Oxytocin, a Mediator of Anti-stress, Well-being, Social Interaction, Growth and Healing

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Abstract

The neuroendocrine and physiological systems related to pain and stress have long been subjected to study. More recently, the corresponding systems promoting anti-stress and restoration have also come into focus. It is not only important to investigate the mechanisms underlying disease but also to examine the physiological and psychological mechanisms which protect and heal the body and soul.

The nonapeptide oxytocin, originally known to stimulate labour and milk ejection, appears to play an important role in this regard. Oxytocin can induce anti-stress-like effects such as reduction of blood pressure and cortisol levels. It increases pain thresholds, exerts an anxiolytic-like effect and stimulates various types of positive social interaction. In addition, it promotes growth and healing.

Repeated exposure to oxytocin causes long-lasting effects by influencing the activity of other transmitter systems, a pattern which makes oxytocin potentially clinically relevant.

Oxytocin can be released by various types of non-noxious sensory stimulation, for example by touch and warmth. Ingestion of food triggers oxytocin release by activation of vagal afferents. Most likely, oxytocin can also be released by stimulation of other senses such as olfaction, as well as by certain types of sound and light. In addition, purely psychological mechanisms may trigger the release of oxytocin. This means that positive interaction involving touch and psychological support may be health-promoting. The social interaction of daily life, as well as a positive environment, continuously activate this system. In addition, various types of psychotherapy involving transfer of support, warmth and empathy are likely to induce similar effects, which thus contribute to the positive effects of these kinds of therapies.

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Key words

Oxytocin – Anti-Stress – Well-Being – Social Interaction

Oxytocin

Oxytocinergic neurons in the hypothalamic paraventricular (PVN) and the supraoptical nuclei (SON) reach the neurohypophysis whence oxytocin is released into the circulation.

In addition, paraventricular oxytocinergic neurons project to several areas within the central nervous system (CNS), such as the olfactory bulb, the frontal cortex, the amygdala, the locus coeruleus (LC), the hippocampus, the periaqueductal grey (PAG), the raphe nuclei, the striatum, the vagal nuclei (DMX and NTS), and the spinal cord [1]. Different effect spectras are induced when oxytocin is released simultaneously in various areas of the brain. So far, only one oxytocin receptor has been demonstrated, the uterine type of oxytocin receptor, and this receptor has been found also in the CNS [2]. It is likely that there are other oxytocin receptors or subtypes since some fragments of the oxytocin molecule can induce different oxytocin-like effects. In further support of the existence of multiple oxytocin receptors, is the fact that some of the effects of oxytocin induced in the CNS are not possible to prevent by an oxytocin antagonist [3].

The oxytocinergic nervous system is equally developed in males and females, although it is under strong influence by the female steroid hormones [3, 4]. Estrogens stimulate synthesis and release of oxytocin and increases the number of oxytocin receptors in some areas of the brain [4, 5, 6]. For example, the estrogen β-receptor mediates oxytocin release, and recently it was shown that the estrogen induced increase in oxytocin receptors within the amygdala is mediated through the estrogen α-receptor [7, 8, 9]. Thus there is a strong connection between estrogens and oxytocin, which leads to sex differences with regard to some of the effects of oxytocin.

The enervation of the PVN is complex and the release of oxytocin is for example stimulated by acetylcholine [10], noradrenaline (α-1-adrenoreceptors) [11], dopamine (D2-D3 receptors) [12, 13], serotonine (5-HT1a receptors) [14], vasoactive intestinal polypeptide (VIP) [15] and cholecystokinin-8 (CCK-8) [16]. Interestingly, oxytocin itself stimulates its own release [17]. This kind of positive feed-back is unusual, and a possible explanation behind this effect might be an oxytocin-mediated reduction of GABAergic inhibition of the release of oxytocin [18]. Furthermore, oxytocin autoreceptors have been detected on some of the oxytocinergic neurons [19]. Strong stimuli of oxytocin release, for example exerted by suckling, parturition, and osmotic stimuli, induces a very specific firing pattern of the magnocellular neurons in both the PVN and the SON. The numbers of synapses increase and the glial coverage

decreases so that both the somatic and the dendritic surfaces of the oxytocinergic neurons become juxtaposed which allows interaction and synchronisation of the neurons. In connection with these changes, all the neurons start to burst in synchrony, causing a pulsatile release of oxytocin into the circulation [20]. Whether these changes occur also in the parvocellular oxytocinergic neurons are not known.

Opioids [21], GABA [22] and the c-terminal oxytocin fragment [own unpublished observation] inhibit the release of oxytocin.

Acute effects of oxytocin

Besides the classical endocrine effects on uterine contraction and milk ejection, oxytocin causes a wide spectrum of behavioural and physiological effects mediated through receptors within the brain. Maternal, sexual, social behaviours as well as the bonding between parent and infant and pair bonding among monogamous mammals are all stimulated by oxytocin [23, 24, 25, 26]. Administration of oxytocin can induce both anxiolytic-like effects and, in higher doses, sedative effects [27, 28]. The anxiolytic-like effect seems to be mediated within the amygdala, which is richly provided with oxytocin receptors [29]. The amygdala is also of great importance for social recognition, especially by olfactory stimuli. In support of this, oxytocin knockout mice have social amnesia, which can be restored when oxytocin is applied into the amygdala. [30, 31]. Both the anxiolytic-like effect and the effect on social recognition are important aspects of the ability of oxytocin to increase social interaction.

Oxytocin increases nociceptive thresholds through an enhancement of enodogenous opioids. This effect has been linked to the PAG and the dorsal horn of the spinal cord [32, 33, 34]. Besides these effects, oxytocin induces several anti-stresses like effects; for example heart rate, blood pressure and the levels of stress hormones decrease and simultaneously the activity within the gastrointestinal tract and the endocrine pancreas increases. These effects of oxytocin are probably mediated through the hypothalamus and the vagal nuclei (DMX and NTS) [25, 35, 36, 37, 38]. However, oxytocin acts also directly in the pancreas and the adipose tissue, where it influences insulin and glucagon secretion and stimulates lipogenesis [36, 39, 40].

Systemic administration of oxytocin in rats induces an acute anti-inflammatory effect, and in vitro, oxytocin can induce antioxidative effects [41, 42]. Moreover, oxytocin stimulates proliferation of several cell types such as osteoblasts, pituitary cells and blastocysts [43, 44, 45].

Long-term effects of oxytocin

Oxytocin (1 mg/kg s.c. or 1 μg/kg i.c.v. indicating that the effects are mediated within the CNS) administered once a day for 5 days in rats decreases blood pressure for more than 1 week or as long as 3 weeks after the last oxytocin injection, in males and females, respectively (the more long-lasting effect in females is probably caused by the female steroid hormones [3, 46, 47]. Besides the reduction of blood pressure, this treatment increases nociceptive thresholds [48], decreases the levels of corticosterone (corresponding to cortisol in humans) [49], improves the ability to learn [50], and changes spontaneous motor activity, for more than 10 days after the last oxytocin injection [3, 50]. Oxytocin also acts as an antidepressant in animal models of depression [51]. In addition, oxytocin treatment increases the activity within the gastrointestinal tract and some slowly growing strains of female rats grow faster without an increase in food intake [52, 53]. Plasma levels of thyroid hormones are decreased compared to controls [54], while wound healing is increased and the levels of several growth hormones, such as insulin-like growth factor-I (IGF-1) and nerve growth factor (NGF), are increased [55, 56].

Oxytocin treatment during the neonatal period induces life-long effects of the same type as these described above. Thus, rat pups which are treated with oxytocin postnatally have lower blood pressure and corticosterone levels, increased nociceptive thresholds and increased weight in adulthood. These effects, in response to oxytocin, are even more pronounced when the animals have been exposed to prenatal stress [57, 58, 59]. The postnatal oxytocin treatment may also influence the offspring of the postnatally oxytocin treated rats, since female rats which have been treated with oxytocin postnatally have larger placentas and foetuses [60].

