Effects of early experiences on mother-offspring interaction and adult behaviour.

Abstract
In recent years numerous studies focusing on early experiences have been carried out in order to examine and understand how early experiences effects the behaviour of the adult animal. The development of the nervous system in an animal is a dynamic process and depends largely on the individual’s interactions with its environment before as well as after birth and this hence influences the behavioural development. And there is a reason to believe that there is a window of opportunity during the neonatal phase for influences that can lead to phenotypic alterations of the adult animal, for instance in the response to stress. In fact the mother-offspring relationship during the neonatal phase has been shown to be an important factor in the so-called HPA (hypothalamus-pituitary-adrenal) stress response. In rodents, the strategies animals use to cope with stress as adults are affected by the amount of maternal care received during their early development. The licking and grooming in the rat may also serve to transmit information regarding the quality of the maternal environment to the offspring and such parental effects are believed to function as a source of phenotypic plasticity that in concert with environmental demands may influence offspring phenotype.

Introduction
Through the domestication process and despite thousands of years of artificial selection for tameness, studies of free-range and feral livestock have shown that the behaviour of our domesticated animals closely resembles those of their wild ancestors. One example of this is when pigs released into natural habitats will perform the full range of wild boar behaviour around farrowing, including isolate themselves from the group and the nest building behaviour (Jensen 1989). But there are also several cases where domestication has shown to have a profound impact in changed phenotypic expression. Perhaps one of the most famous example is the early canid domestication process where the Russian geneticist Belyaev showed that the selection for one single behavioural trait e.g. tameness toward humans in farm-foxes, resulted in morphological and physiological changes, such as diverse coloration, shortened legs, floppy ears, curly tails and changed reproductive cycle. The domestication process has also led to an increase in human animal interaction and a lot of the domesticated species like chickens, cows, pigs and sheep do not always find the interactions with humans a rewarding or pleasant event. Other outcomes of the domestication process is diverse husbandry conditions, such as dense population, vaccination, restraint, movement between cages, weaning and transportation etc. and these can all be considered to be potential stressors that could affect the animals and which could result in a significant biological cost to the animal. Repeated exposure to several of such acute unrelated stressors, or if exposed to prolonged stress could potentially cause a stress response or even inflict a pathological state (Moberg 2000) and lead to reduced welfare.
The way in which personality is affected by early experiences is an interesting area of research for applied ethology because these factors may alter the mental development and phenotypic expression in the adult animal. In recent years numerous studies focusing on early experiences have been carried out in order to examine and understand how early experiences effects the behaviour of the adult animal. The development of the nervous system in an animal is a dynamic process that depends largely on the individual’s interactions with its environment before as well as after birth and this hence influences the behavioural development. Many altricial species such as dogs are born in a state of large neural immaturity, but the nervous system rapidly develops via an intense synaptogenesis in which external stimulation plays an important role (Gazzano et al. 2008). It is therefore reason to believe that there is a window of opportunity during the neonatal phase for influences that can lead to phenotypic alterations of the adult animal, for instance in the response to stress.

The mother-offspring relationship during the neonatal phase has been shown to be an important factor in the so-called HPA (hypothalamus-pituitary-adrenal) stress response. In rodents, the strategies animals use to cope with stress as adults are affected by the amount of maternal care received during their early development. In stress studies using the technique of neonatal handling, neonatal handled rat pups received more maternal care than non-handled pups and the handled pups responded less intensely and for shorter periods of time to restraint stress as adults compared to non-handled pups ( Caldij et al. 1998). If handling have the same affect in other species as in rats it is likely that the effect is mediated not by the handling procedure itself but by the fact that this early experience of handling is followed by the reception of more maternal attention.

### Early experiences

Ontogeny is the development of an individual from the moment the egg is fertilized until death and early life experiences, together with genetic inheritance, influence all living creatures and affects both the physiological and the psychological expression and hence the behaviour of the animal throughout their lives. In the moment of fertilization a zygote is formed. The zygote then undergoes rapid cell division and cell differentiation during early prenatal development. By the third week the embryonic disc will form the so-called primitive streak and form three specialized layer, the ectoderm (creates the central nervous system (CNS) and the skin), the mesoderm (form the spinal cord, skeleton and skeleton muscles) and the endoderm (the respiratory and circulatory systems, the intestinal and digestive system, glands and genitals) (Eakin and Behringer 2004). This process lead to the development of the mammalian embryo, but where does early life experience begin in the sense that environmental cues, such as maternal hormone, influence the embryo or fetus and have an impact of the behavior of the offspring?

