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Faculty of Veterinary Medicine and Animal Science

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Oxytocinets genetiska bakgrund och betydelse för soggans modersegenskaper

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Abstract

Oxytocin is today widely spoken of as a "feel good" hormone. Recent research has increased interest in the hormone and its role in social and sexual interactions, as well as its importance for complex behavioral patterns. There is evidence that oxytocin is released during physical contact and is said to suppress anxiety and stress. In animals and humans, oxytocin, which is a neuropeptide and likewise a hormone, is necessary for parturition and lactation. Synthesis of oxytocin occurs in brain neurons and in specific organs involved in reproduction. Although oxytocin is believed to have existed for more than 700 million years, the structure is almost unchanged since its inception. This suggests a well conserved gene that is less affected by evolutionary development. Pig production confirms that; sows have, despite intense selection for various traits, still similar maternal abilities as their ancestors. This bachelor thesis is a literature review of genetic aspects of oxytocin and its importance for maternal ability of sows.

Sammanfattning

Oxytocin är idag vida omtalat som ett "må bra"-hormon. Ny forskning har ökat intresset för hormonet och dess roll i sociala och sexuella interaktioner samt dess betydelse för komplexa beteendemönster. Det är bevisat att oxytocin frisätts vid fysisk beröring och sägs dämpa oro och stress. Hos djur och människor är oxytocin, som är en neuropeptid och tillika ett hormon, nödvändigt för att sätta igång förlossning och mjölkutsöndring. Syntes av oxytocin sker i hjärnans nervceller och i specifika organ som medverkar vid reproduktion. Trots att oxytocin tros ha funnits längre än 700 miljoner år är strukturen nästintill oförändrad sedan dess uppkomst. Detta tyder på en väl bevarad gen som inte påverkats i stor utsträckning av evolutionär utveckling. Grisproduktionen styrker detta; då suggor trots hård selektion för diverse egenskaper fortfarande vidbehållit liknande modersegenskaper som sina förfäder. Denna kandidatuppsats är en litteraturstudie över oxytocinets genetiska bakgrund och betydelse för suggans modersegenskaper.

Introduction

Recent research results on oxytocin have been quickly picked up by the media and oxytocin received much attention as a "feel-good" hormone. A lot has been written about this hormone and popular headers based on scientific research results are various; "Oxytocin - the love hormone" (Wudarczyk et al., 2013), "Oxytocin makes people dishonest" (Scheele et al., 2013) and "Lying connected to oxytocin" (Poulin et al., 2012). But there is much more to this hormone than popular newspaper articles suggest. Oxytocin is of great relevance not only for human, but also for complex behavioral patterns and relevant physiological mechanisms in livestock animals.

Oxytocin is a posterior pituitary hormone, made and released by neurons of the hypothalamo-neurohypophysial system (Brownstein et al., 1980). Its function on uterus contraction and milk secretion was discovered in 1906 and 1910, 1911 (Dale, 1906; Ott & Scott, 1910; Schafer & Mackenzie, 1911), only a few years after the discovery of a component released by the pituitary gland which had an impact on blood pressure (Oliver & Schäfer, 1895). One of the special characters of the neuropeptide oxytocin is that it is well conserved, with an almost unchanged gene structure and expression (reviewed by Donaldson & Young, 2008). Despite the conservation there are differences in the genetic regulation of oxytocin receptors that might emphasize natural variation in social behavior in various species shown in several

studies and lately reviewed (Donaldson & Young, 2008). Especially the relevance of oxytocin on social interactions is an interesting aspect, which also has relevance for animal welfare.

It is generally known today that livestock production, not least in Sweden, is widely affected by economic factors. Highly productive animals are therefore required of the farmers. Animal welfare has to be taken into account because it may influence the productivity (Grandinson, 2003). Reproductive status, level of production, health and access to replacement of animals is of great matter (Engblom, 2007). The maternal behaviour of the sow is of big importance in pig production. A sow not performing sufficient results, as high number of weaned and well grown piglets, might soon to be culled out of the production (Budimir et al., 2013). In Sweden almost 50% of the sows are replaced every production period, mainly because of reproduction problems. Sows showing good results tend to stay in the production until old age (Engblom, 2007).