In summary, repeated administration of oxytocin induces an anti-stress like pattern through a decreased activity in the hypothalamo-pituitary-adrenal (HPA) axis and the sympathetic nervous system. Additionally, oxytocin induces calmness and increases nociceptive thresholds. Simultaneously, anabolism, healing and growth are promoted, for example through an increase in parasympathetic vagal nerve activity. By this way, energy is used for anabolism and growth instead of energy expenditure, which occurs, for instance, during motor activity.

Oxytocin interacts with other neurotransmitters

The long-lasting effects in response to oxytocin treatment is probably induced through secondary mechanisms, since oxytocin seems to change the activity in other transmitter

systems. The long-lasting increase in nociceptive thresholds appears to be related to an increased activity within the endogenous opioid system [48], and many of the anti-stress like effects seem to be induced through an increase in CNS α-2-adrenoreceptor function. When rats are pre-treated with oxytocin, only half as much of the α-2-adrenoreceptor agonist clonidine is required to reduce the firing of the noradrenergic LC neurons by 50% (measured by single-cell recording techniques) [61]. At the same time, the reduction of blood pressure and the sedative effect of clonidine are potentiated in oxytocin treated animals [3]. In rats treated with oxytocin, an increased number of α 2-adrenoreceptors have been demonstrated by autoradiography in for example the hypothalamus, the amygdala and the nucleus of the solitary tract [62].

As mentioned above, oxytocin decreases plasma corticosterone levels, and oxytocin influences HPA-axis activity through effects at several levels of the HPA-axis. For example, the amount of mineralocorticoid mRNA as well as the amount of glucocorticoid mRNA are changed in the hippocampus of oxytocin-treated rats [63]. A possible explanation to these central changes might be an increased activity of α-2-adrenoreceptors which in turn influences the HPA-axis at several levels. In addition, activation of α-2-adrenoreceptors decreases the activity of the sympathetic nervous system [64].

Oxytocin also induces changes in the function of the serotoninergic (5-HT) system. Rats treated with oxytocin have an increased synthesis of 5-HT in the frontal cortex as well as increased levels of 5-HT in the brain stem (own unpublished observation). Besides the mechanisms described above, oxytocin may induce long-lasting changes of the cholinergic transmission as well as other signalling mechanisms [37, 65, 66] (fig. 1). The duration of the long-term effects of oxytocin seems to be age dependent since rats treated with oxytocin postnatally have changed α-2-adrenoreceptor function in several brain areas as adults [67].

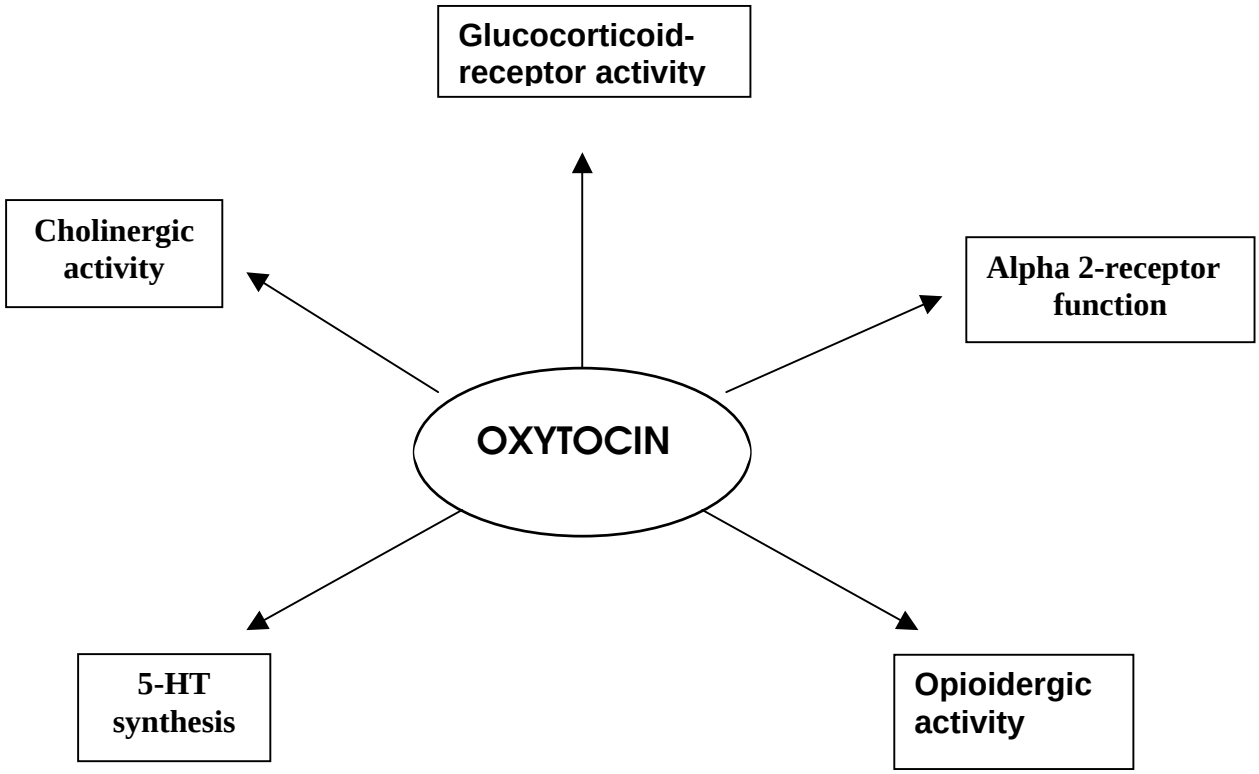

Figure 1: Mechanisms by which oxytocin influences the activity of other transmitter systems within the central nervous system to induce long-term effects.

Non-noxious sensory stimulation releases oxytocin and induces oxytocin-like effects

Labour and lactation, or suckling, are followed by a release of oxytocin into the circulation and into the brain. Elevated levels of oxytocin have been found in the cerebrospinal fluid (CSF) and in more specific parts of the brain, such as the amygdala and the spinal cord. This means that oxytocin, in parallel to being released in the circulation, can be released in those parts of the brain that are reached by oxytocin containing nerves. Other types of sensory stimulation, such as sucking, food intake, warmth, touch, light pressure, massage-like stroking and sexual stimulation elevate oxytocin levels in the circulation as well as in the CSF [34, 68, 69, 70].

Feeding and sucking does not only give rise to oxytocin release but also to an anti-stress pattern which is similar to that caused by oxytocin. It has been shown that oxytocin is released after sucking, feeding, and after administration of the gastrointestinal hormone cholecystokinin (CCK). CCK induces oxytocin release via activation of vagal afferents; thereby some of the effects which follow after food intake may be secondary to the release of oxytocin [16].

Regarding touch, both thick A-β-fibres and a subpopulation of more slowly conducting C fibres, which are activated by low intensity stimulation, may be involved in the release of oxytocin. Activation of these fibres have been demonstrated to induce changes in the insular cortex, a part of the brain, which is related to emotions and interpretation of tactile stimuli [71, 72]. In addition, the front side of the chest, the abdomen and the urogenital organs are provided with a specific type of vagal innervation. These fibres do not enter the spinal cord, but project directly to the nodose ganglion and the NTS [73, 74]. The NTS is linked to the PVN via noradrenergic fibres which may mediate oxytocin release (fig. 2).

