Prenatal and perinatal complications in the development of psychosis: canaries in the coalmine

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Prenatal and perinatal complications and later psychosis - the canary in the coalmine

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Although first mooted as early as the 1930's, the study of obstetric complications and later psychosis came to the fore in the late 1980's when proponents of the neurodevelopmental aetiological model of schizophrenia cited the association between obstetric adversity and later schizophrenia as an essential building block for this theoretical approach [1,2] An intensive period of research into pregnancy and birth complications in patients with schizophrenia culminated in several meta-analytic reviews [3.4] which showed that there were no specific obstetric complications associated with psychotic disorder – rather a host of pre- and perinatal risk factors of small effect size (typically with odds ratios of less than 2). Although work continued to be published on the topic of obstetric complications, the field of psychosis research then focussed on the search for genetic risk factors, before a further decade of investigation came to a similar conclusion regarding the genetic underpinnings of psychosis – many risk alleles of very small effect.[5]

In this issue of Lancet Psychiatry, and almost 20 years on from the last meta-analytic review, Davies and colleagues present an impressive synthesis of the literature on obstetric risk factors for psychosis up to the present day.[6] Reviewing 15,000 records and 500 full-text articles and amassing evidence from 152 studies, the authors uncover 30 significant risk factors and 5 significant protective factors for psychosis. These findings are presented in 4 descriptive groupings: parental and familial factors; pregnancy factors; labour and delivery factors and foetal growth and development factors. In general, the effect sizes for these risk factors, although statistically significant, represent less than a doubling of the odds of psychosis, indicating that they are mostly of small to moderate effect, though the authors note in their Discussion that multiple small effects can have a significant impact. However, unlike the previous meta-analytic reviews, (and somewhat controversially), Davies and colleagues included parental psychopathology as a prenatal risk factor and the results are decidedly different in the category of parental and familial factors, with odds ratios consistently over 2 and much larger than for the pregnancy, labour and delivery or foetal growth categories. Davies and colleagues find that maternal stress increases the risk of later psychosis in offspring by more than 2-fold; maternal psychopathology increases risk for later psychosis by a factor of 4 while maternal psychosis increases the risk more than 7-fold. Paternal psychopathology also increases the risk by almost 3-fold. The only "traditional" obstetric complications to have effects sizes over 2 are polyhydramnios, premature rupture of membranes and congenital malformations. As acknowledged by the authors, maternal psychopathology or, indeed, paternal psychopathology may not represent a true pre- or perinatal factor or a genetic vulnerability but also a rearing environment risk factor, a moot point which is likely to be a combination of all of the above. [7] Information would also be needed on the exact timing of the psychopathology to parse this effect.

Certainly, the work by Davies and colleagues shows that it is time to move beyond merely reporting individual pre- and peri-natal risk factors. Recent developments in the field of causal inference and mediation analyses allow a more nuanced approach. (See Figure) Some consideration should be given to the direct effects of pre- and perinatal complications on, for instance, infant temperament, the developing neuroendocrine system and the developing brain, and also the mediating effects of known environmental risk factors for psychosis such as adversity and adolescent cannabis use on an already-sensitized neural system.[8,9] Recent work underscores the importance of examining the joint effect of polygenic risk score and early life complications on increasing susceptibility to schizophrenia. [10]

Regarding preventive strategies, improving the number of antenatal care visits would appear to be an achievable goal using tools such as incentivized or outreach prenatal care. Children born pre-term are known to have increased risks for psychiatric illness and should be monitored into the adolescent years . [11] It is also important to consider the impact of clustering of a range of pre- and perinatal factors as they rarely occur in isolation. The findings of Davies and colleagues show that the offspring of women who have non-optimal obstetric profiles (for a wide variety of reasons) are most at risk for later psychosis.[6] Additionally, it is noteworthy that the meta-analysis of Davies and colleagues shows that women with mental illness, particularly psychosis, women with a partner with mental illness and women exposed to stress, are at the highest risk to have children who go to develop psychosis.[6] Too often, the response of public health and psychiatry is to focus only on the mentally-ill parent (for instance with medications and clinic appointments), but the needs of the children of mentally-ill parents, who often need basic day-today supports, can go un-noticed.[13] A recent Lancet commission has issued a call to place the needs of children at the centre of the Sustainable Development Goals.[14] Just as the canaries acted as sentinels for the miners, the clustering of early life complications and parental mental illness can act as an early warning sign of difficulties ahead and herald the opportunity to intervene to improve intergenerational outcomes.

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