The aim of this review is to get an overview of the genetic background of oxytocin and its importance for maternal behavior of sows. It will highlight factors defining good maternal behavior and also tell the general role of oxytocin, as its functional elements, location of production, secretion, transport pathways and receptors. The role of oxytocin and maternal behavior will be discussed separately and in combination.

Oxytocin

The genetic background of oxytocin

For more than 700 million years homologs of oxytocin have existed (Acher et al., 1995; Donaldson & Young, 2008). It is believed that oxytocin and vasopressin emerged from a gene-duplication before vertebrates arose. The genes are found on the same chromosome close to each other (Donaldson & Young, 2008). Neurohormones, similar those of mammals are found in both worms and fish. Social and reproductive behaviour and water homeostasis are connected to oxytocin and vasopressin (Acher et al., 1995; Donaldson & Young, 2008). In females pair bonding, lactation, parturition, maternal and sexual behaviour are affected by oxytocin. While in males, sexual and social behaviour, erection and ejaculation are affected by vasopressin. Nevertheless, females and males are influenced by both oxytocin and vasopressin (Donaldson & Young, 2008).

A human cell normally contains 46 chromosomes, 23 chromosome pairs (U. S. National Library of Medicine, 2014; DNA Learning Center, 2014), while the cell of a domestic pig contains 38 chromosomes, totally 19 chromosome pairs (McConnell et al., 1963). The oxytocin gene (OXT) is located in chromosome 20 in human (DNA Learning Center, 2014) and in chromosome 17 in pigs (National Center for Biotechnology Information, 2014). When OXT is induced in uterine the myometrium becomes more sensitive to OXT. During contractions an upgrade of oxytocin receptor gene (OXTR) mRNA occurs simultaneously with OXT. Uterine contraction also contributes to a major increase of OXTR in the myometrium. OXTR is a G protein-coupled receptor. OXT is hydrolysed and inactivated by an enzyme, leucyl/cystinyl aminopeptidase (LNPEP). Degradation of the hormone determines the availability of OXT to the OXTR. During pregnancy LNPEP levels in the maternal blood increases and plays a major role for maintenance of pregnancy as it regulates the amount of OXT (Kim et al., 2013).

Recent studies have shown that one single nucleotide polymorphisms (SNP) identified in the oxytocin receptor (OXTR) gene (rs53576) is connected to parenting and social behaviour.

Likewise, oxytocin in rodents affects similar behaviours (Michalska et al., 2014). They proved that positive parenting and social behaviour in women are correlated. Further they demonstrated that positive parenting and brain responses to child stimuli were related to the presence of a specific SNP (rs53576) variant identified in the OXTR (Michalska et al., 2014). The effect was also shown in an experiment in humans, where plasma oxytocin was found in higher levels in parents than in individuals with no child, but did not differ between genders. Individuals which were homozygote at two loci of the OXTR (rs2254298, rs1042778) gene showed lower levels of plasma oxytocin than heterozygotes, while heterozygotes had more physical contact with their infants. The children of heterozygotes in turn showed higher levels of oxytocin, than children of homozygotes, as an answer to frequent body contact. Parents who received a high amount of body contact as children tend to give their own children a high amount of body contact as well (Feldman et al., 2012).

A posterior pituitary hormone and neuropeptide

The nonapeptide oxytocin contains nine amino acids (Figure 1). Oxytocin and vasopressin in mammals differ only at the position of two amino acids (Donaldson & Young, 2008).

