Oxytocin effects in mothers and infants during breastfeeding

Oxytocin integrates the function of several body systems and exerts many effects in mothers and infants during breastfeeding. This article explains the pathways of oxytocin release and reviews how oxytocin can affect behaviour due to its parallel release into the blood circulation and the brain. Oxytocin levels are higher in the infant than in the mother and these levels are affected by mode of birth. The importance of skin-to-skin contact and its association with breastfeeding and mother-infant bonding is discussed.

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Key points

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1. Oxytocin is released in the mother and infant during breastfeeding and skin-to-skin contact.
2. Milk ejection patterns vary between women.
3. Oxytocin is released into circulating blood and brain structures, in parallel.
4. Oxytocin levels are higher in the infant than in the mother and differ with mode of birth.

Oxytocin – a system activator

Oxytocin, a small peptide of just nine amino acids, is normally associated with labour and the milk ejection reflex. However, oxytocin is not only a hormone but also a neurotransmitter and a paracrine substance in the brain[1,2]. During breastfeeding it is released into the brain of both mother and infant where it induces a great variety of functional responses.

Through three different release pathways (**FIGURE 1**), oxytocin functions rather like a system activator and often influences the release of other signalling substances such as opioids, serotonin, dopamine and noradrenaline. Through these activations, different behavioural and physiological effects are facilitated and coordinated into adaptive patterns, which are influenced by the type of stimuli and environmental factors[3].

Through the endogenous release of oxytocin or its administration, for example by nasal spray in humans, various types of socially interactive behaviours can be stimulated. These include maternal and sexual behaviours as well as the development of bonding and attachment[4]. Oxytocin stimulates well-being, it induces anti-stress effects, decreases sensitivity to pain, decreases inflammation and stimulates processes related to growth and healing. In addition, repeated exposure to oxytocin may give rise to long-term effects by influencing the production or function of other signalling systems. For example, noradrenergic activity in the brain may decrease as a consequence of the increased function of inhibitory alpha-2 adrenoceptors[3].

The regulation of the release of oxytocin is complex and can be affected by different types of sensory inputs, by hormones such as oestrogen and even by the oxytocin molecule itself. This article will focus on four major sensory input nervous pathways (**FIGURES 2 and 3**) activated by:

1. Sucking of the mother's nipple, in which the sensory nerves originate in the breast.
2. Sucking in the infant, in which the sensory nerves originate in the infant oral mucosa.
3. The presence of food in the gastrointestinal tract, affecting vagal sensory nerves.
4. Skin-to-skin contact in both mothers and infants, in which the sensory nerves that originate in the skin respond to warmth, touch, stroking and light pressure.

The mother

Milk ejection

Oxytocin is critical for milk removal in, perhaps, its most renowned role: the milk ejection reflex. Following sucking, the release of oxytocin causes the contraction of myoepithelial cells in the breast pushing milk from the alveoli, through the milk ducts and toward the nipple.

In general, it takes around a minute of infant sucking or stimulation with a breast pump before milk ejection occurs[5,6]. Interestingly, the milk ejection reflex can be