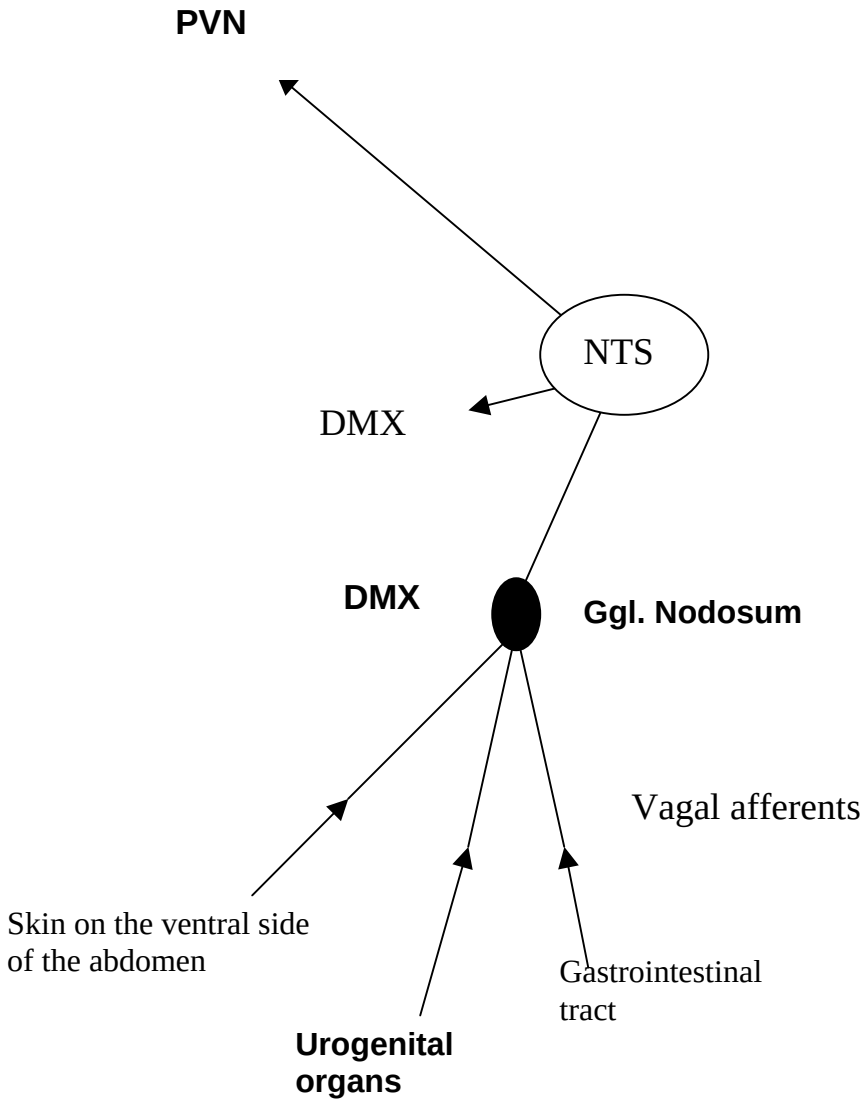

Figure 2: A schematic illustration of the projection of vagal afferents to the nucleus of the solitary tract (NTS) and from thereon to the paraventricular nucleus (PVN) from which oxytocin is released in response to stimulation of these sensory nerves.

When we discuss the effects of touch below, it is not the experience of the cortically registered sensation of touch which is in focus, but rather the effects of touch on emotions and the autonomic nervous system residing in deeper limbic areas of the brain. In support of this, non-noxious sensory stimulation such as touch or low intensity electrical stimulation of somatosensory afferents in anaesthetized rats gives rise to a physiological anti-stress pattern which is similar to that induced by suckling and breastfeeding [75-83]. If conscious rats, males or females, are stroked on the front side (40/min) oxytocin levels rise and an oxytocin-like effect spectrum is induced. Pulse and blood pressure decrease, the levels of gastrointestinal hormones increase, nociceptive thresholds increase and the animals get calmer. Oxytocin antagonists antagonise some of these effects, for example the effect on nociceptive thresholds [84, 85, 86]. Repeated treatment with this kind of massage-like stroking does, like repeated treatment with oxytocin, give rise to long-lasting effects of the same type as those induced by acute stimuli. The animals also increase more in weight, in particular if they have been stressed. They become more interactive and their ability to learn is ameliorated (in a test for conditioned avoidance) [Lund et al. to be published]. Obviously, the animals treated with the massage-like stroking exhibit an effect pattern which is similar to that induced by oxytocin injections. This similarity together with the fact that oxytocin is released by the treatment and that oxytocin antagonists block several of the massage induced effects, for example the increased nociceptive thresholds, indicate that oxytocin is an important mediator of the effects induced by massage-like stroking. It is possible that repeated release of endogenous oxytocin gives rise to effects that are similar to those induced by repeated administration of exogenous oxytocin, for example secondary changes in the activity of other transmitter systems such as an increased activity in the α-2-adrenoreceptor function. Addition of extra sensory stimulation in the neonatal period is followed by a more rapid growth and also to the fact that the animals become calmer and have a reduced activity within the HPA-axis as adults. In addition, their blood pressure is lower. This treatment has been shown to be followed by an increased activity in α-2-adrenoreceptor function in adult rats [67, 87, 88, 89]. It is possible that some of these postnatal effects are in part indirectly mediated by oxytocin release.

Oxytocin release can also be induced by odours, sound and light. Oxytocin treated animals release an odour which elevates nociceptive thresholds and counteracts stress in animals kept in the same cage. In addition, endogenous oxytocin is released in the animals reached by the olfactory stimuli. The olfactorily induced effects can be antagonized by an oxytocin antagonist and also by local anaesthesia of the nasal mucosa. This data indicate that the

effects are mediated by oxytocin also in the recipient animals [90, 91]. An odour with calming properties which induces social behaviour has been isolated from lactating dogs [92].
Another important fact is that oxytocin release can be conditioned to other stimuli such as sound, odours and people [93]. Even thoughts, associations and memories can, most likely, induce a release of oxytocin.

Oxytocin, closeness and breastfeeding

Newborn babies are placed skin to skin on their mothers' chest immediately after birth. If the babies' spontaneous activity is not interfered with, they start to breastfeed within one to two hours [94]. Before suckling, they massage their mothers' breasts with their hands. The mothers' oxytocin levels exhibit a pulsatile pattern during this period. It is possible that the children's own motor activity lies behind these oxytocin pulses since the amount of massage-like movements performed by the newborn as well as the rate of sucking relate to the amount of maternal oxytocin pulses [95]. Oxytocin released into the blood stimulates ejection of milk but it also dilates the cutaneous blood vessels on the chest whereby the mother may transfer warmth to the infant [96]. It is likely that in parallel to the release of oxytocin into the circulation there is also a release of oxytocin into the CNS of the mother, as previously demonstrated in animals, and that this oxytocin contributes to increased maternal interaction and bonding to the infant and also to her own well-being.
The physiological relaxation is expressed by decreased levels of cortisol and blood pressure and an increased activity of the gastrointestinal tract [80, 97, 98]. The mothers' well-being is reinforced by the feeling of warmth caused by the dilatation of cutaneous blood vessels.

The closeness is of course reciprocal. The infant is also influenced by the contact with the mother and the warmth stimulates the interaction with the mother which is expressed by the spontaneous breastfeeding behaviour [94]. The infant also becomes calmer and it does not scream as long as it is kept skin to skin on its mother's chest [99]. The physiological relaxation is followed by an increased peripheral circulation and thereby the feet of the infant become warm. The fine-tuned interplay between mother and infant is revealed by a relation between the maternal skin temperature and the increase of temperature in the feet of the infant. The warmer the mother is the warmer are the feet of the infant [100].
The release of oxytocin has not been studied in the newborn, but since the levels of the hormone cortisol decrease and since the levels of the gastrointestinal hormone CCK increase (effects which may be secondary to an increased release of oxytocin in the hypothalamus and

the DMX) in premature infants which have been allowed to have ventral skin contact (kangaroo care) it might be assumed that oxytocin release is stimulated [101, 102]. The infants sucking during breastfeeding, reinforces the effects induced by touch [80, 98, 103]. Even stimulation of other senses (vision, sound and odours, and also eye contact – an indirect touch between mother and infant) play an important role for these reciprocal effects.

Figure 3: The ventral side is of importance in close relationships. The vagal nerve afferents originating in this area are activated by touch and closeness and may be of importance for the psychophysiological reactions triggered by ventral closeness.

