Birth and beyond:

The far-reaching influence of oxytocin

Although long associated with attachment, reproduction and parental care, the diverse functions of the hormone oxytocin remain relatively obscure. Dr Sue Carter, Director of The Kinsey Institute at Indiana University, has pioneered the use of the prairie vole as a model to study the mechanism of action of oxytocin (and its partner, vasopressin) in human behaviour and development. Her findings may impact not just on how we understand the biology of human social behaviour, but how we impact upon it through the use of labour-suppressing or labour-inducing drugs during childbirth.

Photo credit: Dr Lowell Getz

What on earth could human beings have in common with the prairie vole, a small grassland rodent from central North America? In fact, according to Dr Sue Carter, this diminutive mammal may be one of the closest animal analogues of human social behaviour and may have much to teach us about ourselves.

With a human-like autonomic nervous system (the system responsible for unconscious control of functions such as heart rate, breathing, digestion, and sexual arousal), the prairie vole also forms highly social societies with long-lasting and highly selective pair-bonds and shared parental responsibility. These features, says Dr Carter, make them an ideal model for studying the neurological, physiological, and hormonal mechanisms underlying social behaviour and monogamy.

THE LOVE HORMONE

As in humans, prairie voles are also known to have high levels of the hormone, oxytocin. Oxytocin is a ubiquitous small, but potent, molecule comprising a string of nine amino acids, produced in the hypothalamus, deep at the base of the brain. Oxytocin acts as a neurotransmitter, carrying signals between nerve cells, and Dr Carter describes it as having a "unique and unusually broad profile of biological and behavioural effects." As such, it is involved in regulating the cardiovascular and immune systems, stress responses, mental health and social behaviour. However, it is perhaps best known for its role in childbirth, breastfeeding, cuddling, and orgasm.

According to Carter, writing with colleague and psychophysiologist Professor Stephen Porges – who is also her husband – love is not a hazy social concept but is "deeply biological", originating in the most primitive parts of the brain. A physiological explanation for love is now starting to become apparent, and oxytocin features repeatedly in this story. The chemical is released in response to experiences such as holding a baby, but also in acutely stressful encounters, perhaps to protect the body against overwhelming fear and trauma. Experiments have shown that social behaviours such as eye contact and empathy are strengthened in subjects treated with synthetic oxytocin (e.g., via a nasal spray). In general, says Carter, oxytocin is associated with "immobility without fear." That is, it promotes a state of physiological relaxation that may facilitate processes such as birth, lactation, motherhood and consensual sex.

Dr Carter also believes that oxytocin has been a powerful force in human evolution. By creating strong contractions oxytocin can facilitate birth; thus humans can deliver babies with a large skull, despite the constraints of a fixed pelvis imposed by our upright gait. By permitting the development of a large cortex this hormone has indirectly facilitated the development of complex thought, structured societies, and language. After birth, by supporting breastfeeding and parental (or other caregiver) attachment, oxytocin promotes the emotional health of both mother and child. In other words, says Dr Carter, the birth process accommodates an enlarged nervous system, including the brain, while parental investment supports the elaboration of this nervous system – all under the influence of oxytocin. Further evidence suggests that oxytocin may shield both mother and child from the pain of childbirth, and may help protect against postnatal depression.

MOLECULAR DANCES

However, oxytocin does not act in isolation. In particular, it interacts with a related hormone, vasopressin, and the interplay between these two chemicals is crucial to social relationships. In the prairie vole, Dr Carter found that social interactions between animals could continue in the absence of oxytocin as long as vasopressin was still present. The action of both hormones had to be blocked before an impact on behaviour was observed. The "intricate molecular dances" of oxytocin and vasopressin, says Carter, help to fine-tune social activities such as parental care and protection.

Furthermore, the receptor molecules that allow cells to recognise and respond to oxytocin are themselves regulated by other hormones and 'epigenetic' factors – events that modify the way our genes are expressed without actually changing their DNA sequence. In fact, says Dr Carter, love itself could almost be characterised as an "epigenetic phenomenon." The very presence of oxytocin receptors can be altered by life experiences – either social situations or exposure to biologically active chemicals. This can allow the body to adapt and prepare itself for likely future situations. However, says Carter, epigenetic changes – especially early in life – can also have long-lasting effects on the development of the nervous system and social or emotional behaviours. Humans may be particularly susceptible to such changes because a considerable amount of brain development occurs after birth, during a time when babies are exposed to behavioural and hormonal stimuli emanating from those around them. The nervous system, says Carter, "seems to be especially sensitive to early

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Photo credit: Dr Lowell Getz

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life experiences and these experiences may have life-long consequences."