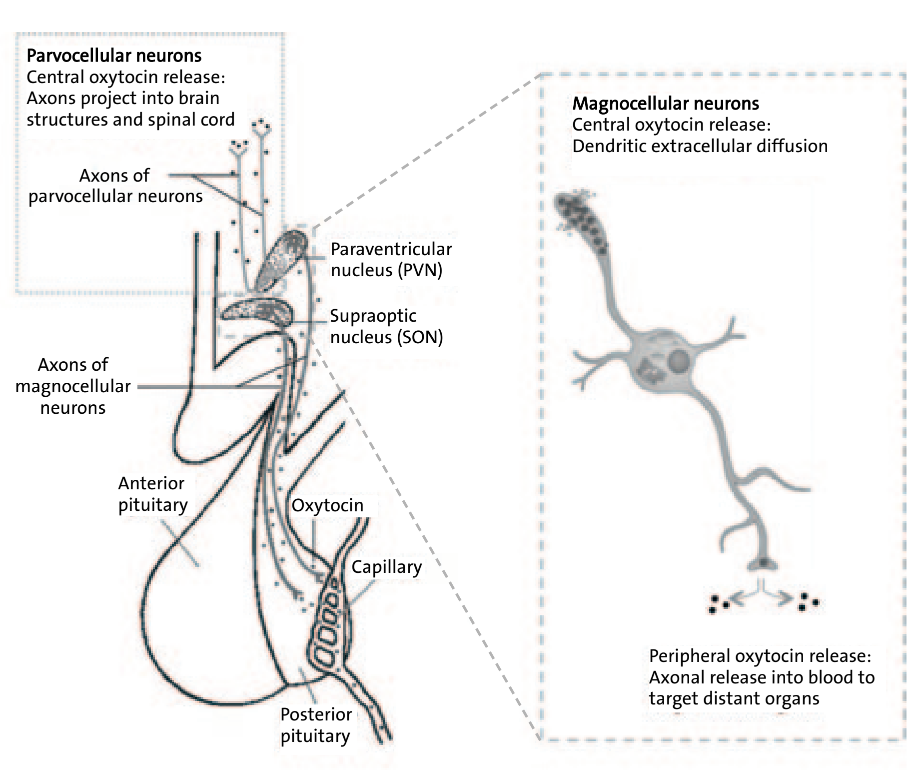


FIGURE 1 The release of oxytocin from the supraoptic (SON) and paraventricular (PVN) nuclei of the hypothalamus. Magnocellular neurons in the SON and PVN release oxytocin centrally and peripherally from the posterior pituitary, resulting in effects that include milk ejection and uterine contraction. Parvocellular neurons, located in the PVN, project axons directly into brain structures involved in the regulation of social interaction, anxiety, the activity of the hypothalamic-pituitary-adrenal axis, well-being and the autonomic nervous system (eg the amygdala, hypothalamus, anterior pituitary, nucleus accumbens, nucleus tractus solitarius and the dorsal vagal motor nucleus).

easily conditioned and many women can experience spontaneous milk ejections between feeds[7,8] as the sight, thought, sound and smell of the infant (or even a breast pump in pump-dependent mothers) can cause milk ejection and dripping of milk from the nipples. Indeed, it is common that milk ejection occurs prior to the physical attachment of the infant or a breast pump[7,9].

Milk ejection can be associated with different sensations that vary dramatically between women. These may be localised to the breast such as a 'drawing' pain or tingling, to more systemic sensations such as nausea, thirst, fainting or even mental anxiety and depression[8].

Sucking- and pumping-induced oxytocin release has been described as pulsatile[7,10]. On average, oxytocin pulses occur with 90-second intervals over the first 10 minutes of breastfeeding in the first few days after birth[11,12]. The amount of oxytocin that is released within a 10 minute breastfeed is much higher at four months when compared to four days after birth, but there is still a strong correlation between the amount of oxytocin released on the two occasions within individual women[13].

One pulse of oxytocin is generally associated with one milk ejection and there is a relationship between the amount of oxytocin released and the number of oxytocin pulses during the first 10 minutes of breastfeeding[12]. The number of milk ejections during breastfeeding ranges from one to 17 over a period of up to 25 minutes[6,7]. Similarly, pulsatile patterns of two to 14 milk ejections are seen during a 15 minute breast expression[5]. The similarity between the milk ejection pattern resulting from breastfeeding and breast pumping is demonstrated in **FIGURE 4**.

Tracking an individual mother over time, it appears that her pattern of milk ejection repeats throughout the first nine months of lactation[5]. If a mother has two or three milk ejections she will continue that pattern, removing all her milk in these brief episodes. Other mothers may follow a more constant pulsing profile in that they have continuous milk ejections throughout the milk removal session. Both of these patterns can remove similar volumes of milk successfully, but the second scenario would require more time to reach that same level of milk removal[5]. Similar repeatability has been observed in individual infants at successive breastfeeds[14]; these mother-derived patterns may explain why some infants are quick feeders and others take a bit more time.

