

# Role of oxytocin in improving the welfare of farm animals — A review

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Submitted Dec 25, 2015; Revised Feb 15, 2016;  
Accepted Feb 29, 2016

**Abstract:** Recently, increasing attention has been paid to the welfare of farm animals, which have been evaluated using behavioral and physiological measures. However, so far, the measures have almost always been used to estimate poor welfare. In this review, firstly we focus on how oxytocin (OT) relates to positive social behavior, pleasure, and stress tolerance, and second on which management factors stimulate OT release. OT induces maternal and affiliative behaviors and has an anti-stress effect. Further, OT is produced during enjoyable events, and has positive feedback on its own release as well. Therefore, to some extent, the relationship of OT to positive normal behavior was mutually beneficial—heightened OT concentration owing to comfortable rearing conditions induces positive social behavior, which in turn may increase OT concentration. Hence, studies on animal welfare should pay more attention to increasing comfort and the stress tolerance, rather than only focusing on when stress occurs in farm animals.

**Keywords:** Behavior; Farm Animals; Management; Oxytocin; Welfare

## INTRODUCTION

Recently, the topic of animal welfare has been paid more and more attentions. In order to improve the welfare of farm animals, studies have been carried out using several methods, including behavioral and physiological measures. Of the behavioral measures, stereotypies [1] have been widely used as behavioral indicators of poor welfare in addition to escape behavior [2] and so on. On the other hand, activation of the hypothalamic-pituitary-adrenal (HPA) system and the sympathetic-adrenal-medullary system has been widely used as physiological indicators of poor welfare in human and animal experiments. Most welfare assessments have been conducted when the animals were under stressful conditions. Duncan and Olsson [3] advocated that freedom from the state of suffering is assured by providing environmental requirements, while the establishment of pleasurable states requires environmental enrichment. Thus, studies on animal welfare are gradually moving from merely the reduction of stress to methods of increasing pleasure and stress tolerance in the animals' lifetime. Consequently, assessments of good welfare are becoming increasingly important. Under these circumstances, affiliative behavior and positive social interaction have been used as good welfare indicators. In addition, dopamine, endorphin, and serotonin have been used as indicators to evaluate good animal welfare. However, it has been pointed out that the release of dopamine induces the release of catecholamine [4], which is a stress indicator, whereas endorphin and serotonin influence sedation rather than pleasure and have no particular correlation with behavior [5,6].

Interestingly, it was reported that hormone oxytocin (OT) mediate not only the affiliative and social behaviors related to good welfare mentioned above, but also responses to pleasurable events [7,8]. Thus, OT as a good welfare indicator [9] has recently gained

importance in this topic [10]. There are many reviews on the topic of animal welfare. The concept of animal welfare has been discussed based on viewpoints of theoretical foundation and its increasing developments [11,12]. Even if those were reviewed with animal production, those were almost based on the critical aspects [13-15].

We tried to review OT studies from the viewpoint of increasing welfare in farm animals. In this review, we focus on how OT, as a good welfare indicator, is playing roles on the welfare of farm animals, and what kind of animal management increases OT concentration.

## ROLES OF OXYTOCIN ON ANIMAL WELFARE

### Role of oxytocin on positive social behavior

OT, discovered in 1909, had been studied as a hormone involved in milk ejection and uterine contractions. It is produced by two kinds of oxytocinergic neurons: The magnocellular neurons sending their projections to the neurohypophysis releasing OT into blood circulation, and the parvocellular neurons sending their projections mainly to the campus, ventral tegmental area, frontal cortex, brainstem, pons, medulla, and spinal cord [16].

According to Ross and Young [8], in the late 1970s, pharmacological studies began to reveal a role for OT not only in birth and lactation, but also in synchronizing maternal behavior. During pregnancy and parturition, mothers nurture the fetus and protect the offspring after birth; this induces a series of hormonal changes in the mothers and offspring. Subsequently, Pedersen and Prange [17] firstly indicated the effect of OT on maternal behavior in rats. The study showed that 6 of 13 animals in the group administered intracerebroventricular OT became fully maternal (including 5 items designed by authors), whereas none of the 12 animals in the saline control group became fully maternal. Thus, the role of OT in maternal behavior began to receive more attention. Daily brief separation from pups induced maternal behaviors in dams, which heightened the sensitivity of OT receptors in the brain [18]. Further, the effect of the administration of OT on the incidence of maternal behavior in virgin rats was summarized by Pedersen et al [19], though not all studies demonstrated OT-induced maternal behavior. OT secretion from the paraventricular nucleus also induced maternal behavior in sheep [20]. However, this effect has not been ascertained in cattle [21].

Maternal behavior includes licking, grooming, and nursing of the offspring, and plays an important role in supporting the life of the offspring. From the above, it is evident that studies on OT in relation to maternal behavior in farmed animals are important for improving the welfare and survivability of the offspring.