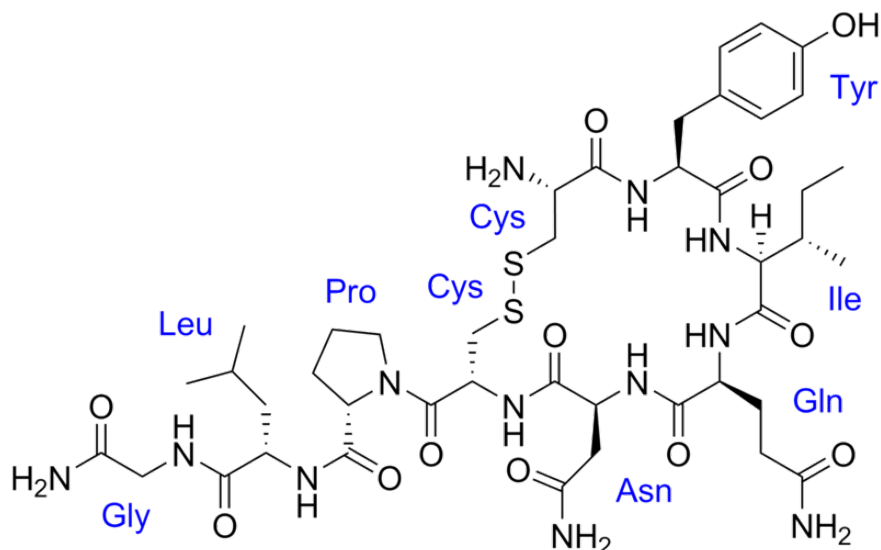


Figure 1: Chemical structure of oxytocin containing nine amino acids (designed by Edgar181, 2009. From <http://en.wikipedia.org/wiki/Oxytocin> (downloaded 2014-05-06)).

Oxytocin is synthesized in the hypothalamic paraventricular, neuronal nucleus, and in supraoptic nuclei, nuclei of neuroendocrine cells synthesizing oxytocin during late embryogenesis (Figure 2 & Figure 3).

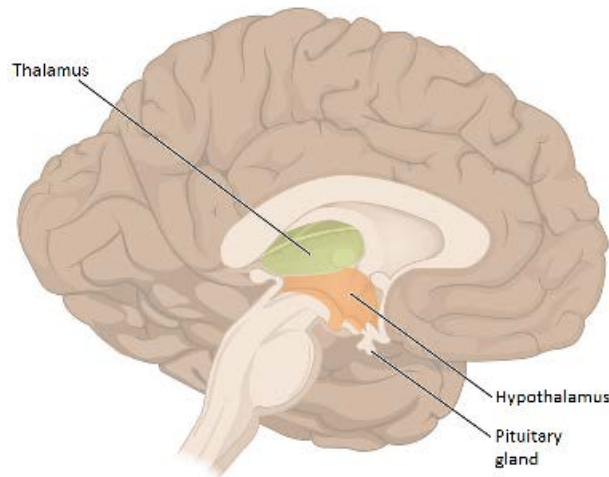


Figure 2: A schematic picture of thalamus, hypothalamus and pituitary gland. (Designed by OpenStax College, 2013. From http://commons.wikimedia.org/wiki/File:1310_Diencephalon.jpg (downloaded 2014-06-02). Modulated by Freja Engström).

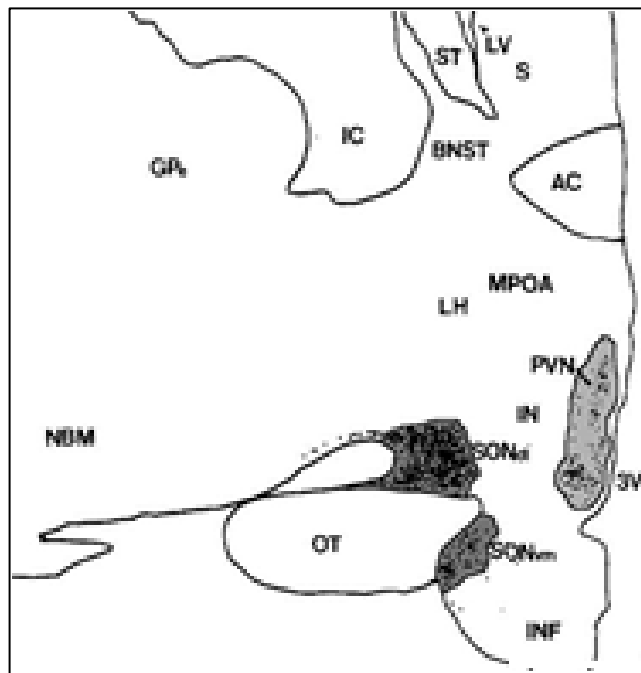


Figure 3: The black area shows the supraoptic nuclei (SON) and the gray area shows the paraventricular nucleus (PVN) in the hypothalamus (designed by Sammyj, 2007. From http://en.wikipedia.org/wiki/Supraoptic_nucleus (downloaded 2014-05-06) and http://en.wikipedia.org/wiki/Paraventricular_nucleus (downloaded 2014-05-06). Modulated by Freja Engström).