Oxytocin-induced effects in the brain

It is not known why mothers have such varied milk ejection patterns but, since oxytocin is involved in so many functions, these release patterns may not only impact on milk removal. Systemic oxytocin release and its release into the brain may result in many other outcomes involving breastfeeding and mother-infant interactions. For example, breastfeeding in mothers is associated with physiological and psychological adaptations including:

- Increased social interaction
- Decreased anxiety
- Decreased cortisol levels
- Decreased blood pressure
- Increased gastrointestinal tract function[15-17].

These effects are exerted in the brain but are associated with circulating oxytocin levels, supporting the concept that oxytocin is released systemically and into the brain in parallel, as has previously been demonstrated in sheep in response to suckling[18].

The infant

Infants produce oxytocin too and in fact, the production of oxytocin begins in the fetus. An understanding of the infant oxytocin system is complicated by difficulties in collecting repeat blood samples and measuring circulating oxytocin levels in the newborn. Nevertheless, some studies exist in which oxytocin levels have been measured in the newborn while other studies have demonstrated the release of oxytocin indirectly via expression of oxytocin-linked effect patterns. Information can also be drawn from animal experiments, as oxytocin exerts similar effect patterns in all mammals.

Infant oxytocin levels are affected by the mode of delivery

In infants born by vaginal delivery, oxytocin levels in umbilical arterial blood were actually higher than in infants born by caesarean section: 69pg/mL (range 20-315pg/mL) vs 33pg/mL (range 9-195pg/mL), respectively. Mothers also had higher oxytocin levels if they delivered vaginally, compared to caesarean section. In the first 30 minutes after birth, infants (born both vaginally and by caesarean) had higher oxytocin levels than those of mothers: approximately 30pg/mL (range 13-158pg/mL). Over subsequent hours and days the differences due to mode of birth diminish, yet infants will maintain a higher oxytocin level than their mothers (**FIGURE 5**). In addition, oxytocin levels recorded postpartum in infants born vaginally correlate inversely with fetal arterial pH and also with the duration of labour. This suggests that the elevated oxytocin levels recorded postpartum are linked to the stress of being born (Bystrova et al 2013, unpublished results)[19].

Ingestion of oxytocin from maternal milk

Human milk contains many different hormones and growth factors and it also contains small amounts of oxytocin. The concentration of oxytocin in maternal milk is approximately 8pg/mL in the first few days after birth and then decreases with increased milk production. Even if the ingested oxytocin was able to survive the acid milieu of the stomach and was absorbed from the small intestine of the fetus, the dilution within the circulation would limit any significant rise of oxytocin levels. It would also be unlikely that transport to the brain would occur because of the blood-brain-barrier.

Oxytocin release by sucking

While the intake of oxytocin from human milk has negligible effects, sucking in newborns is associated with infant oxytocin release. In calves, the act of sucking at the udder is associated with a rise in oxytocin levels but not when drinking/lapping milk from a bucket[20]. This effect is caused by activation of sensory nerves in the oral mucosa during sucking. Furthermore, oxytocin is released when milk reaches the gastrointestinal tract (**FIGURE 3**). Food intake is linked to release of the gut hormone cholecystokinin (CCK) which, via activation of the afferent (sensory) vagal nerve fibres, triggers oxytocin release[21]. In support of this, infant plasma levels of CCK have been shown to rise during breastfeeding[22].