Long-term effects by closeness and breastfeeding

Skin to skin contact between the newborn baby and the mother and breastfeeding immediately after birth are not only followed by immediate changes as described above but also by more long-lasting effects. The bonding between mother and infant may be reinforced by this treatment as expressed by a more frequent interaction between mothers and infants four days after birth and also to a reduced occurrence of abandonment of the babies. In addition, some studies show that milk production is ameliorated and the time for breastfeeding prolonged [104-109].

Breastfeeding women, after a period of breastfeeding, become calmer and more socially interactive as measured by the Karolinska Scale of Personality (an inventory measuring personality traits) [110-113]. In addition, their blood pressure is lower, and the cortisol release induced by physical activity reduced [114, 115]. Moreover, the vagal control of the levels of gastrointestinal hormones is changed in a way which is consistent with optimal digestion and storing of nutrients [116]. The idea that oxytocin contributes to the psychological changes during breastfeeding is supported by the fact that the number of oxytocin pulses in connection with the breastfeeding session is related not only to the amount of milk which is received by the infant during breastfeeding but also to the mothers level of calm and interest in social interaction. Even the prolactin levels in these mothers correlate to maternal levels of calm and relaxation [110, 111].

There is further experimental data supporting the notion that oxytocin may be of physiological importance during the neonatal period. Women who have been delivered by Caesarean section have, on the average, fewer pulses of oxytocin in connection with breastfeeding measured 2-3 days after birth, compared to those delivered vaginally (fig. 3). Nor are they as calm and socially interactive as the mothers having had a vaginal delivery. Obviously, the development of the breastfeeding related oxytocin pattern and the behavioural adaptation is delayed by Caesarean section. It is not possible to decide whether these effects are due to a reduction of labour related oxytocin release or to a delayed skin to skin contact between mother and infant [111, 117]. Alternatively, pain or stress in connection with the surgical intervention may have antagonised oxytocin release and oxytocin induced effects in the newly delivered mother. Anyway, it seems as if reduced exposure to oxytocin during this critical period delays the development of the psychophysiological adaptation taking part in connection with birth, in particular in primiparous. In a longer time perspective this may be related to problems with breastfeeding and reduced interaction between mother and child. Also other pain relieving interventions in connection with labour as for example epidural anaesthesias reduce the release of oxytocin and may therefore influence the developing mother infant interaction [118].

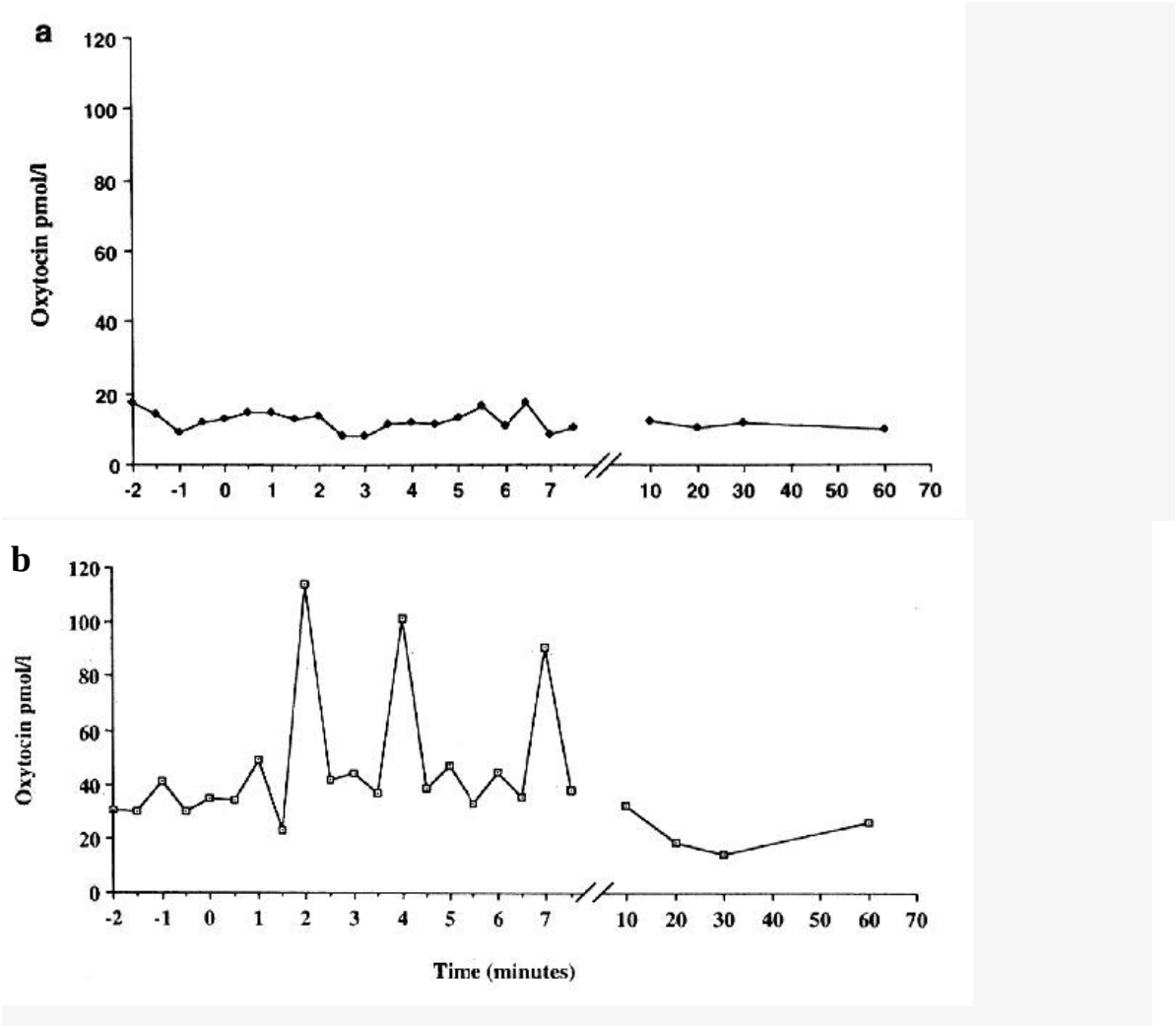

Figure 4: Oxytocin levels in response to breastfeeding 2 days after birth. The upper panel shows the flat oxytocin pattern in a woman having had an emergency caesarean section. The lower panels show the pulsatile oxytocin pattern in two women having had a vaginal delivery. (from Nissen et al. 1996 [117]).

Oxytocin release in other types of relations and therapeutic situations

The psychophysiological effects, described above, which occur in response to closeness between mother and infant can be regarded as a model for a reaction pattern which is triggered in many different types of contacts and relations among humans of different ages and sexes. Sexual activity, in particular, is connected to a very powerful release of oxytocin in both sexes [119]. Despite the differences, basically, the same psychophysiological system, including calm, social interaction, relaxation, and stimulation of restoration processes is induced by many kinds of social contacts. These effects induced are of course health promoting and may be one of the reasons why people with good social relations have a better health [120, 121, 122].

It is well-known that the fight-flight pattern can be triggered by threatening situations. External as well as internal situations which by a certain individual are experienced as dangerous or uncontrollable give rise to stress responses via activation of the amygdala/hippocampus region. The activity within the LC is increased as well as the release of CRF in the hypothalamus leading to stimulation of the HPA-axis and the sympathetic nervous system [123, 124]. By analogy, it is likely that a psychophysiological pattern related to calm and relaxation can be triggered by purely psychological mechanisms for example by a calm, supportive and warm surrounding. It remains to be established if oxytocin is involved in such responses of antistress nature. The fact that oxytocin release can be induced in response to sensory stimuli as well as by thoughts and associations support this assumption.

A doula is a woman who touches, holds and supports a woman in labour, physically and mentally. With this type of support it has been shown that women give birth more quickly and that the need for Caesarean section and pain relief is significantly reduced. The experience of labour becomes more positive. Recently some well documented articles have been published which show that the presence of a doula also gives rise to beneficial long-term effects. Two months after birth, mothers who have been helped by a doula during labour, have been shown to have a better relation to their children and also to their partners, when compared to those who did not have this type of support. In addition, they are less depressed [125, 126, 127]. It is possible that it is the combination of physical touch and emotional support given by the doula which lies behind these effects. Perhaps, the doula changes the activity in different neurotransmitter systems in the brain in a way similar to those induced by repeated oxytocin administration in animal experiments. It is possible that such neurochemical changes lie behind the stimulation of social interaction and decreased levels of mental and physiological stress observed in the mother that have been supported by a doula.