The synthesis of oxytocin occurs not only in the brain but also in the corpus luteum, uterus, placenta, amnion and testis (reviewed by Nishimori et al., 1996). It is stored in granules or vesicles (Brownstein et al., 1980) to then be secreted into the circulation by neurons of the brain via the posterior pituitary (Brownstein et al., 1980; Nishimori et al., 1996). Carrier protein transports the granule along the axon to the nerve ending. Exocytosis occurs when nerve ending membrane depolarise (Brownstein et al., 1980). It has been reviewed by Nishimori et al. (1996) that a cloned and sequenced receptor for oxytocin is expressed in tissues involved in activity of endogenous and exogenous oxytocin. This specific receptor

inhibits exogenous oxytocin release and responds to adrenal and gonadal steroids. Studies in rodents showed that the levels of oxytocin and oxytocin receptors in uterus increase during pregnancy and parturition (reviewed by Nishimori et al., 1996). Oxytocin is expressed within the hypothalamus (Donaldson & Young, 2008) and its action potential affects the amount of hormone release (Sjaastad et al., 2010). Peptide hormones are water-soluble and circulate accessibly in the blood. This enables a fast enzymatic degradation and excretion in the urine and bile. Oxytocin has a plasma half-life of only 3-5 minutes which requires a persistent secretion. A continuously secretion enables a precise regulation (Sjaastad et al., 2010).

The general role of oxytocin

Oxytocin is said to regulate social behaviour in mammals (Donaldson & Young, 2008). The synthesis of oxytocin has been shown important for mating behaviour and to play a role in the function of lordosis, copulation and ejaculation. Oxytocin is additionally said to influence onset for maternal behaviour in rodents (reviewed by Nishimori et al., 1996) and to ease anxiety, play a part in stressed situation and social emotional interactions (Yun et al., 2013; Donaldson & Young, 2008).

In pigs, the level of oxytocin increases significantly during pre-farrowing and farrowing. Peaks of oxytocin release are subsequent after each piglet born (Yun et al., 2013). Since oxytocin also affects the ability to nurse it is of big importance for piglet survival (Nishimori et al., 1996). Oxytocin triggers milk let-down; close to and during milk let-down the oxytocin levels in sows rise, although the hormonal peak showed to vary considerably between animals in a study by Valros et al. (2004). They proposed that oxytocin might affect more functions than solely milk let-down as facilitate milk production, but more related studies needs to be done.

Use of oxytocin in pig production – onset of farrowing

Oxytocin is used for onset of farrowing, even though an increased activity of uterine contractions could lead to intra-partum stillborn piglets since the blood flow increases the gaseous exchange in the uterus and might injure unborn piglets (Mota-Rojas et al. 2006). In a study Mota-Rojas et al. (2006) showed that when oxytocin was administered, crated sows had a significant number of stillborn piglets. Furthermore, higher number, high frequency and longer duration of uterine contractions were shown in the oxytocin treated sows (Mota-Rojas et al. 2006). Further an experiment performed in Mexico showed that penned sows injected with oxytocin directly after the first piglet born got shorter intervals between following born piglets (Alonso-Spilsbury et al., 2004). But added oxytocin increases frequency of ruptured umbilical cords and the appearance of meconium stained skin stillborn piglets is more common in oxytocin treated sows as compared with control group (Alonso-Spilsbury et al., 2004; Mota-Rojas et al., 2006). Also the number of abnormal deliveries was noticeably higher in the oxytocin administered groups (Alonso-Spilsbury et al., 2004).