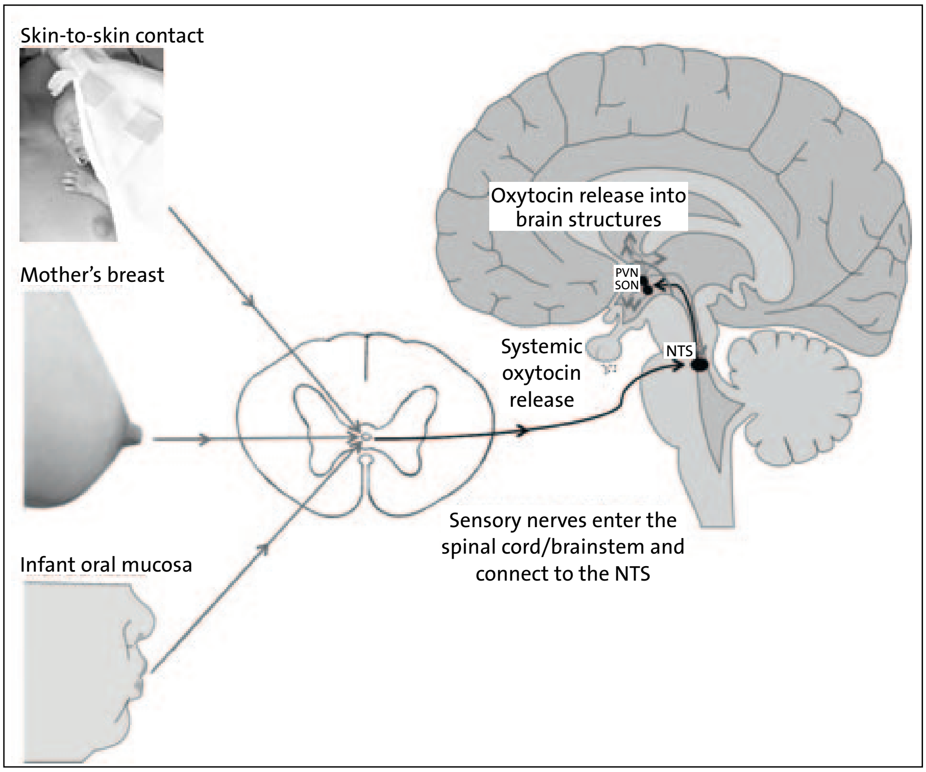


FIGURE 2 Different kinds of sensory nerves can release oxytocin during mother-infant interaction. While various sensory nerves can initiate this pathway, the nucleus tractus solitarius (NTS) acts as a common relay station for sensory input to the oxytocin-producing paraventricular (PVN) and supraoptic (SON) nuclei. (Image © Medela.)

