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Brain Research



Review

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



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ARTICLE INFO

Article history:

Accepted 21 February 2015

Available online 28 February 2015

Keywords:

Schizophrenia

Development

Hypothesis

Immune system

Infection

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.

This article is part of a Special Issue entitled SI: Neuroimmunology in Health And Disease.

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Contents

1. Introduction	94
1.1. Many diverse findings are associated with schizophrenia risk	95
2. Early immune system programming: Schizophrenia's missing link?	97
3. Schizophrenia findings for which the hypothesis provides a unifying explanation	98
3.1. Finding #1: Prenatal exposure to certain infections and stressful environmental factors, which increases risk for schizophrenia after puberty, also impairs post-pubertal immune competence and thymic structure and function	98
3.2. Finding #2: Prenatal exposure to a number of infectious agents increases risk for schizophrenia, but most individuals with such exposure don't develop the disorder.	99
3.3. Finding #3: The effects of early infections may not appear until after puberty, when they can produce neurologic and psychiatric symptoms	100
3.4. Finding #4: Prenatal exposure to adverse environmental factors increases risk for schizophrenia at the same geographic site, but the prevalence rate for schizophrenia is actually higher in many countries with the best prenatal care and nutrition.	101
3.4.1. Latitude, vitamin D, and schizophrenia prevalence	101
3.5. Finding #5: Gene expression studies find that, among the many genes whose expression differs greatly in schizophrenic patient vs. controls, there is a strong overrepresentation of genes involved in immune function and response to infection.	102
3.5.1. Need for experimental tests of causal hypotheses.	102
3.6. Finding #6: Many of the diverse environmental factors that increase risk for schizophrenia also increase risk for infection and immune dysfunction	102
3.6.1. Urban residence	102
3.6.2. Immigrant status	102
3.7. Finding #7: Many genetically influenced factors, including male sex, that increase risk for schizophrenia are also associated with differences in immune function and resistance to infection	103
3.7.1. Genetic factors	103
3.7.2. Genetic vulnerability to infectious pathogens	103
3.7.3. Sex differences	103
3.8. Finding #8: Environmental factors, such as psychosocial stress, which tend to worsen symptoms of schizophrenia, also tend to disrupt immune function	103
3.8.1. Stress and symptoms in schizophrenia	103
3.8.2. Stress and impaired immune function and disease resistance	104
3.9. Finding #9: Immune dysfunctions, such as imbalances of pro- and anti-inflammatory cytokines, may contribute to the onset of psychotic symptoms and the progressive loss of brain tissue in schizophrenia	104
3.10. Finding #10: Many medications that reduce psychotic symptoms also combat infection	104
4. Summary	105
5. Novel treatment and prevention strategies suggested by the hypothesis	105
5.1. New treatment strategies	105
5.1.1. Bolstering immune function.	105
5.1.2. Diagnosing and treating unrecognized infections and immune disorders.	105
5.2. New prevention strategies	105
5.2.1. Reducing exposure to new infections.	105
5.2.2. Primary prevention by optimizing prenatal care and nutrition	106
6. Experimental tests of the hypothesis in humans are warranted	106
Conflict of interest statement	107
References	107

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

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