STARTING AT THE BEGINNING

The obvious time to start exploring these epigenetic changes, then, is at birth. In our modern medicalised society, childbirth is often accompanied by medical interventions which include the administration of artificial oxytocin analogues (mimics) or antagonists (chemicals that block the oxytocin receptor). Dr Carter's current research programme, funded by the US National Institutes of Health, aims to use the prairie vole as a model to explore for the first time, the behavioural, hormonal, nervous and epigenetic consequences of exposure to these chemicals during childbirth.

The synthetic form of oxytocin, known medically as Pitocin, is widely used to stimulate labour (for instance, where babies are overdue according to doctors' calculations) and to prevent maternal haemorrhaging after birth. Conversely, oxytocin antagonists, such as Atosiban, are used to attempt to slow labour down (for instance, where birth has started prematurely). Yet little is known about the impact of these drugs on the infant in the longer-term. Carter's research aims to examine whether these interventions could have long-lasting effects upon the brain and behaviour of the child, and the mechanisms through which such effects could be mediated.

Dr Carter's experiments with the prairie voles have already shown that manipulating oxytocin or vasopressin levels around the time of birth can cause differences in the way individuals are 'programmed' to behave socially. For example, new-born females exposed to small increases in oxytocin showed an enhanced ability to pair-bond, and boosted production of their own oxytocin by the hypothalamus, in later life. However, when given in larger amounts the effects of these same hormones may be negative.

Research in rats suggests that oxytocin released during birth triggers a switch in the brain of the foetus which temporally inhibits nerve cell activity, protecting them from any shortages of oxygen which may occur during birth which might cause lasting damage to the nervous system.

Photo credit: Dr Lowell Getz

The intricate molecular dances of oxytocin and vasopressin help to fine-tune social activities such as parental care and protection.

Administration of oxytocin antagonists before birth prevents this switch from occurring and puts the developing baby's brain at greater risk of damage from hypoxia. This is just one of several reasons Dr Carter believes that such pharmacological treatments should be applied with caution.

Most of the women giving birth in Westernised cultures now receive Pitocin at some stage during or after labour, one in eight babies are born prematurely making them targets for Atosiban, and one in three babies are born by caesarean-section. Thus, oxytocin is manipulated in a large proportion of births. While in many cases the use of such chemical birth interventions saves lives, Dr Carter hopes that her work could be used to optimise their use in order to further improve birth outcomes for mother and child – both in the short and long term.

Behind the Research

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Research Objectives

Dr Carter's research focuses on neuropeptide and steroid hormones, including oxytocin, vasopressin, corticotropin-releasing hormone, and estrogen. Her programme has discovered important developmental functions for oxytocin and vasopressin and implicated these hormones in the regulation of long-lasting neural and effects of early social experiences.

Detail

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Bio

Dr Sue Carter is Director of the Kinsey Institute and Rudy, Professor of Biology at Indiana University. Dr Carter previously held professorships at the University of Illinois and the University of Maryland. Dr Carter is known for her research on the neurobiology of social monogamy and the introduction of the prairie vole as a model for examining the functions of oxytocin and vasopressin.

Funding

NIH

Collaborators

- Stephen W. Porges, a psychophysiologist and originator of the polyvagal theory.
- Lowell Getz, mammologist.
- Diane Witt, graduate student.
- Jessie Williams, postdoctoral fellow.
- Karen Bales, postdoctoral fellow.
- John M. Davis, a psychiatrist and mentor.
- Jessica Connelly, an expert in the epigenetics of oxytocin.

References

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Personal Response

To what extent do you think our behaviour (particularly around relationships and childbirth) is 'programmed' by our genes, to what extent is influenced by external factors, and to what extent do we have control over it?

"We believe that oxytocin has a complex role in brain function, emotional health and throughout the body. Thus, a deeper understanding of the causes and consequences of both physiological and behavioural experiences associated with birth and parenting remains "a major challenge for the medical sciences of the twenty-first century."

What impact do you hope your work will have in future on the way we manage the human birth process?

Knowledge is power. As we have a deeper understanding of the physiology of birth and parenting, I believe we can respect and optimise the highly evolved natural processes that permitted modern humans to exist and to care for their offspring. In the future, a biologically-informed perinatal medicine may help us minimise excessive or harmful interventions, while supporting the health and safety of future generations. It is increasingly clear that motherhood and love are based on the same neurobiology and chemistry that underlies birth. Birth and breastfeeding help to prepare both the child and mother to cope with later stress. Embedded in the knowledge of these processes are secrets that may allow us to be born in joy, successfully manage trauma throughout life and live in peace.