The relationship of OT with maternal behavior with reference

to the pair-bond between mothers and offspring, caused interest among researchers about the mechanism by which OT might mediate behavior in pair bonding. One of the first reports in this regard indicated that centrally administered OT induced affiliative behavior and facilitated bonds in female prairie voles [22]. Additionally, [23] indicated that affiliative behaviors might induce hypothalamic OT expression, which in turn may attenuate stress responses in delayed gastric emptying and accelerated colonic transit. These results are supported by those of Dhakar et al [24], who showed that OT-receptor knockout rats performed exhibited aggressive behavior than intact animals. Further, centrally administered OT also induced grooming behavior in male rats [25], affiliative response of huddled sitting in the subordinate squirrel monkey [26], and flexible behaviors such as locomotors activity in the open field under stress condition [27].

Dunbar [28] reported that social grooming, as an affiliative behavior, plays a particularly important role in social bonding and has a major effect on an individual's lifetime reproductive fitness in humans and primates. Social grooming in cows plays a role in functional significance for the formation and maintenance of social bonds and the stabilization of social relationships [29].

As a consequence, the evaluation of OT with relation to positive social behavior, such as maternal and affiliative behavior, may contribute greatly towards improving the welfare and fitness of farm animals.

### Role of oxytocin on positive emotion

OT has been examined in relation to pleasurable events and positive interactions. For example, massage-like stroking of the abdomen of anaesthetized rats lowered blood pressure, and this effect was diminished by intravenous injection of an OT antagonist [30]. Morhenn et al [31] reported that comfortable physical contact increased endogenous OT concentration in human. Their results indicated that serum OT increased during massage followed by trust, but did not increase either with trust or with massage alone, suggesting that increased OT concentration is associated with pleasurable emotion. Further, the supportive interaction "warm touch" between married couples increased their salivary OT concentration [32]. In calves, serum OT concentration was higher in the natural suckling rearing system than in bucket-suckling calves [33]. In sows, Algers et al [34] reported that stimulation of the udder by piglets increased OT levels.

The OT-mediated pleasurable emotion described above may be a response to sensory activation. Uvnäs-Moberg [7] reported that social behavior and affiliative interaction involves sensory stimuli capable of releasing OT, which stimulates the attachment of bonding and in turn induces more OT release.

### Role of oxytocin on stress tolerance

OT was involved in the HPA axis in exerting an anti-stress effect. It was reported that intranasal OT administration attenuated the adreno-cortico-tropic-hormone response in monkeys [35], and centrally administered OT attenuated cortisol secretion in Holstein steers [36]. Further, intranasal OT injection had an anxiolytic-like effect on rats [37,38]. Thus, since the modern intensive livestock industry comprises many stressors to animals, studies on the anti-stress effects of OT should be paid more attention.

#### Role of oxytocin on positive feedback effects

Moos et al [39] found that intraventricular injection of OT induced a dose-dependent rise in OT release from the nuclei of both male and lactating rats, whereas an OT antagonist significantly reduced basal OT release in magnocellular nuclei. These findings suggest that OT has a positive feedback effect on its own release. Da et al [20] (1996), noting that central OT-induced maternal behavior in sheep, also suggested that OT exerted positive feedback, as the intracerebroventricular administration of OT induced maternal behavior, which in turn facilitated OT release in both of central terminal and peripheral into the blood. In addition, Neumann et al [40] reported that OT exerts positive feedback in the supraoptic nucleus during suckling, suggesting that natural suckling may increase basal serum OT concentrations in rats. Although the positive feedback of OT has not been reported during other behaviors so far, it may be exerted not only during suckling and maternal behavior but also during other positive normal behaviors associated with pleasant feelings. Owing to this, we postulate that OT and positive social behavior and positive emotion is mutually beneficial—OT concentration induces positive social behavior and positive emotion, which in turn increases OT concentration. The heightened OT concentration may be beneficial to animals, since it increases the stress tolerance [7] (Uvnäs-Moberg 1998) and engenders positive emotional states [41].

### MANAGEMENT PRACTICES FOR INCREASING OT CONCENTRATION IN ANIMALS IN ANIMAL HUSBANDRY

An instantaneous increase in serum OT concentrations has been reported in calves during natural suckling that lasts only for 1 min [42]. In our previous study, we found that the basal serum OT concentration in 1-month-old calves was higher under the natural suckling system than the bucket-suckling system [33]. We speculated two possible causes for this finding. Heightened serum OT concentration might be due to the positive feedback by instantaneous secretion, firstly during long-term natural suckling, similar to results obtained with rats [40] and secondly during physical interactions with dams and peers. This postulated might be in agreement with that of Odendaal and Meintjes [43] that positive behavioral interactions stimu-

late OT secretion in both humans and dogs. Hence, from these views, the welfare of farm animals would be improved under the natural suckling rearing system via an increase in serum OT concentration. This may be supported by the arguments of Krohn [44], who concluded that natural suckling systems, where calves are nursed by dams and have social contact with other calves and cows, are more beneficial to calf welfare, with results such as a greater positive effect on daily gain and vitality of the calf than is seen in the artificial rearing systems. These results might be partly mediated by OT.