It is important to note that the openness to impressions of all kinds is very high during birth, when oxytocin levels are high. Therefore a loving and caring treatment may influence the individual in a deep going and long-lasting way just as a difficult and extremely painful labour can be traumatizing for the mother and induce a posttraumatic stress syndrome.

A combination of touch and a positive supportive psychological support may have even more favourable anti-stress effects than either treatment alone. If an individual is very anxious and afraid it may be difficult to reach this person by psychological mechanisms. Touch may sometimes work better, since somatosensory stimulation activates the release of oxytocin from PVN via a direct mechanism which cannot easily be blocked by anxiety.

It is possible that openness to the positive effects of supportive treatments may be induced by a combination of physical and mental support in people of all ages and sexes. Such a combined treatment is, and should perhaps be used more often, in many therapeutically situations, involving psychological and somatic treatments.

The fact that oxytocin levels are decreased in patients with depression, stress-related disorders, anxiety and chronic pain support the idea that stimulation of oxytocin release may have health promoting properties [128-133]. Interestingly, some of the pharmacological drugs used to treat these disorders may involve oxytocinergic mechanisms. Thus oxytocin release is triggered by 5HT1a-receptors and oxytocin levels even increase in response to the administration of SSRI in animal experiments [134,135]. These data indicate that oxytocin is a common mediator of several pharmacological, physiological and psychological treatments.

References

1. Buijs RM, De Vries GJ, Van Leeuwen FW. The distribution and synaptic release of oxytocin in the central nervous system. In: Amico JA, Robinson AG, editors. Oxytocin: Clinical and Laboratory Studies. Elsevier Science Publishers BV 1985. p. 77-86.
2. Freund-Mercier MJ, Stoeckel ME, Palacios JM, Pazos A, Reichhart JM, Porte A, Richard P. Pharmacological characteristics and anatomical distribution of [3H]oxytocin-binding sites in the wistar brain studied by autoradiography. Neuroscience 1987;20:599-614.
3. Petersson M, Lundeberg T, Uvnäs-Moberg K. Oxytocin enhances the effects of clonidine on blood pressure and locomotor activity in rats. J Auton Nerv Syst 1999;78:49-56.
4. Yamaguchi K, Akaishi T, Negoro H. Effect of estrogen treatment on plasma oxytocin and vasopressin in ovariectomized rats. Endocrinol Japon 1979;26:197-205.
5. Schumacher M, Coirini H, Johnson A, Flanagan L, Frankfurt M, Pfaff D, McEwen B. The oxytocin receptor: a target for steroid hormones. Regul Pept 1993;45:115-9.
6. Tribollet E, Audigier S, Dubois-Dauphin M, Dreifuss JJ. Gondadal steroids regulate oxytocin receptors but not vasopressin receptors in the brain of male and female rats. An autoradiographical study. Brain Res 1990;511:129-40.

7. Patisaul HB, Scordalakes EM, Young LJ, Rissman EF. Oxytocin, but not oxytocin receptor, is regulated by oestrogen receptor beta in the female mouse hypothalamus. J Neuroendocrinology 2003;15:787-93.

8. Somponpun S, Sladek CD. Role of estrogen receptor-beta in regulation of vasopressin and oxytocin release in vitro. Endocrinology 2002;143:2899-904.
9. Choleris E, Gustafsson JA, Korach KS, Muglia LJ, Pfaff DW, Ogawa S. An estrogen-dependent four-gene micronet regulating social recognition: a study with oxytocin and estrogen receptor-alpha and –beta knockout mice. Proc Natl Acad Sci 2003;100:6192-7.
10. Clarke G, Fall CHD, Lincoln DW, Merrick LP. Effects of cholinoceptor antagonists on the suckling-induced and experimentally evoked release of oxytocin. Br J Pharmacol 1978; 63:519-27.
11. Tribollet E, Clarke G, Dreifuss JJ, Lincoln DW. The role of central adrenergic receptors in the reflex release of oxytocin. Brain Res 1978;142:69-84.
12. Crowley WR, Parker SL, Armstrong WE, Wang W, Grosvenor CE. Excitatory and inhibitory dopaminergic regulation of oxytocin secretion in the lactating rat: Evidence for respective mediation by D-1 and D-2 dopamine receptor subtypes. Neuroendocrinology 1991;53:493-502.
13. Melis MR, Argiolas A, Gessa GL. Apomorphine increases plasma oxytocin concentration in male rats. Neurosci Lett 1989;98:351-355.
14. Bagdy G, Kalogeras KT. Stimulation of 5-HT1A and 5-HT2/5-HT1C receptors induce oxytocin release in the male rat. Brain Res 1993;611:330-332.
15. Ottesen B, Hansen B, Fahrenkrug J, Fuchs A-R. Vasoactive intestinal peptide (VIP) stimulates oxytocin and vasopressin release from the neurohypophysis. Endocrinology 1984;115:1648-50.
16. Verbalis JG, McCann MJ, McHale CM, Stricker EM. Oxytocin secretion in response to cholecystokinin and food intake: Differentiation of nausea from satiety. Science 1986; 232:1414-19.
17. Moos F, Freund-Mercier MJ, Guerné Y, Guerné JM, Stoeckel ME, Richard PH. Release of oxytocin and vasopressin by magnocellular nuclei in vitro: Specific facilitatory effect of oxytocin on its own release. J Endocrinol 1984;102:63-72.
18. Brussaard, AB. Oxytocin suppresses the GABAergic synaptic input in supraoptic neurones from the rat. In: Ivell R, Russell JA, editors. Oxytocin: Cellular and

Molecular Approaches in Medicine and Research. Plenum Press, New York.1995. p. 105-15.

19. Freund-Mercier MJ, Stoeckel ME. Somatodendritic autoreceptors on oxytocin neurons. In: Ivell R, Russell JA, editors. Oxytocin: Cellular and Molecular Approaches in Medicine and Research. Plenum Press, New York. 1995. p. 185-94.
20. Hatton GI, Tweedle CD. Magnocellular neuropeptidergic neurons in hypothalamus: Increases in membrane apposition and number of specialized synapses from pregnancy to lactation. Brain Res Bull 1982;8:197-204.
21. Wright DM, Clarke G. Inhibition of oxytocin secretion by μ and δ receptor selective enkephalin analogues. Neuropeptides 1984;5:273-76.
22. Randle JCR, Renaud LP. Actions of G-aminobutyric acid on rat supraoptic nucleus neurosecretory neurones in vitro. J Physiol 1987;387:629-47.
23. Carter CS. Neuroendocrine perspectives on social attachment and love. Psychoneuroendocrinology 1998;23:779-818.
24. Insel TR. Oxytocin – A neuropeptide for affiliation: evidence from behavioral, receptor autoradiographic, and comparative studies. Psychoneuroendocrinology 1992;17:33-5.
25. Windle RJ, Shanks N, Lightman SL, Ingram CD. Central oxytocin administration reduces stress-induced corticosterone release and anxiety behavior in rats. Endocrinology 1997; 138:2829-34.
26. McCarthy MM, Altemus M. Central nervous system actions of oxytocin and modulation of behavior in humans. Mol Med Today 1997;3:269-75.
27. Uvnäs-Moberg K, Alster P, Hillegaart V, Ahlenius S. Oxytocin reduces exploratory motor behaviour and shifts the activity towards the centre of the arena in male rats. Acta Physiol Scand 1992;145:429-30.
28. Uvnäs-Moberg K, Ahlenius S, Hillegaart V, Alster P. High doses of oxytocin cause sedation and low doses cause an anxiolytic-like effect in male rats. Pharmacol Biochem Behav 1994;49101-6.
29. Ferguson JN, Aldag JM, Insel TR, Young LJ. Oxytocin in the medial amygdala is essential for social recognition in the mouse. J Neurosci 2001;158:278-85
30. Winslow JT, Hearn EF, Fergusson J, Young LJ, Matzuk MM, Insel TR. Infant vocalization, adult aggression and fear behaviour of an oxytocin null mutant mouse. Horm Behav 2001; 39:11-21.