Maternal behaviour

What defines maternal behaviour and which behavioural patterns are desirable? Most pig farmers might have similar goals and add certain values to maternal behaviour, being of big importance for the production. Relevant traits in sows are high fertility as high numbers of weaned and well grown piglets are desirable (Budimir et al., 2013). A study in Sweden showed that one of the primary reasons for culling sows in commercial production is reproduction problems (Engblom et al., 2007). Reviewed by Yun et al. (2013), oxytocin is well-known as a pituitary hormone affecting maternal behaviour in mammals. It influences

both parturition and lactation (Yun et al., 2013). Additional aspects need to be taken into account; the doctoral thesis by Wallenbeck (2009) stated that the animal behaviour is affected not only by genetic effects but also by environmental effects. What could these environmental factors be? Many pigs, especially in densely populated regions in Europe, are today kept in closed buildings leaving little room for natural behaviour as observed in wild pigs. Many studies have especially analysed the effect of crates, as recently reviewed by Yun et al. (2013). They summarized that crated sows, common in commercial husbandry, have no possibility of nest-building during farrowing. This has a negative effect on their ability to express natural behaviour and thus a negative effect of the maternal behaviour (Yun et al., 2013).

Nest-building

Many studies have been focusing on the investigation of the nest-building behaviour in pigs. In Yun et al. (2013) it is reviewed that performing natural behaviour as foraging, rooting and building a nest to protect the infants against predators is important for the sow. Crated sows with no possibility of nest-building show increased stress levels and decreased nursing behaviour and maternal reactions towards infants (Yun et al., 2013). Wallenbeck (2009) summarized that nest-building before farrowing is common in both outdoor and indoor environments. A study by Gustafsson et al. (1999) proved no differences in maternal behaviour between outdoor held domestic and wild-type sows, bred from a domestic mother and a wild boar as father. Both type of sows showed the same motivation for nest-building (Gustafsson et al., 1999). Nest-building follows the same pattern in a wild boar-crossed sow or a domesticated sow; this behavioural pattern is therefore greatly established in sows (Gustafsson et al., 1999; Wallenbeck, 2009). Because of material access, affecting the timing and quality of nest-building, the period of nest-building by indoor sows is longer compared to loose-housed sows (Wallenbeck, 2009). The nest-building behaviour persists for 24 h (Gustafsson et al., 1999; Wallenbeck, 2009) and reaches its peak 6 to 12 h before farrowing (Wallenbeck, 2009). The oxytocin level starts to increase during nest-building. Higher oxytocin concentration contributes to end nest-building prepartum (Castrén et al., 1993).

Nursing behaviour and milk let-down

Many factors impact the ability of the sow to connect to the piglets. The environment during parturition and lactation has been reviewed being one of them (Yun et al., 2013). Nursing is of big importance for piglet growth (Valros et al., 2002) and survival (reviewed by Nishimori et al., 1996). A study in mice has proven that lack of oxytocin does not affect the fertility but is fundamental for the milk ejection (reviewed by Nishimori et al., 1996). The first milk, colostrum, is vital for the piglets to ingest during the first 6 hours alive. Colostrum contains a major amount of antibodies important for viability and infection resistance. After 24 hours the udder is emptied of colostrum milk. Production of colostrum starts 105 days into pregnancy and is stored in the udder until farrowing (Mattsson & Mattson, 2012). The hormonal release of oxytocin contributes to contraction of the alveolar myoepithelium and milk ejection (Algers et al., 1990). In 1990, a study by Algers et al. (1990) showed that milk let-down occurs after piglets massaging the udder for approximately 1.5-2 minutes, which is followed by oxytocin release. The sow starts grunting at a low rate, to invoke piglet attention, then escalating to a grunting peak when milk let-down happens (Algers et al., 1990). An experiment made in Denmark in 1987 showed that grunt rates of the sow correlate with the frequency of piglets at the udder. 8 hours after farrowing a pattern with peaks of high grunt rates had occurred and within the first 24 hours alive the piglets have learned to understand the high rated sound (Castrén et al., 1989). Algers et al. (1990) further showed that plasma oxytocin reaches its peak within 10 seconds of suckling, but the amount of oxytocin is

independent of pre-massaging of the udder before milk let-down. Plasma oxytocin is back to basal values again only 1 minute after milk let-down. Higher number of piglets stimulating the udder decreases time before reaching grunting peak. Furthermore reported was that the intergraded grunting rate, 1 minute before and 1 minute after grunting peak, and levels of oxytocin at different time points are positively correlated. As grunting rate rises the levels of oxytocin do as well (Algers et al., 1990).

