Prenatal Stress and Schizophrenia

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In rodents, prenatal stress (PS) is associated in the adult offspring with behavioral changes, persistent changes in HPA axis activity, as well as changes in glucocorticoid receptor density (Takahashi et al. 1992; Henry et al. 1994; Lordi et al. 2000; Szuran et al. 2000). In non-human primates, prenatal stress results in attentional difficulties, neuromotor abnormalities, decreased locomotion, and hyperresponsiveness to stress in adult offspring (Schneider et al. 2002). PS in primates results in increased levels of dihydroxyphenlacetic acid (DOPAC), a dopamine metabolite, in offspring suggesting increased dopamine activity. In longitudinal research in humans, schizophrenia has been correlated with exposure to several forms of maternal PS, including death of the father during gestation (Huttenen & Niskanen 1978), unwanted pregnancy (Myhrman et al. 1996), exposure to wars and catastrophes, such as the 1940 invasion of Holland (van Os & Selten 1998), and the nuclear attack on Nagasaki (Koenig et al. 2002). Elevated rates of schizophrenia are also related to maternal depression during pregnancy (Jones et al. 1998). Depression is often associated with hypercortisolemia.

In my paper “The schizophrenias: Neuroscience, Neurophenomenological and Psychoanalytic Perspectives,” I noted the following on the connection between PS and later rates of schizophrenia:

“The link between exposure to stress during gestation and subsequent schizophrenia was suggested by a study that prenatal death of father was associated with increased risk of schizophrenia (Kuh & Ben-Sholomo 1997). In a population-based study on increased risk of schizophrenia, it was observed that subjects exposed during the first trimester of pregnancy to the stress of invasion by the Nazi army in the Netherlands had increased rates of schizophrenia.
An additional population-based study conducted in the Netherlands discovered a (non-significant) increased risk of developing schizophrenia in subjects prenatally exposed to the 1953 Dutch flood disaster (Selten, van der Graaf, et al 1999- "Psychotic illness after prenatal exposure to the 1953 Dutch flood disaster.” Schizophrenia Research, 35, 243-245). Rates of schizophrenia were significantly higher in subjects whose mothers were told of their husbands’ deaths during the war between Finland & Russia while in the 2nd & 3rd trimester as opposed to hearing the news after birth. I wonder if the connection between maternal starvation and later development of schizophrenia made by Susser & Lin (1992-”Schizophrenia after prenatal exposure to Dutch hunger winter of 1944-1945,” Archives of General Psychiatry, 49, 983-988), could also be contributed to by the effects of maternal stress secondary to a lack of food supply. Verdoux and Sutter (2002-”Obstetrical complications, maternal psychopathology, and the risk of psychosis” ) noted: “The association between prenatal exposure to maternal stress and later schizophrenia may be mediated by the direct impact of stress, such as fetal hypoxia induced by vasoconstriction; or more indirectly, by increasing the risk of OC’s [obstetrical complications], such as prematurity, or by increasing the risk of maternal prenatal or postnatal depression” (p.108).