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Prenatal exposure to viral infection and conversion among adolescents at high-risk for psychotic disorders

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Dear editors,

A considerable body of literature suggests that prenatal exposure to a viral teratogen (PEVT) is associated with the etiology of psychotic disorders (e.g., Brown et al., 2004; Mednick et al., 1988). Because a steady stream of research is also beginning to suggest that identifying and treating high-risk individuals may help to ameliorate course and potentially prevent the onset of psychotic illness onset, the need for understanding the intricate relationships between risk factors and etiology among these individuals is rapidly becoming a research priority (Haroun, Dunn, Haroun, & Cadenhead, 2006). To date there have been no prospective investigations designed to evaluate whether PEVT is associated with conversion among high-risk individuals.

In the present study, adolescent participants with schizotypal personality disorder (SPD; a disorder with a roughly 30% rate of conversion to psychotic disorders; Yung et al., 1998) were evaluated for a history of PEVT and then followed for a three-year period with annual diagnostic assessments. It was hypothesized that among participants, the group comprising those who eventually converted to an Axis I psychotic disorder would show a significantly greater history of PEVT than those who did not convert. Further, we predicted that PEVT would be positively associated with psychotic symptomatology.

This report presents data on 40 participating high-risk adolescents who underwent an initial assessment and 3 annual follow-up assessments: to determine the presence of SPD (Structured Interview for DSM-IV Personality Disorders, SIDP-IV; Pfohl et al., 1997), to rule-out the presence of and Axis I disorder at baseline and to determine conversion status during follow-up assessments (Structured Clinical Interview for Axis I DSM-IV Disorders, SCID-I; First, Spitzer, Gibbon, & Williams, 1995), and to determine level of prodromal symptoms (the Structured Interview for Prodromal Symptoms, SIPS, contains an instrument, the Scale of Prodromal Symptoms, SOPS, which rates the severity of relevant symptoms among dimensions ranging from healthy to pathological; Miller et al., 2002). The mean SOPS symptom category scores were used as measures of positive, negative, and global symptoms (in addition to meeting criteria for SPD, participants in the present study met SOPS criteria for Attenuated Positive Symptom Syndrome ((APS)), which is defined by moderate to severe

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positive symptoms and associated with heightened risk of conversion to psychosis; Miller et al., 2002). PEVT was assessed at baseline by parental report, typically completed by the mother, using the McNeil-Sjöström Scale for obstetric complications (McNeil, Cantor-Graae, Sjöström, 1994). Demographic characteristics of the sample are presented in Table 1 (Please see: Mittal et al., 2007 for an in-depth description of recruitment, sample, and study procedures).

Of the 40 participating high-risk adolescents, 10 converted to an Axis I psychotic disorder. This conversion group consisted of 3 individuals with schizophrenia, 3 with schizoaffective disorder, 3 with bi-polar disorder (with psychotic features) and 1 with depression (with psychotic features). Conversion status and PEVT were found to be significantly related, Pearson $X^2(2, n = 40) = 3.38$, $p = .03$; a .50 proportion (5/10 participants) of the *Converted* group showed a history of PEVT in comparison to .20 proportion (6/30) of the *Non-converted* group. It is noteworthy that while there were significant group differences in PEVT, *t* tests indicated that there were no significant group differences in baseline symptomatology. Spearman correlations were conducted to determine the relationship between PEVT and baseline prepsychotic symptoms. There were positive relationships between PEVT and positive symptoms ($r = .29$. $p = .03$); however, for negative, and global symptoms the associations did not approach significance.

The findings in the present study are consistent with the notion that prenatal exposure to maternal viral infection enhances risk of psychotic disorders. However, it is important to note that influenza epidemics are rare, and these viruses probably account for a small proportion of the total number of patients with schizophrenia worldwide. Only a small minority of mothers who are exposed give birth to a pre-schizophrenic child. Nonetheless, the results from influenza studies are important because they suggest that a particular environmental factor occurring at a specific time in fetal development can increase risk for schizophrenia.

A significant limitation in this present investigation is the reliance on parental report of PEVT, as several studies have found that mothers of both schizophrenia and high-risk children show a tendency to over-report OCs (McIntosh et al., 2002). Future studies examining the effects of PEVT would benefit from prospective methodology using more precise assessment such serological levels to assess for virus (e.g., Brown, 2004).

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Table 1

Characteristics of Sample

	Converted	Non-converted	Total	Group Differences
Sex				
Males	5	23	28	
Females	5	7	12	
Mean Age (yrs.)	14.5(SD = 1.65)	14.07(SD = 1.70)	14.16(SD = 1.81)	Not Significant
Baseline SIPS Symptoms				
Positive	2.46(SD = 1.04)	2.25(SD = .99)	2..29(SD = .99)	Not Significant
Negative	2.33(SD = 1.43)	1.72(SD = .96)	1.85(SD = 1.05)	Not Significant
Total	2.18(SD = 1.14)	1.81(SD = .73)	1.90(SD = .82)	Not Significant
PEVT	5/10 (50%)	6/30 (20%)	11/40 (27.5%)	$p \leq .05$