Reviewed by Valros et al. (2002) was that sows turning much of their body storage into milk have a higher nursing frequency. Individual sows have their own behaviour characteristics (Valros et al., 2002). Studies in Sweden and the Netherlands have shown that the nursing pattern was changing within different periods of lactation and with the age of piglets (Valros et al., 2002; Gustafsson et al., 1999). Jensen (1988) displayed that nasal contact between Landrace free-ranging sows and their piglets change by period of lactation. Foraging increased the first 4 weeks after farrowing, then decreasing until weaning. Nose contact initiated by the sow showed higher frequency in the beginning of lactation and decreased after 4 weeks. Between the 1st and 4th week, the piglets often initiated nose contact after milk let-down and before final massage of the udder. Aggression towards piglets increased during lactation (Jensen, 1988). Gustafsson et al. (1999) showed that domestic sows are less active and have less nose-contact with their piglets compared to the wild-type. Total duration for nursing in general and mean duration of sow terminated nursing was decreasing with the increase of piglet age (Valros et al., 2002). Further, the frequency of termination of the nursing by the sow, increased with piglet age (Valros et al., 2002; Jensen, 1988). Successful nursing proved having a positive effect on the average daily gain during the beginning of lactation but stabilized after day 15. Successful nursing had the same frequency during entire lactation (Valros et al., 2002).

Disturbance of maternal behaviour

Fear and aggressiveness

The doctoral thesis by Grandinson (2003) tells that negative stress may have effects on the productivity and welfare of animal. Pigs being handled negatively by human show increased levels of the stress hormone cortisol (Grandinson, 2003). Chronic stress and increased cortisol levels have negative effects on oestrus behaviour and parturition duration in gilts (Hellbrügge et al., 2009). Gilts showing less fear of humans have increased amount live born piglets (reviewed by Grandinson, 2003; Hellbrügge et al., 2009) and decreased amount crushed piglets (Hellbrügge et al., 2009). Oxytocin reduces anxiety and plays a major role for fear response (Kirsch et al., 2005; Guzmán et al., 2013). Amygdala in the brain is linked to fear and trust. In many mammals amygdala express a high amount of oxytocin receptors. In human, a fearful face can activate amygdala and thus influence social behaviour. Increased activity of amygdala represents a danger signal and has been observed in humans avoiding social interactions and humans with phobia (Kirsch et al., 2005). Guzmán et al. (2013) increased the level of fear in mice by enhance oxytocin receptors in lateral septal. The experiment showed that increased level of oxytocin receptors contributes to maintenance of social memory rather than to lower the level of fear (Guzmán et al., 2013).

It has been suggested in a review by Forde (2002), to cull sows showing aggressiveness toward stockperson, but a selection of that sort could adversely affect the total production (Forde, 2002) as protection of infants is a good natural maternal behaviour (Forde, 2002; Grandinson, 2003). Aggressiveness of the sow towards the stockperson mainly depends on intention to protect her piglets, defending herself or showing dominance (Forde, 2002).

An experiment by Forde (2002) showed that almost 8% of domestic gilts killed piglets by savaging, aggressively attacking their piglets. Of the savaging sows 80% were held in farrowing pens and 20% in crates. Savaging turned out to decrease, and aggressiveness directed towards stockperson increase with each litter. Sows causing danger for the stockperson were solely from the farrowing pen system. No correlation between the human-pig relation and savaging behaviour could be identified in that study (Forde, 2002). However, differences in productivity occurred. Gilts showing dangerous aggressiveness towards stockperson had higher piglet growth and level of live born piglets compared to gilts savaging piglets. In the presence of humans the savaging gilts moved less, were quieter, had higher heart rate and less will to interact with human, unlike the aggressive sows, which had higher levels of contact with human (Forde, 2002).

Litter size affects piglet mortality and crushing

Piglet loss before weaning is a problem in modern pig production. It is not always easy to predict what causes piglet mortality and especially why piglets are crushed under the sow. Several factors can affect such as incautiousness of the sow, litter size, weight of the piglets and their development of coordination. Wallenbeck (2009) observed sows that were rather active at the beginning of farrowing, which is unusual as onset of farrowing should result in a more passive sow. The risk of piglets being crushed during their first hours is reduced if sows are more passive, showing behaviour such as lying down with little response to the piglets, during the first or second hour after onset of farrowing, (Wallenbeck, 2009).