31. Ferguson JN, Young LJ, Hearn EF, Nazuk MM, Insel TR, Winslow JT. Social amnesia in mice lacking the oxytocin gene. Nat Genet 2000;25:284-8.
32. Uvnäs-Moberg K, Bruzelius G, Alster P, Lundeberg T. The antinociceptive effect of non-noxious sensory stimulation is mediated partly through oxytocinergic mechanisms. Acta Physiol Scand 1993;149:199-204.
33. Ågren G, Lundeberg T, Uvnäs-Moberg K, Sato A. The oxytocin antagonist 1-deamino-2-D-Tyr-(Oet)-4-Thr-8-Orn-oxytocin reverses the increase in the withdrawal response latency to thermal, but not mechanical nociceptive stimuli following oxytocin administration or massage-like stroking in rats. Neurosci Lett 1995;187:49-52.
34. Lund I, Yu LC, Uvnäs-Moberg K, Wang J, Yu C, Kurosawa M, et al. Repeated massage-like stimulation induces long-term effects on nociception: contribution of oxytocinergic mechanism. Eur J Neurosci 2002;16:330-8
35. Uvnäs-Moberg K. Antistress pattern induced by oxytocin. News Physiol Sci (NIPS) 1998; 13:22-6.
36. Björkstrand E, Eriksson M, Uvnäs-Moberg K. Evidence of a peripheral and a central effect of oxytocin on pancreatic hormone release in rats. Neuroendocrinology 1996;63:377-383.
37. Björkstrand E, Ahlenius S, Smedh U, Uvnäs-Moberg K. The oxytocin receptor antagonist 1-deamino-2-D-Tyr(OEt)-4-Thr-8-Orn-oxytocin inhibits effects of the 5-HT1a receptor agonist 8-OH-DPAT on plasma levels of insulin, cholecystokinin and somatostatin. Regul Pept 1996;63:47-52.
38. Siaud P, Puech R, Assenmacher I, Alonso G. Microinjection of oxytocin into the dorsal vagal complex decreases pancreatic insulin secretion. Brain Res 1991;546:190-4.
39. Bonne D, Cohen P. Characterization of oxytocin receptors on isolated rat fat cells. Eur J Biochem 1975;56:295-303.
40. Dunning BE, Moltz JH, Fawcett CP. Modulation of insulin and glucagon secretion from the perfused rat pancreas by the neurohypophyseal hormones and by desamino-D-arginine vasopressin (DDAVP). Peptides 1984;5:871-5.
41. Petersson M, Wiberg U, Lundeberg T, Uvnäs-Moberg K. Oxytocin decreases carrageenan induced inflammation in rats. Peptides 2001;22:1479-84.
42. Moosmann B, Behl C. Secretory peptide hormones are biochemical antioxidants: structure-activity relationship. Mol Pharmacol 2002;61:260-8.

43. Petersson M, Lagumdzija A, Stark A, Bucht E. Oxytocin stimulates proliferation of human osteoblast-like cells. Peptides 2002;23:1121-6.
44. Pawlikowski M, Majak J, Stepien H. Influence of vasopressin and oxytocin upon mitotic activity of adenohypophyseal cells in rat. Endokrynol Pol 1975;4:417-20
45. Furuya K, Mizumoto Y, Makimura N, Mitsui C, Murakami M, Tokuoka S, Ishikawa N, Nagata I, Kimura T, Ivell R. A novel biological aspect of ovarian oxytocin: gene expression of oxytocin and oxytocin receptor in cumulus/luteal cells and the effect of oxytocin on embryogenesis in fertilized oocytes. Adv in Exp Med Biol 1995;395:523-28.
46. Petersson M, Alster P, Lundeberg T, Uvnäs-Moberg K. Oxytocin causes a long-term decrease of blood pressure in female and male rats. Physiol Behav 1996;60:1311-15.
47. Petersson M, Lundeberg T, Uvnäs-Moberg. Short-term increase and long-term decrease of blood pressure in response to oxytocin – potentiating effect of female steroid hormones. J Cardiovasc Pharmacol 1999;33:102-8.
48. Petersson M, Alster P, Lundeberg T, Uvnäs-Moberg K. Oxytocin increases nociceptive thresholds in a long-term perspective in female and male rats. Neurosci Lett 1996;212:87-90.
49. Petersson M, Hulting A-L, Uvnäs-Moberg K. Oxytocin causes a sustained decrease in plasma levels of corticosterone in rats. Neurosci Lett 1999;264:41-4.
50. Uvnäs-Moberg K, Eklund M, Hillegaart V, Ahlenius S. Improved conditioned avoidance learning by oxytocin administration in high-emotional male Sprague-Dawley rats. Regul Pept 2000;88:27-32.
51. Arletti R, Bertolini A. Oxytocin as an antidepressant in two animal models of depression. Life Sci 1987;41:1725-30.
52. Petersson M, Hulting AL, Andersson R, Uvnäs Moberg K. Long term changes in gastrin, cholecystokinin and insulin in response to oxtytocin treatment. Neuroendocrinology 1999;69:202-208.
53. Uvnäs-Moberg K, Alster P, Petersson M. Dissociation of oxytocin effects on body weight in two variants of female Sprague-Dawley rats. Integr Physiol Behav Sci 1996;31:44-55.
54. Petersson M. Oxytocin decreases plasma levels of thyroid-stimulating hormone and thyroid hormones in rats. Regul Pept 2002;108:83-87.

55. Petersson M, Lundeberg T, Sohlström A, Wiberg U, Uvnäs-Moberg K. Oxytocin increases the survival of musculocutaneous flaps. Naunyn Schmiedebergs Arch Pharmacol 1998; 357:701-704.

56. Luppi P, Levi-Montalcini R, Bracci-Laudiero L, Bertolini A, Arletti R, Tavernari D, Vigneti E, Aloe L. NGF is released into plasma during human pregnancy: an oxytocin-mediated response? Neuroreport 1993;4:1063-1065.

57. Sohlström A, Carlsson C, Uvnäs- Moberg K. Effects of oxytocin treatment in early life on body weight and corticosterone in adult offspring from ad libitum fed and food restricted rats. Biol Neonate 2000;78:33-40.

58. Uvnäs-Moberg K, Alster P, Petersson M, Sohlström A, Björkstrand E. Postnatal oxytocin injections cause sustained weight gain and increased nociceptive thresholds in male and female rats. Pediatr Res 1998;43:344-8.

59. Olausson H, Uvnäs-Moberg K, Sohlström A. Postnatal oxytocin alleviates adverse effects in adult rat offspring caused by maternal malnutrition. Am J Physiol (Endocrinol Met) 2003;284(3):E475-80.

60. Sohlström A, Olausson H, Brismar K, Uvnäs-Moberg K. Oxytocin treatment during early life influences reproductive performance in ad libitum fed and food-restricted female rats Biol Neonate 2002;81(2):132-8.

61. Petersson M, Uvnäs-Moberg K, Erhardt S, Engberg G. Oxytocin increases locus coeruleus alpha 2-adrenoceptor responsiveness in rats. Neurosci Lett 1998;255:115-8.

62. Díaz-Cabiale Z, Petersson M, Narváez JA, Uvnas-Moberg K, Fuxe K. Systemic oxytocin treatment modulates alpha2/adrenoceptors in telencephalic and diencephalic regions of the rat.Brain Res 2000;887:421-5.

63. Petersson M, Uvnäs-Moberg K. Systemic oxytocin treatment modulates glucocorticoid and mineralocorticoid receptor mRNA in the rat hippocampus. Neurosci Lett 2003;343:97-100.