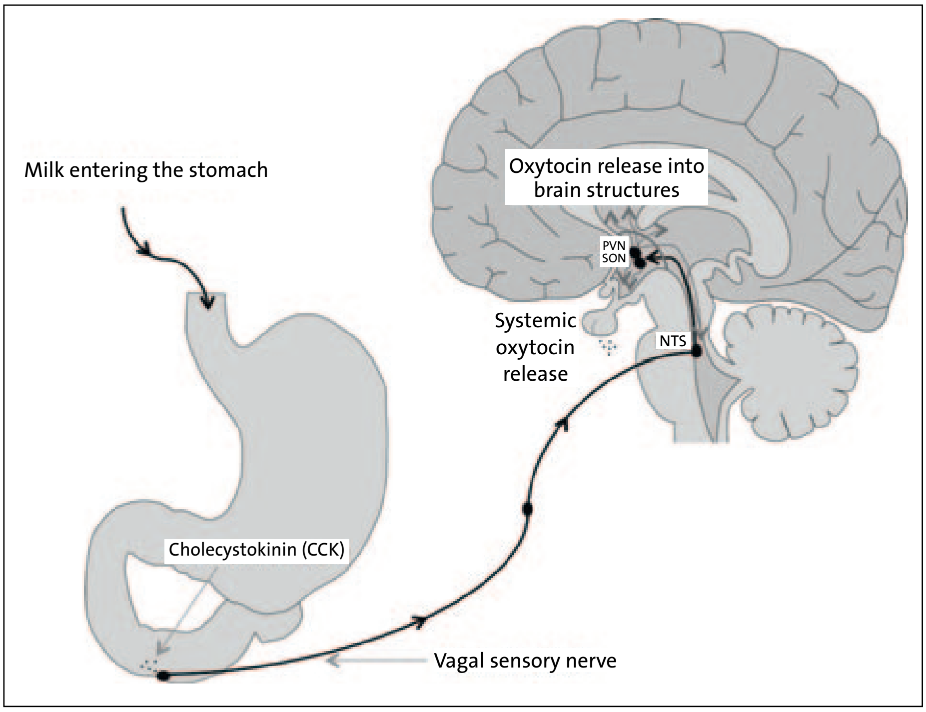


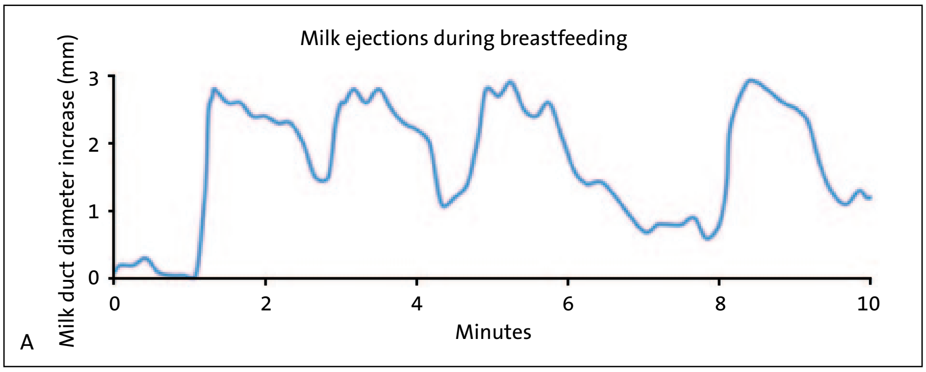
FIGURE 3 The ingestion of food into the infant's stomach can trigger oxytocin release. Food intake results in the release of the gut hormone cholecystokinin (CCK), which, via activation of sensory vagal nerve fibres, results in central and peripheral oxytocin release. (Image © Medela.)

The mother and infant

Skin-to-skin contact

Oxytocin can be released by activation of several types of sensory nerves originating from the skin, nipples, gastrointestinal tract and urogenital tract. Light pressure, warmth and stroking contribute to oxytocin release caused by 'pleasant' or 'non-noxious' sensory stimulation of the skin[23].

When newborn infants are put on their



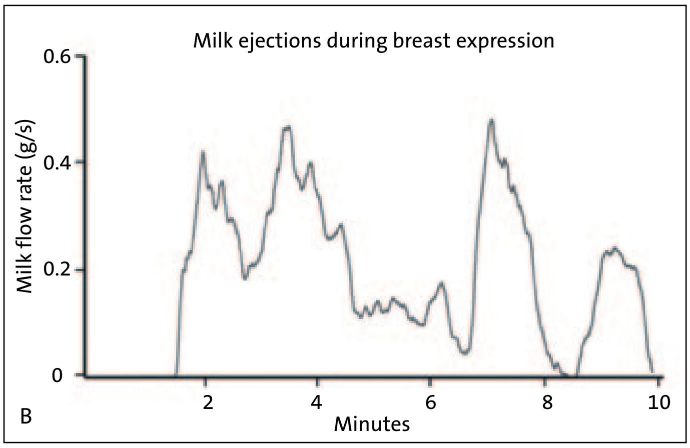


FIGURE 4 Examples of the pulsatile patterns of milk ejection during breastfeeding and breast expression. Graph A demonstrates four pulses measured during a breastfeed by monitoring the size of the milk duct with ultrasound; as milk is ejected through the ductal system the milk duct diameter expands (image courtesy of Dr Donna Geddes, Australia). Graph B demonstrates four pulses measured during breast expression by monitoring the rate of flow of milk; as milk is ejected through the ductal system the milk flow rate increases.

mother's chest immediately after birth, oxytocin is released into the maternal circulation (**FIGURE 2**). The effect is, in part, linked to massage of the breasts by the infant[24]. However, the oxytocin release that is induced by skin-to-skin contact does not occur in short pulses in the same way as oxytocin induced by sucking, but rather in a few protracted pulses. It is not associated with milk ejection, but may instead 'prime' the ensuing breastfeeding interaction.

