Badawi and colleagues (p 85) report on a positive association between newborn encephalopathy (NE) in term neonates and the risk of autism spectrum disorder (ASD). The study they conducted has several strengths worth mentioning that include the population-based nature of their sample, the systematic ascertainment of cases of NE in a well-defined population, the selection of a proper control series, and a comprehensive independent assessment of case status at follow-up.

The authors report a rate of ASDs of 5%, which represents a six-fold increase in the risk of ASDs in newborns with encephalopathy as compared with study controls and with known population estimates from Australia and other countries. Although based on a relatively small sample of cases, the increase in risk was statistically significant and, furthermore, being able to compare their case series to both controls and newborns with NE but without autism, the authors could assess the specificity of risk factors and documented that episodes of antepartum bleeding, trauma, or infection during pregnancy were mediating this risk association.

The findings are important for two reasons. First, they point towards insults occurring during gestation in the fetus as important mechanisms leading to neurodevelopmental disorders, and in particular, to ASDs. This is consistent with previous studies of obstetric and prenatal complications in autism which identified increased rates of adverse events during pregnancy (such as bleeding during the second trimester) and other prenatal events. It is also noteworthy that the environmental risk factors which have been associated thus far to ASDs consist of prenatal exposures to particular teratogens that include thalidomide, valproic acid, or misoprostol. Although these exposures or adverse events might explain only a relatively small proportion of the overall population risk to autism, they are important pointers towards possible biological mechanisms underlying susceptibility to autism and indicate that fetus maldevelopment is a likely pathway to autism, even though the onset of first symptoms as recognized by parents might only occur in the second or third year of life.

Unfortunately, and as discussed by Badawi and colleagues, it is not possible from their study and the present state of knowledge to differentiate in the causal pathways to ASD the respective contribution of genetic factors and of early prenatal environmental insults, and to evaluate their interactions. The findings, however, draw attention to the need for future research to address these issues with appropriate research designs.

Secondly, there are practical implications from this study for clinicians engaged in the clinical follow-ups of children born with encephalopathy. A six-fold increase in the risk of a disorder which has a population-based rate of almost 1% in most recent surveys is significant and calls for pediatricians to implement systematic early detection of early signs of autism in these vulnerable infants. Major advances have been made recently in the field of early detection of signs of autism in infants as young as 8 months old, and simple screening tools now exist for the clinicians to use to detect deficits in pointing, orienting to name, eye gaze, and social responsiveness in toddlers that might prompt an appropriate referral to a more specialized team. The importance of early detection of autistic deviation in the development of young children has been emphasized in the last 15 years as new intensive intervention programs for children with autistic symptoms have shown that the earlier and more intensive the intervention, the better the outcome. The findings of this study, taken together with preliminary reports of a similar increase in the risk of ASDs in children born with very low birthweights, should alert pediatricians to the need to screen systematically toddlers born in difficult circumstances for the emergence of autistic symptoms in the first 3 years of life. As ever, the results from Badawi et al.’s study need replication but they provide useful pointers on prenatal risk mechanisms involved in autism and also draw the attention of practitioners to the immediate need to detect deviant development at an early age in vulnerable infants.

**Eric Fombonne**

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**References**