There are no conflicts of interest.

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