It has not yet been demonstrated that peripheral oxytocin levels rise in response to skin-to-skin contact in human newborns. Even if circulating oxytocin levels do not rise, it may be assumed that oxytocin levels increase in the infant brain in response to these types of stimuli. In the following sections a number of effect patterns, both short- and long-term will be described. These can be attributed to oxytocin release and/or function in the brain and are triggered in both the mother and the infant during breastfeeding and skin-to-skin contact.

Social interaction, well-being and stress levels

When the mother and the newborn infant are placed in skin-to-skin contact after birth, the infant expresses an inborn breast-seeking behaviour – a 'social approach behaviour'[25]. Both mother and infant become more socially interactive and synchronise their interactions[26]. Mother and infant become calmer, the infant cries less, the pain threshold increases, cortisol levels decrease and skin temperature of the mother's breast and of the infant increases[27,28]. As discussed below, these effects are likely to involve oxytocin release in the brain.

Oxytocin and inhibition of stress

It is well known that cortisol release is controlled by the hypothalamic-pituitary-adrenal (HPA) axis. In this mechanism of interactions, corticotrophin releasing factor (CRF) released from the hypothalamus, stimulates the release of adrenocorticotrophic hormone (ACTH) from the anterior pituitary, which in turn releases cortisol into the circulation from the adrenal cortex. Oxytocin can inhibit the function of the HPA axis at each of these levels[29].

What is not well-known is that noradrenergic neurons originating in the locus coeruleus (LC) and the nucleus tractus solitarius (NTS) in the brainstem, exert a powerful influence on the activity of the HPA axis by stimulating production of CRF in the hypothalamus and activity in the sympathetic nervous system. Oxytocin may decrease stress levels by counteracting the activity in these noradrenergic pathways: administration of oxytocin or the release of oxytocin from oxytocinergic nerves that terminate in the LC and the NTS, increases the number or function of inhibitory alpha-2 adrenoceptors located on the noradrenergic neurons[30,31].

This type of oxytocin-linked, anti-stress pattern is facilitated in certain situations, for example, when the skin is exposed to touch, warmth and light pressure, which explains why mothers and newborn infants experiencing skin-to-skin contact exhibit a marked anti-stress pattern. The high levels of oxytocin seen in both mothers and infants after vaginal birth (**FIGURE 5**) may play an important role.

Bonding and attachment

The act of sucking may also enhance bonding between mothers and newborn infants and the infant's attachment to their mother. In support of this, newborn lambs that are allowed to suck at the udder soon after birth recognise and follow their mothers more quickly than those that are separated from their mothers in the early days after birth[32]. It seems that neural reflexes induced from the oral mucosa by the touching of the nipple (**FIGURE 2**) and also the presence of colostrum in the gastrointestinal tract are involved in the creation of this primitive 'attachment' behaviour (**FIGURE 3**).

Long-term effects

Research has shown that mothers who have breastfed for several weeks have lower basal, systolic and diastolic blood pressure and also lower stress reactivity. This supports the existence of a long-term, anti-stress influence of oxytocin in humans. The finding of a reduced risk for certain kinds of cardiovascular disease and type 2 diabetes in mothers who have breastfed, is further support of the connection between repeated exposure to endogenous oxytocin and long-term, anti-stress effects[33].

