

Neuro-endocrinology

12 BRIEFINGS

THE MATERNAL BRAIN

SUMMARY

A mother's brain is prepared by the hormones of pregnancy to show the strong maternal feelings that ensure the newborn is cared for. These hormones induce a cascade of changes in the brain, reducing stress reactions, evoking maternal behaviour and preparing the neuroendocrine circuits that drive the birth process and ensure that the suckling infant gets milk. The nerve cells that make oxytocin are involved in all of these aspects of motherhood, and details are emerging of how their performance is adapted by pregnancy.

An oxytocin neurone prepared to burst into activity for delivery.

During pregnancy oxytocin neurones store more oxytocin, are restrained from premature activation and made ready to discharge in synchronised bursts.

The brakes are released at term, allowing the stimulated neurones to secrete oxytocin in large pulses, contracting the uterus and expelling the fetus.

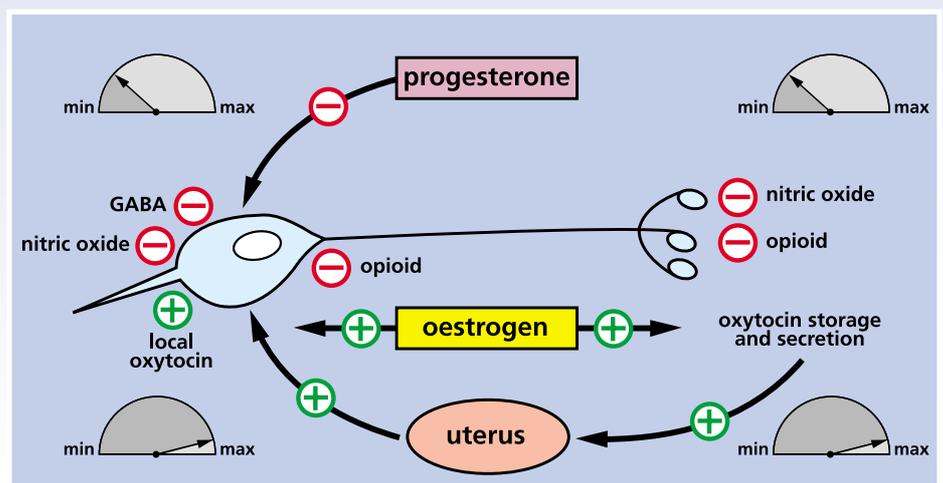
Adaptive circuits

Females of few mammalian species show maternal behaviour unless they have been through pregnancy. This implies 'change' in the pregnant mother's brain, but assuring that maternal behaviour occurs at birth is just one aspect. The brain automatically controls many adaptations to pregnancy, such as increased appetite, expansion of blood volume and deeper breathing. Through the pituitary gland, the brain prevents further ovulations, and the risk of another competing pregnancy, and when the time is right it drives contractions of the uterus to expel the fetus and then stimulates the mammary glands to produce milk. The adaptations in neural circuitry in the mother's brain are prepared by actions of pregnancy hormones. While the neural circuits for birth, maternal behaviour and lactation

are ready for sudden action at term, they must be restrained until birth. So the circuits have powerful inhibitory as well as excitatory controls.

Pregnancy hormones and the brain

The corpus luteum formed from the ovulated follicle in the ovary, and the placenta and fetus, secrete massive amounts of hormones into the mother's circulation. The female sex-steroid hormones, oestrogen and progesterone, are of key importance. Being lipid soluble, they readily enter the brain and act on the many nerve cells bearing oestrogen and progesterone receptors in the 'maternity circuits'. The actions of oestrogens on genes and the direct actions of progesterone on the cell surface of neurones change the balance between inhibition and



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excitation. Other hormones, peptides such as relaxin and lactogen that are only ever secreted in pregnancy, can also act on the brain. The stage of pregnancy is signalled to the brain by the pattern of secretion of hormones; as term approaches the progesterone to oestrogen ratio plummets.

A model maternal neurone

Details of adaptive changes in the brain in pregnancy are emerging from extensive studies of one particular type of neuroendocrine neurone. Oxytocin is a hormone important in labour because it stimulates expulsive uterine contractions. If it is secreted too soon, preterm labour may result, the baby is born immature and may not survive, or suffers brain damage; this remains a major health problem. Oxytocin is secreted into the blood in the posterior pituitary gland from the terminals of neurones that have their cell bodies in the hypothalamus, at the base of the brain.

As the fetal head is pushed through the birth canal the oxytocin neurones are reflexly stimulated to secrete oxytocin in pulses every few minutes. When the newborn suckle at the nipples the oxytocin neurones again secrete in pulses, and without these the young can get no milk since the hormone pulses cause milk ejection. Before breast feeding starts, oxytocin is released within the brain from neural projections to forebrain areas where maternal behaviours are organised. This oxytocin reduces the anxiety of the first exposure to squirming and noisy newborn, encouraging maternal behaviour. This anti-anxiety action of oxytocin may underlie the reduced neuroendocrine responses to stress recently

“oxytocin released in the brain acts on the circuitry for maternal behaviour”

described as a consequence of pregnancy in women and in animals.

Brakes on . . . brakes off

Oxytocin builds up in the posterior pituitary during pregnancy because less is released and more is produced. Oestrogen stimulates the oxytocin gene when progesterone secretion falls, though we do not yet know how the oestrogen receptor expressed in oxytocin neurones regulates this gene. Oxytocin neurones are strongly inhibited by three mechanisms which prevent them from releasing the stored oxytocin prematurely.

First, progesterone, acting through an intermediary, intensifies actions of the inhibitory neurotransmitter GABA on oxytocin neurones . . . **brakes on**. Second, stimulated oxytocin neurones produce nitric oxide, which diffuses from the cells and their terminals, restraining oxytocin cell activation and secretion . . . **more braking**. During pregnancy, oestrogen and progesterone increase neuronal nitric oxide synthase (nNOS) activity and also activate the third mechanism, which uses brain peptides with opiate-like activity. These opioid peptides restrain oxytocin secretion first via receptors in the posterior pituitary and later at the nerve cell bodies . . . **safety stop ?**

The brakes come off . . . when progesterone secretion collapses near term: GABA is less effective and the nNOS gene is turned down. However, the opioid restraint

remains, stopping the oxytocin neurones from running out of control, as excitation now predominates. A boost is given by oxytocin itself, breaking out from the nerve cell dendrites and driving the oxytocin neurones to operate near full power. Finally, oxytocin released in the brain acts on the circuitry for maternal behaviour, sensitised through induction of oxytocin receptors by oestrogen.

Cost/benefit ?

Research on oxytocin neurones, which are essential for successful motherhood, is revealing how the hormonal signals from the fetus, placenta and ovary cause adaptive changes in the maternal brain. These changes benefit the offspring, but there can be costs for the mother, for example the post partum blues and depression in women, the neural mechanisms of which are not yet understood.

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