AFFECTIVE DISORDERS

Baby blues

Pregnancy and the post-partum period are sensitive times for both mother and baby. Two recent papers address different aspects of maternal depression during this period. Noorlander *et al.* show that exposure to antidepressants *in utero* can have long-lasting effects on the offspring's serotonin system, and Maguire and Mody describe a convincing mouse model of post-partum depression (PPD) which suggests that altered sensitivity of GABA (γ-aminobutyric acid) type-A receptors ($GABA_A$Rs) might predispose women to the disorder.

The pregnancy-related surge in sex-hormone levels and their subsequent fall after giving birth are thought to play a part in the aetiology of PPD, but it is unclear why some women develop depression whereas others do not. Sex-hormone derivatives called neurosteroids bind to several receptor types, including $GABA_A$Rs. Maguire and Mody therefore set out to determine whether altered sensitivity of $GABA_A$Rs for neurosteroids might underlie PPD.

They found that, in mice, expression of $GABA_A$R γ-subunits and δ-subunits decreased during pregnancy but quickly returned to pre-pregnancy levels after birth. Similarly, both tonic (mediated by δ-subunit-containing $GABA_A$Rs) and phasic (mediated by γ-subunit-containing $GABA_A$Rs) inhibition of granule cells in the dentate gyrus were reduced during pregnancy and normalized post partum.

To study the possible behavioural effects of changes in $GABA_A$R-mediated inhibition during and after pregnancy, the authors examined mice that lacked the δ-subunit of $GABA_A$Rs (*Gabrd*$^{-/-}$ mice). These mice displayed reduced tonic inhibition of dendate gyrus granule cells (relative to virgin wild-type mice) before and during pregnancy. Furthermore, unlike in wild-type mice, the lower levels of inhibition remained reduced after pregnancy. Post-partum, *Gabrd*$^{-/-}$ mice showed higher levels of depressive-like behaviour and increased anhedonia compared with wild-type and virgin *Gabrd*$^{-/-}$ mice.

Gabrd$^{-/-}$ mice also showed abnormal maternal behaviour in the post-partum period, characterized by impaired nest building and reduced pup gathering. Approximately 40% of pups of *Gabrd*$^{-/-}$ mothers died owing to neglect or cannibalism. The reduced survival rate was not caused by a lack of $GABA_A$R in the pups themselves, as wild-type pups fostered to *Gabrd*$^{-/-}$ mice were also more likely to die. Restoring $GABA_A$R function in *Gabrd*$^{-/-}$ mothers by adding a $GABA_A$R δ-subunit agonist to the drinking water increased the pups' survival rate.

Research into the causes of PPD has so far been hampered by a lack of adequate animal models for the disorder, but these findings suggest that *Gabrd*$^{-/-}$ mice might provide a useful model of PPD, as they show both depressive-like behaviour and abnormal maternal care. Moreover, the data indicate that impaired restoration of $GABA_A$R levels post partum might have a role in the development of PPD.

Women who are prone to PPD or women who are depressed during pregnancy are often advised to take antidepressant medication while pregnant. Noorlander *et al.* examined the effects that this might have on the fetus and found that, in mice, fetal exposure to clinical doses of a selective serotonin-reuptake inhibitor reduced post-natal survival of the pups and, in adulthood, caused decreased serotonin transporter levels in the raphe nucleus and anxiety-like behaviour.

Together these papers highlight not only the importance of developing animal models of depression during and after pregnancy, but also the value of research into the short- and long-term effects of antidepressant medication on offspring.

Leonie Welberg

Rubber Ball

ORIGINAL RESEARCH PAPERS Macguire, J. & Mody, I. $GABA_A$R plasticity during pregnancy: relevance to postpartum depression. *Neuron* **59**, 207–213 (2008) | Noorlander, C. W. *et al.* Modulation of serotonin transporter function during fetal development causes dilated heart cardiomyopathy and lifelong behavioral abnormalities. *PLoS One* **3**, e2782 (2008)