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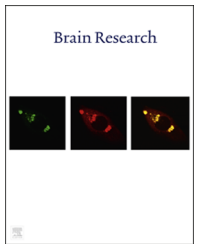

Review

Abnormal immune system development and function in schizophrenia helps reconcile diverse findings and suggests new treatment and prevention strategies

Sherry Anders[a], *Dennis K. Kinney*[b,c,*,1]

[a]*Clinical Psychologist in Independent Practice, Boxborough, MA, USA*
[b]*McLean Hospital, Belmont, MA, USA*
[c]*Department of Psychiatry, Harvard Medical School, Boston, MA, USA*

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ABSTRACT

Extensive research implicates disturbed immune function and development in the etiology and pathology of schizophrenia. In addition to reviewing evidence for immunological factors in schizophrenia, this paper discusses how an emerging model of atypical immune function and development helps *explain a wide variety of well-established – but puzzling – findings* about schizophrenia. A number of theorists have presented hypotheses that early immune system programming, disrupted by pre- and perinatal adversity, often combines with abnormal brain development to produce schizophrenia. The present paper focuses on the hypothesis that disruption of early immune system development produces a latent immune vulnerability that manifests more fully after puberty, when changes in immune function and the thymus leave individuals more susceptible to infections and immune dysfunctions that contribute to schizophrenia. Complementing neurodevelopmental models, this hypothesis integrates findings on many contributing factors to schizophrenia, including prenatal adversity, genes, climate, migration, infections, and stress, among others. It helps explain, for example, why (a) schizophrenia onset is typically delayed until years after prenatal adversity, (b) individual risk factors alone often do not lead to schizophrenia, and (c) schizophrenia prevalence rates actually tend to be *higher* in economically advantaged countries. Here we discuss how the hypothesis explains 10 key findings, and suggests *new, potentially highly cost-effective, strategies for treatment and prevention* of schizophrenia. Moreover, while most human research linking immune factors to schizophrenia has been *correlational*, these strategies provide ethical ways to *experimentally test* in humans theories about immune function and schizophrenia.

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*Correspondence to: 18 Locust Avenue, Lexington, MA 02421, USA. Mobile: +1 617 271 5156.
E-mail addresses: dr.dkinney@gmail.com, dkinney@partners.org (D.K. Kinney).
[1]Retired.

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Contents

1. Introduction

A large and growing body of research implicates atypical immune function and development in the etiology and pathology of schizophrenia. Like other recent review papers, this paper reviews evidence for the role of immunological factors in schizophrenia. In addition, this paper emphasizes several related points that have generally received less attention.

First, we discuss how a hypothesis involving atypical immune function and development helps provide a *unifying explanation for a large and diverse set of empirical findings* about schizophrenia, findings that come from many diverse disciplines, including epidemiology, genetics, immunology, neurophysiology, and pharmacology. The hypothesis helps explain a number of puzzling findings, and provides a way of reconciling some paradoxical, seemingly contradictory, findings.

The hypothesis, described at length by Kinney et al. (2009a/2010), proposes that early immune system programming, influenced by the disruptive effects of pre- and perinatal adversity, often combines with abnormal central nervous system (CNS) development to produce schizophrenia. These early effects on