Further, OT in relation to feeding behavior acts not only by maintaining homeostasis but also through the feelings of reward and hedonism. Olszewski et al [45] concluded that OT, as a feeding inhibitor, maintains homeostasis and is capable of mitigating some aspects of feeding behavior and energy metabolism. In addition, it was reported that feeding behavior induced serum OT release in dogs and sows [46], and dairy cows [47,48]. Though the mechanism of feeding-induced OT release is still unknown, it is a popular hypothesis that feeding behavior is controlled by not only the homeostatic system but also by the reward and hedonic system [49]. Researchers speculated two possibilities: one is that vagal fibers (secreting cholecystokinin, somatostatin, glucagon, and thyrotropin-releasing hormone) activate the brain [50], and the other is that sensory nerves in the oral mucosa are activated during feeding [42]. Sinomiya et al [51] reported that serum OT concentration tended to be higher in grazing cows than housing cows. It might be reasonable to suppose that the grazing system leads to more feeding and chewing behavior and more comfort to cows than the housing system, and that this increased comfort induces serum OT release in cows. Although it is difficult to conclude that the grazing system is more beneficial to animals than the housing system [52], animal welfare might be improved under the grazing system.

On the other hand, serum OT concentrations differed among individual calves, and the individual difference was stable in the same rearing system for several months [53]. However, different rearing systems may cause divergent physiological changes. In rats, chronic stress of repeated unavoidable stress induced an escape and a decrease in extra neuronal dopamine basal concentration [54]. Chronic stress of long term tethered housing pigs induced a greater increase in the adreno-cortico-tropic-hormone and cortisol than in loose-housed pigs [55]. Hence, physiological characteristics might be changed by the use of a long-term rearing system. OT also has a long-term effect. It was reported that intracerebroventricular OT administration decreased blood pressure and was effective for 8 days after the last injection [56], increased nociceptive thresholds for 3 weeks after the last injection of 10 days after a previous 5-day treatment [57], and decreased corticosterone for 10 days after the last injection of a regime administered once a day for 5 days [58] in rats. As mentioned above, manual brush-

ing [59] suckling [42,33], and massaging [31] caused instantaneous increases in serum OT concentration. Thus, we consider that, if animals are reared in a long-term comfortable state, are provided stimuli such as brushing and massaging, and are reared under natural suckling or grazing rearing systems, they would have a higher basal OT concentration, which in turn might induce more positive normal behavior.

However, studies about serum OT have a limitation. As is well known, OT is produced in the supraoptic and paraventricular nuclei of the hypothalamus. However, it is difficult to directly inject OT into the brain and measure OT concentration in the brain in both humans and larger domestic animals. Administering OT via intranasal spray into the brain and measuring OT concentration in serum might solve these problems, and has been widely employed in many studies in humans and some domestic animals, although these studies have been criticized by Churchland and Winkielman [60]. They claim that the blood-brain barrier might prevent OT pullout from the blood into the brain, and that OT in the brain has a short life, and intranasal OT might hence not reach the OT receptor sites in the brain. In particular, it is of increasing importance to clarify the relationship of brain and serum OT concentrations. A few studies exist on serum OT, such as the study examining the feedback effects of OT mentioned above, facilitating OT release in both brain and blood [39,20], as well as the studies demonstration that feeding behavior induces increases in serum OT [46-48]. Although studies on nasal administration of OT continue to be criticized, it may be considered certain that the relationship of OT with positive social behavior is mutually beneficial to some extent—the higher the OT concentration (modulated by general management practices, such as natural suckling, maternal care, and grazing; enrichment, such as manual brushing; and intranasal administration) the greater the degree of induction of positive social behavior, which in turn increases OT concentration.

## CONCLUSION

OT is a key indicator of good welfare, enhancing pleasure, suppressing stress, and stimulating its own release. The release of OT is related to the performance of positive normal behavior, and enrichment, such as brushing, which can further accelerate OT secretion. Hence, studies on the welfare of farm animal should pay more attention to methods to improve management practices to induce OT and hence improve the comfort and stress tolerance of the animals, and not merely focus on how to control stress in farm animals.

## CONFLICT OF INTEREST

We certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

## ACKNOWLEDGMENTS

This review was supported by the Laboratory of Land Ecology, Graduate School of Agricultural Science, Tohoku University. We would especially like to thank Assistant Professor Yu Yoshihara and Professor Shin-ichiro Ogura from the Laboratory of Land Ecology, and Associate Professor Sang-gun Roh from the Laboratory of Animal Physiology, Tohoku University.

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