A study by Hellbrügge et al. (2008) showed a negative correlation between crushing and weaning weight of the piglets. The genetic correlation (r_g) between birth weight and early crushing was -0.13. High individual birth weight decreased endanger of being crushed, especially during the piglets first three living days. Hellbrügge et al. (2008) also discussed that the highest risk for piglet losses was during the day of birth since both sow and piglets are weaker after farrowing. Uncoordinated movements by new-born piglets and lack of sufficient heat for the smallest piglets increased the risk of mortality, as did selection for larger litter size (Hellbrügge et al., 2008).

Discussion

Oxytocin in pig production

As several maternal abilities are connected to the genetics of the sow (Nishimori et al., 1996; Yun et al., 2013) they are of importance to study and discuss. Oxytocin is well-known as a hormone affecting the maternal behaviour in pigs during farrowing (Yun et al., 2013) and lactation (Nishimori et al., 1996). For sows with lower oxytocin level, the farrowing might take longer, since oxytocin has an effect on the onset of farrowing and the ability to increase uterine contraction frequency (Mota-Rojas et al., 2013). If the farrowing takes long, the sow will be exhausted, therefore administration of oxytocin can be useful to decrease the total farrowing time (Alonso-Spilsbury et al., 2004) and thus avoid piglet mortality. I have not found any other reasons for use of oxytocin in pig production except from shorten farrowing time. It has come to my knowledge that oxytocin also is used to stimulate milk let-down after farrowing, but more research have to be done as there is barely nothing written about it. Unfortunately, addition of oxytocin has numerous not desirable effects that need to be taken into account. Mota-Rojas et al. (2013) showed that administration of oxytocin increases the occasion of intra-partum stillborn piglets. High frequency of uterine contractions cause increased gaseous exchange from the sow's blood stream into the piglets (Mota-Rojas et al., 2013). In a study, in penned sows, oxytocin was injected and it was observed that the number

of abnormal deliveries were noticeably (Alonso-Spilsbury et al., 2004). Both Alonso-Spilsbury et al. (2004) and Mota-Rojas et al. (2013) observed an increased appearance of meconium stained skin and higher frequency of ruptured umbilical cords in the groups given additional oxytocin. However, in crated sows administering of oxytocin might help onset of farrowing, as onset could be disturbed because lack of ability to perform natural maternal behaviour as nest building (Yun et al., 2013). Oxytocin administration in penned sows is to be considered in cases of long farrowing time. It could contribute to shorter farrowing as the interval between each piglet born gets shorter (Alonso-Spilsbury et al., 2004) and the sow less tired. This in turn might lead to increased number of living piglets. However, it has to be considered, that detailed studies on the effect of oxytocin levels in the blood are rare, since the measurement of oxytocin levels is difficult. As shown by Algers et al. (1990), oxytocin rises in fairly short peaks and only the use of sows with cannula might enable the measurement of its levels, since blood samples would need to be taken regularly. Such experiments can usually not be done on a larger scale and are restricted to fewer animals. Furthermore, ethical aspects must be carefully considered and it has to be proven if the number of sows in such a study will be enough, to confirm or deny the scientific question asked.

Effect of genetic changes

The phenotype of pigs has undergone major changes during and due to domestication and selection for specific traits. In contrast, changes in the genetics and behaviour pattern have been less. This was demonstrated by Gustafsson et al. (1999); domesticated sows and wild boar-crossed sows showed the same motivation for nest-building. Also the pattern of nest-building was similar (Gustafsson et al., 1999). This seems to acknowledge that changes of behavioural patterns, likely also related to the contribution of genetic effects, were established at a lower frequency during domestication. Reason for this could be higher selection for phenotypes different from behavioural pattern which again did not impact genotypes related to behaviour. Either this is the reason of less variability of the genetic sequence of the oxytocin gene, or the general character of oxytocin is, that it is more likely to be well conserved, with fewer changes occurring with time. Gustafsson et al. (1999) gives nest-building as an example where selection has not been done frequently to remove the maternal behaviour. This could be because the few hours of nest-building before each farrowing have not been considered as a significant problem. As crated sows are not able to perform nest-building a removal of this behaviour might make the sows feel less stressed before delivery. Again, if such patterns are not genetically correlated with production traits, for which animals have been selected for, behaviour will unlikely change substantially.