The act of skin-to-skin contact between mother and infant during the first two hours after birth has been associated with long-term outcomes. These include enhanced interaction between mother and infant and a better ability to handle stress

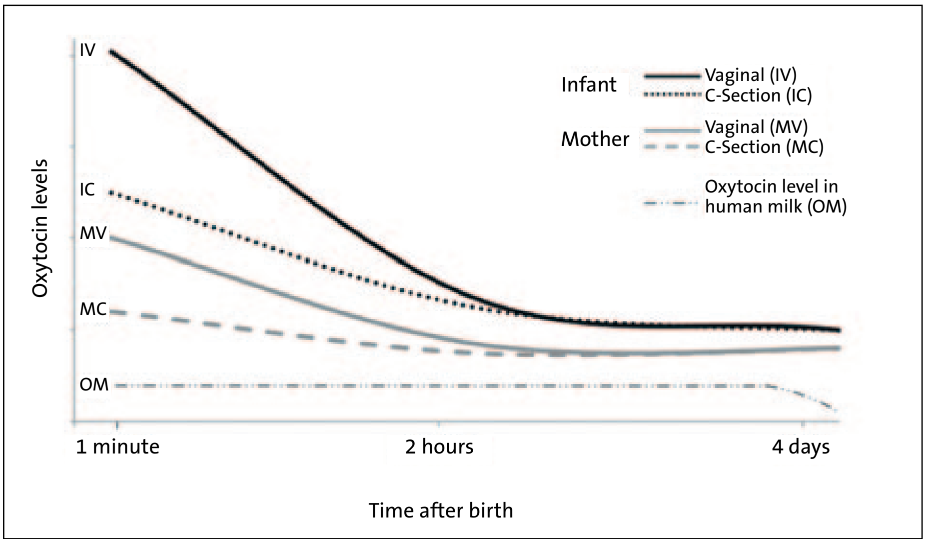


FIGURE 5 The relative levels of blood oxytocin in the mother and infant in relation to the mode of birth. The graph shows that infants have much higher oxytocin levels than mothers. In both mother and infant it is shown that one minute after birth oxytocin levels are much higher in mothers and infants that have delivered/been born vaginally compared to those who were delivered/born via caesarean section. The magnitude of this difference decreases with time such that the levels of oxytocin are similar between birth modes from approximately two hours after birth. Also indicated is the very low level of oxytocin in the mother's milk, which further decreases as milk production increases.

in the infant – effects which may be measured as long as one year after birth[34,35].

As an example of a mechanism behind these long-term effects, decreased levels of anxiety and increased social interaction seen in rats exposed to extra sensory stimulation after birth has been attributed to an increased production/function of oxytocin receptors in the amygdala. The anti-stress effects have been attributed to a decreased function of the HPA axis[36].

Medical interventions during birth

It can be concluded that oxytocin stimulates socially interactive behaviour and induces anti-stress effects and that these effects may become long lasting if induced early in life. Many medical interventions during birth interfere with spontaneous oxytocin release. For example:

- Caesarean section may be linked to a reduced oxytocin release during labour (or none at all if there is no labour)
- Epidural analgesia may be linked to reduced oxytocin release as the Ferguson reflex is partly blocked
- Infusions of oxytocin may influence spontaneous oxytocin release via a feed-back inhibitory mechanism.

Recent data suggest that such effects can be documented at two days after birth[11,37].

Development of secure attachment

Oxytocin release is easily conditioned and, after a while, its release and the consequent oxytocin-related effects will be triggered in the infant by just the sight, voice or smell of the mother. With time, the infant may learn to hold the 'image' of its mother even when she is not present and in this way the infant may remain calm and happy even when alone. Only when the infant becomes fearful does it need to return to the secure base, or in physiological terms, receive activation of sensory nerves from the skin, when being held close by the mother (or another caregiver) to become happy and calm again. In the long-term, the function of the oxytocin system may become well established in those infants receiving closeness and friendly encounters by primary caregivers: a chronic state of satisfaction and calm develops – secure attachment.

Conclusion

Oxytocin is an integral component of many body systems with long-term implications for both mother and baby. It is not only involved in milk ejection from the mother, but is also a key hormone for the infant and can be influenced by skin-to-skin contact and birthing practices. Consolidation of current understanding of oxytocin should encourage consideration of the value of the natural interaction between mother and infant, at and after birth.

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