64. Rajkowski J, Kubiak P, Ivanova S, Aston Jones G. State related activity, reactivity of locus ceruleus neurons in behaving monkeys. In: Goldstein D, Eisenhofer G, Mc Carty T, editors. Advances in Pharmacology, catecholamines briding basic science with clinical medicine. San Diego, Ca: Academic Press: 1998. p. 740-6.

65. Rogers RC, Hermann GE. Dorsal medullary oxytocin, vasopressin, oxytocin antagonist, and TRH effects on gastric acid secretion and heart rate. Peptides 1985;6:1143-8.

66. Gilbey MP, Coote JH, Fleetwood-Parker S, Peterson DF. The influence of the paraventriculo-spinal pathway and oxytocin and vasopressin on sympathetic preganglionic neurones. Brain Res 1982;251:283-96.

67. Diaz-Cabiale Z, Olausson H, Sohström A, Narváez A, Uvnäs-Moberg K, Fuxe K. Postnatal oxytocin treatment increased the density and reduced the affinity of alfa2-adrenoceptor agonist binding sites in central autonomic regions of the adult rat in a regionally selective pattern modulated by prenatal stress. Neuropsychopharmacology, in press.

68. Kendrick KM, Keverne EB, Baldwin BA, Sharman DF. Cerebrospinal fluid levels of acetylcholinesterase, monoamines and oxytocin during labour, parturition, vaginocervical stimulation, lamb separation and suckling in sheep. Neuroendocrino-lolgy 1986;44:149-56.

69. Sansone GR, Gerdes CA, Steinman JL, Winslow JT, Otenweller JE, Komisaruk BR, et al. Vaginocervical stimulation releases oxytocin within the spinal cord in rats. Neu-roendocrinology 2002;75:306-15.

70. Stock S, Uvnäs-Moberg K. Increased plasma levels of oxytocin in response to afferent electrical stimulation of the sciatic and vagal nerves and in response to touch and pinch in anaesthetized rats. Acta Physiol Scand 1988;132:29-34

71. Vallbo AB, Olausson H, Wessberg J. Unmyelinated afferents constitute a second system coding tactile stimuli of the human hairy skin. J Neurophysiol 1999;81:2753-63.

72. Olausson H, Lamarre Y, Backlund H, Morin C, Wallin BG, Starck G et al. Unmyelinated tactile afferents signal touch and project to insular cortex. Nature 2002;5:900-4.

73. Eriksson M, Lindh B, Uvnäs-Moberg K, Hökfelt T. Distribution and origin of peptide-containing nerve fibres in the rat and human mammary gland. Neuroscience 1996;70: 227-45.

74. Komisaruk BR, Sansone G. Neural pathways mediating vaginal function: the vagus nerves and spinal cord oxytocin. Scand J Psychol 2003;44:241-250.

75. Uvnäs-Moberg K, Posloncec B, Åhlberg L. Influence on plasma levels of somatostatin, gastrin, glucagon, insulin and VIP-like immunoreactivity in peripheral venous blood of anaesthetized cats induced by low intensity afferent stimulation of the sciatic nerve. Acta Physiol Scand 1986;126:225-30.

76. Lindén A. Eriksson M, Hansen S, Uvnäs-Moberg K. Suckling induced release of cholecystokinin into plasma in the lactating rat: Effects of abdominal vagotomy and lesions of central pathways concerned with milk ejection. J Endocrinol 1990;127:257-63

77. Kurosawa M, Suzuki K, Utsugi T, Araki T. Response of adrenal efferent nerve activity to non-noxious mechanical stimulation of the skin in rats. Neurosci Lett 1982;34:295-300.

78. Araki T, Iro M, Kurosawa M, Sato A. Responses of adrenal sympathetic nerve activity and catecholamine secretion to cutaneous stimulation in anesthetized rats. Neuroscience 1984; 12:231-7.

79. Tsuchiya T, Nakayama Y, Sato A. Somatic afferent regulation of plasma corticosterone in anesthetized rats. Jpn J Physiol 1991;41:169-76.

80. Uvnäs-Moberg K, Widström AM, Marchini G, Winberg J. Release of GI hormones in mother and infant by sensory stimulation. Acta Paediatr Scand 1987;76:851-60.

81. Uvnäs-Moberg K, Lundeberg T, Bruzelius G, Alster P. Vagally mediated release of gastrin and cholecystokinin following sensory stimulation. Acta Physiol Scand 1992;146:349-56.

82. Hotta H, Sato A, Sato Y, Uvnäs-Moberg K. Somatic afferent regulation of plasma prolactin in anaesthetized rats. Jpn J Physiol 1993;43:501-9.

83. Kurosawa M, Nagai N, Sato A, Uvnäs-Moberg K. Somatic afferent regulation of plasma immunreactive glucagon in anesthetized rats. Jpn J Physiol 1194:44:221-3.

84. Kurosawa M, Lundeberg T, Ågren G, Lund I, Uvnäs-Moberg K. Massage- like stroking of the abdomen lowers blood pressure in anesthetized rats: Influence of oxytocin. J Auton Nerv Syst 1995;56.26-30.

85. Uvnäs-Moberg K, Alster P, Lund I, Lundeberg T, Kurosawa M, Ahlenius S. Stroking of the abdomen causes decreased locomotor activity in conscious male rats. Physiol Behav 1996; 60:1409-11.

86. Lund I, Lundeberg T, Kurosawa M, Uvnäs-Moberg K. Sensory stimulation (massage) reduces blood pressure in unanaesthetized rats. J Auton Nerv Syst 1999;78:30-7.

87. Holst S, Uvnäs-Moberg K, Petersson M. Postnatal oxytocin treatment and postnatal stroking of rats reduce blood pressure in adulthood. Auton Neurosci 2002;99:85-90.

88. van Oers, de Kloet E, Whelan T, Levine S. Maternal deprivation effect on the infant´s neural stress markers is reversed by tactile stimulation and feeding but not by suppressing corticosterone. J Neurosci 1998;18:10171-9.

89. Caldji C, Tannenbaum B, Sharma S, Francis D, Plotsky PM, Meaney MJ. Maternal care during infancy regulates the development of neural systems mediating the expression of fearfulness in the rat. Proc Natl Acad Sci (USA) 1998;95:5335-40.
90. Ågren G, Olsson C, Uvnäs-Moberg K, Lundeberg T. Olfactory cues from an oxytocin-injected male rat can reduce energy loss in its cagemates. Neuroreport 1997;8:2551-5.
91. Ågren G, Uvnäs-Moberg K, Lundeberg T. Olfactory cues from an oxytocin-injected male rat can induce anti-nociception in its cagemates. Neuroreport 1997;14:3073-6.
92. Mills DS. Pheromonatherapy – an integral part of modern companion animal practice. UK Vet. 2002;7:1-3.
93. Tindal JS. Stimuli that cause the release of oxytocin. In: Greep RO, Astwood EB, editors. Handbook of Physiology, Endocrinology IV. The pituitary gland, part 1. 1974. p.257-67.
94. Widström AM, Ransjö Arvidsson AB, Christensson K, Matthiesen AS, Winberg J, Uvnäs-Moberg K. Gastric suction in healthy newborn infants. Effects on circulation and developing feeding behaviour. Acta Pediatr Scand 1987;76:566-72.
95. Matthiesen AS, Ransjö-Arvidson AB, Nissen E, Uvnäs-Moberg K. Postpartum maternal oxytocin release by newborns: effects of infant hand massage and sucking. Birth 2001;28:13-9.
96. Eriksson M, Lundeberg T, Uvnäs-Moberg K. Studies on cutaneous blood flow in the mammary gland of lactating rats. Acta Physiol Scand 1996;1:227-45.
97. Uvnäs Moberg K. The gastrointestinal tract in growth and reproduction. Sci Am 1989;261:78-83.
98. Uvnäs Moberg K. Neuroendocrinology of mother child interaction. Trends Endocrinol Metab 1996;7:126-31.
99. Christensson K, Cabrera T, Christensson E, Uvnäs Moberg K, Winberg J. Separation distress call in the human neonate in the absence of maternal body contact. Acta Pediatr 1995;84;467-8.
100. Bystrova K, Widström AM, Matthiesen AS, Ransjö-Arvidsson AB, Welles-Nyström B, Wassberg C, et al. Skin-to-skin contact may reduce negative consequences of “the stress of being born“: a study on temperature in newborn infants, subjected to different ward routines in St. Petersburg. Acta Ped 2003;92(3):320-6.
101. Törnhage CJ, Serenius F, Uvnäs Moberg K, Lindberg T. Plasma somatostatin and cholecystokinin levels in preterm infants during kangaroo care with and without nasogastric tubefeeding J Pediatr Endocrinol Metab 1998;11:645-651

102. Whitelaw A, Heisterkamp EG, Sleath K. Skin to skin contact for very low birth weight infants and their mothers: a randomized trial of “kangoroo care“ Arch Dis Child 1998;63:1377-81.