Lack of oxytocin during milk let-down

Oxytocin is released by teat stimulation (Castrén et al., 1989; Algers et al., 1990) and contributes to milk let-down (Algers et al., 1990; Nishimori et al., 1996). A disorder of hormonal release results in problems. Lower levels of oxytocin make probably the milk release take longer. Waiting for milk let-down could get hungry piglets impatient and incautious. This might lead to the interruption; the sow stands up and do not finish nursing. As a higher number of piglets massaging the udder, decreases the time before milk release (Algers et al., 1990), one selection preference could be for large enough litters or relatively larger litters. This indicates that the greater area of the udder getting stimulated, the faster oxytocin release introduce milk let-down. But pre-massaging before milk let-down does not correlate with the amount of oxytocin (Algers et al., 1990).

Problem with gilts as a result of removal of bad behaving sows

Fear of humans and aggression towards piglets is not a desirable behaviour in domestic sows. Selection for less aggressive sows has been suggested by Forde (2002) and Grandinson (2003). But removing all aggressive sows increase the need of replacement animals. It has been shown that sows are more likely to kill fewer piglets compared to gilts (Forde, 2002). It might therefore be of interest to keep older sows in the production instead of introducing new gilts. Furthermore older sows tend to be more aggressive towards stockperson (Forde, 2002), probably because of experience from earlier litters when learning to protect their infants. As aggressiveness toward the stockperson was proven not to be correlated with savaging behaviour (Forde, 2002) a selection for both traits in sows and gilts might be considered. Selection for less aggressive gilts might in contrast lead to reduced number of weaned piglets (Forde, 2002), which again is not desirable in a farming environment and which might have effects on oxytocin release during nursing as discussed in the section above, if litter sizes become too small. The fact that only penned sows showed aggressiveness against humans (Forde, 2002) questions the ability of the crated sows to perform natural maternal behaviour as protecting their infants. Further studies might be needed to determine if the given option to show even more maternal behavioural patterns will decrease aggressiveness also in penned sows. It is also needed to be taken into account that Gusmán et al. (2013) mentioned that fear do not decrease with higher amount of OXTR but the ability to recognise individuals increased. This indicates that more human-animal contact can benefit the production.

The effect of oxytocin for parental behaviour

Feldman et al. (2012) showed that physical contact is a trigger of oxytocin release. Further, frequency of physical contact seems to be transferred from parent to infant by environmental learning (Feldman et al., 2012). One interesting aspect in Feldman et al. (2012) was that the oxytocin levels differed between parents and non-parents, but not between genders. As oxytocin affects parenting and social behaviour positively (Michalska et al., 2014) it should be considered as a way of choosing maternal material into the pig production. One simple and possible solution for decreasing aggressiveness in sows and gilts is to have spinning brushes, today common in several cow stables, in the pen giving them possibility of massage. As said, physical contact contributes to the release of oxytocin and therefore the massage increases the well-being of the sow. Thus, the social and parental behaviour can be improved. Higher oxytocin level, in addition to selection for decreased savaging, could contribute to a higher number of weaned piglets and better mothers. Breeding for higher level of oxytocin is also a way to get more harmonic pigs. Although breeding for the oxytocin genes are extremely complex, as its gene structure and expression are well conserved (Donaldson & Young, 2008).

Conclusion

The oxytocin gene is ancient and the hormone has likely played an important role for social and maternal behaviour for a long time. Oxytocin is necessary for nursing and milk let-down. Likewise, it is of big importance for onset and duration of farrowing. Chemical oxytocin is commonly used in pig production. However, studies have shown that such administration has to be handled with caution since there might be negative effects on piglet survival.

There has been little research on specific patterns and the relationship between oxytocin levels in the blood and behaviour due to the release mechanisms of oxytocin with short peaks. For the same reason, only little information on the genetic background of oxytocin levels in the blood is currently available and there are, to my knowledge, no results on heritability or

genetic correlations. The study presented here, concludes therefore that more research has to be done, before any advice on the use of (chemical) oxytocin as a part of the ordinary work in farms can be given. Additional knowledge is needed to unravel the contribution of oxytocin as an attribute to increase animal well-being.

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