103. Svennersten K, Gorewit RC, Sjaunja LO, Uvnäs-Moberg K. Feeding during milking enhances milking-related oxytocin secretion and milk production in dairy cows, whereas food deprivation decreases it. Acta Physiol Scand 1995;153:309-10.

104. Widström AM, Wahlberg S, Matthiesen AS, Eneroth P, Uvnäs Moberg K, Werner S, Winberg J. Short-term effects of early suckling and touch of the nipple on maternal behaviour. Early Hum Dev 1990;21:153-63

105. Klaus MH, Jerauld, R, Kreger NC, McAlpine W, Steffa M, Kennel JH. Maternal attachment: importance of the first postpartum days. N Eng J Med 1972;296:460-3.

106. Kramer MS, Chalmers B, Hodnett ED, Sevkovskaya Z, Dzikovich I, Shapiro S, et al. Promotion of breastfeeding intervention trial a randomized trial in the republic of Belarus. Jama 2001;286:413-20.

107. Lvoff NM, Lvoff V, Klaus M. Effect of baby friendly initiative on infant abandonment in a Russian hospital. Arch Pediatr Adolsc Med 2000;154:474-7.

108. O’Connor S, Vietze PM, Sherrod KB, Sandler HM, Altemeier WA. Reduced incidence of parenting inadequacy following rooming in. Pediatrics 1980;66:176-92.

109. Gomes-Pedro J, Patricio M Carvalho A, Goldschmidt T, Torgal-Garcia F, Monteiro MB. Early intervention with portuguese mothers: a 2 year follow up. J Dev Behav Pediatr 1995;18:21-8.

110. Uvnäs-Moberg K, Widström AM, Nissen E, Björvell H. Personality traits in women 4 days postpartum an their correlation with plasma levels of oxytocin and prolactin. J Psychosom. Obstet. Gynecol. 1990;11:261-73.

111. Nissen E, Gustavsson P, Widström AM, Uvnäs-Moberg K. Oxytocin, prolactin, milk production and their relationship with personality traits in women after vaginal delivery or Cesarean section. J Psychosom Obst Gynecol 1998;19:49-58.

112. Sjögren B, Widstöm AM, Edman G, Uvnäs-Moberg K. Changes in personality pattern during first pregnancy and lactation. J Psychosom Obstet Gynecol 2000;21:31-8.

113. Heinrichs M, Neumann I, Ehlert U. Lactation and Stress: ProtectiveEffects of Breast-feeding in humans. Stress 2002;5:195-203

114. Light KC, Smith TE, Johns JM, Brownley KA, Hofheimer JA, Amico JA. Oxytocin responsivity in mothers of infants: a preliminary study of relationships with blood

pressure during laboratory stress and normal ambulatory activity. Health Psychol 2000;19:560-7.

115. Altemus M, Deuster PA, Galliven E, Carter CS, Gold PW. Suppression of hypothalamic-pituitary-adrenal axis responses to stress in lactating women. J Clin Endocrinol Metab 1995;80:2954-9

116. Widström AM, Wahlberg S, Matthiesen AS, Eneroth P, Uvnäs Moberg K, Werner S, et al. Short-term effects of early suckling and touch of the nipple on maternal behaviour. Early Hum Dev 1990;21:153-63

117. Nissen E, Uvnäs-Moberg K, Svensson K, Stock S, Widström AM, Winberg J. Different patterns of oxytocin, prolactin but not cortisol release during breastfeeding in women delivered by Caesarean section or by the vaginal route. Early Hum Dev 1996;45:103-118.

118. Ransjö-Arvidson AB, Matthiesen AS, Lilja G, Nissen E, Widstrom AM, Uvnäs-Moberg K. Maternal analgesia during labor disturbs newborn behavior: effects on breastfeeding, temperature, and crying. Birth 2002 ;28:5-12.

119. Carter S. Oxytocin and sexual behavior. Neurosci Biobehav Res Rev 1992;16:131-44.

120. Uvnäs-Moberg K. Physiological and endocrine effects of social contact. Ann N Y Acad Sci 1997;807:146-63.

121. Uvnäs-Moberg K. Oxytocin may mediate the benefits of positive social interaction and emotions. Psychoneuroendocrinology 1999;23:819-35.

122. Knox SS, Uvnäs-Moberg K. Social isolation and cardiovascular disease: An atherosclerotic pathway? Psychoneuroendocrinology 1998;23:877-90.

123. Pitkanen A, Savander V, Le Doux JE. Organization of intraamygdaloid circuitries in the rat: an emerging framework for understanding functions of the amygdala. Trends Neurosci 1977;20:517-23.

124. Gray TS. Functional and anatomical relationships among the amygdala basal forebrain, ventral striatum and cortex. An integrative discussion. Ann N Y Acad Sci 1999; 877:439-44.

125. Hofmeyr GJ, Nikodem VC, Wolman W, Chalmers BE, Kramer T. Companionship to modify the clinical birth environment: effects on progress and perceptions of labour and breastfeeding. Br J Obstet Gynecol 1991;98:756-64

126. Landry SH, McGrath SK Kennel JH et al. The effects of doula support during labor on mother-infant interaction at 2 months. Pediatr Res. 1998;43:13A

127. Thomassen P, Lundwall M, Wiger E, Wollin L, Uvnäs Moberg K. Doula-ett nytt begrepp inom förlossningsvården. Läkartidningen in press
128. Frasch A, Zetzsche T, Steiger A, Jirikowski GF. Reduction of plasma oxytocin levels in patients suffering from major depression. Adv Exp Med Biol 1995;395:257-8.
129. Beckmann H, Lang RE, Gattaz WF. Vasopressin.oxytocin in cerebrospinal fluid of schizophrenic patients and normal controls. Psychoneuroendocrinology 1985;10:187-91.
130. Linkowski P, Geenen V, Kerkhofs M, Menlewicz J, Legros JJ. Cerebrospinal fluid neurophysins in affective illness and in schizophrenia. Eur Arch Psychiatry Neurosci 1984; 234:162-5.
131. Uvnäs-Moberg K, Arn I, Theorell T, Jonsson CO. Gastrin, somatostatin and oxytocin levels in patients with functional disorders of the gastrointestinal tract and their response to feeding and interaction. J Psychosom Res 1991;35:525-3.
132. Alfvén G, de la Torre B, Uvnäs-Moberg K. Depressed concentrations of oxytocin and cortisol in children with recurrent abdominal pain of non-organic origin. Acta Pediatr 1994; 83:1076-80.
133. Anderberg UM, Uvnäs-Moberg K. Plasma oxytocin levels in female fibromyalgia syndrome patients. Z Rheumatolog 2000;59:373-9.
134. Uvnäs-Moberg K, Björkstrand E, Hillegaart V, Ahlenius S Oxytocin as a possible mediator of SSRI-induced antidepressant effects. Psychopharmacology 1999;142:95-101.
135. Uvnäs-Moberg K., Hillegaart V, Alster P, Ahlenius S. Effects of 5-HT1a agonists, selective for different receptor subtypes, on oxytocin, CCK, gastrin and somatostatin plasma levels in the rat. Neuropharmacology 1996;35:1635-40.

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