Results from a study involving stress during pregnancy ( Kloet et al. 2005) has shown to have long-term effects on the offspring regarding its behavior and reproductive functions, as well as the immune, neuroendocrine and autonomic systems. The development of the nervous system in an animal or a human is a dynamic process and depends largely on the individual’s interactions with its environment before as well as after birth and this hence influences the behavioural development (Gazzano et al. 2008). Many altricial species (i.e. species that require care or nursing after hatching or birth), such as dogs are born in a state of large neural immaturity, but the nervous system rapidly develops via an intense synaptogenesis in which external stimulation plays an important role
(Gazzano et al. 2008). Both altricial and precocial (i.e. young that are able to move around and forage at a very early age) species are sensitive to influences before birth through hormones via placenta, for instance has Braastad et al. (1998) shown that maternal stress during the last third of pregnancy has postnatal effects on adrenal function in the offspring of blue fox. The prenatal period hence seem to be a potential time for formation of alternative outcome at least regarding the influence of prenatal stress, but other cues might work the same way. During the early development a significant neurological growth and differentiation takes place during which environmental influences can have profound, lasting effects on the animal’s behavioural repertoire (Rosenzweig 1984). Post partum various circumstances such as physical stress, diseases, naturally occurring variations in maternal behaviour i.e. licking, grooming and nursing can all contribute to altered neurological development (Chapillon et al. 2002) but just as deprivation and stressful conditions can produce negative effects, many events can also operate positively on ontogenesis (Gazzano et al. 2008). In the early postnatal period, the mother composes the primary environmental cue to her young and she is able to modify their behaviour adaptively to their future environment (Champagne et al 2003). According to Beattie et al. (1995) is the behaviour of the growing pig influenced by the environment in early life and is further retained throughout the life.

The early experiences of human - animal interaction also affects the animals social, emotional and cognitive development and some works suggest that the presence and behaviour of the mother could play a part in the offspring’s socialization to humans in mammals such as dogs (Freedman et al 1961), sheep (Boivin et al 2001; 2002), goats (Ruiz-Miranda and Callard 1992) and horses (Hausberger et al. 2008).

In recent years numerous studies focusing on early experiences have been carried out in order to examine and understand how early experiences affects the behaviour of the adult animal (Gazzano et al. 2008). Johnsen et al. (1998) saw that conditions during the first four weeks of life had a major influence on the subsequent development of the feather pecking in laying hens. Chicks reared on wire for the first four weeks developed sever feather pecking compared to controls (i.e. chicks reared on sand and straw) although they had access to sand and straw from the fifth week of life. Further did the experimental group (i.e. the wire birds) show more cases of cannibalism, higher mortality rates, more damaged plumage, were more fearful and laid fewer eggs compared to controls. Johnsen et al. (1998) suggests that since the dust bathing behaviour develops during the first weeks of life (Huber-Eicher and Wechsler 1998) feather pecking may develop as a mis-imprint on feathers as a substrate for dust bathing behaviour, when reared on wire or in highly dense populations.

It is hence more or less clear that early experiences, such as potential human interaction, differences in rearing condition and maternal care and exposure to stressful events could have an impact of the future behavior.

**Stress**

**The physiological respons**

In their natural habitats, animals have to cope with a variety of stressors and adjust to their biotic (e.g. predators, food availability, interaction with members of the same species) and physical environment (e.g. weather), specific for their ecological niche (Kaiser and Sachser 2009). The primary
function of the stress response is to cope with environmental changes and stress can be defined as the state of an animal when it is not able to act in accordance with its motivational state (Jensen and Toates 1997). A stress response starts as a potential threat to homeostasis (the regulation of the body to a balanced state) and is perceived from internal or external cues by the central nervous system (CNS). Whether or not there is an actual threatening stimulus present or not is irrelevant, it is only the perception of a threat that is critical for the stress response to occur (Moberg 2000). Once the CNS perceives a threat, it reacts with a biological response that consists of some combination of the four general biological defence responses: the behavioural response, the autonomic nervous system response, the neuroendocrine response and the immune response (Moberg 2000).

The behavioural defence response may contain just a removal by the animal away from the threat. For instance seek shade when body temperature arises due to sun exposure. During stress the autonomic nervous system affect a number of biological systems, such as the metabolic system, the cardiovascular system, the gastrointestinal system and the reproductive system (Sapolsky 2002). In the case of the metabolic system, two adaptive metabolic responses take place to mobilize energy for immediate use, when faced with an acute physical stressor. First does the body shut down the store away process of energy substrates already in the bloodstream and second does it get access to previously stored away energy and converts it back to circulating energy substrates (Sapolsky 2002). It is the catecholamine secreted from the adrenal medulla during stress that convert the glycogen to readily utilizable glucose or other metabolic products necessary for gluconeogenesis (Moberg 2000). When a stressor is perceived by the brain the cardiovascular tone also increases. Blood pressure and heart rate rise and parts of the circulatory system shuts down and shunt the blood to the organs and muscles that needs it the most. Other features of the autonomic nervous system stress responses are the inhibition of the reproductive physiology and behavior and the suppression if inflammation and pain perception. The autonomic nervous system responses are thus often understood to have an adaptive role called the fight or flight response (Cannon 1929). By mobilizing energy reserves and shutting down some systems and up regulate others, the body allocate its resources to what is really important, namely survival (Mendl 1999). It is of no use to invest in expensive systems like reproduction if you are for instance under an attack of a lion. Then it is best to prepare the body for fight or flight in order to survive (Moberg 2000). The complex neuroendocrine system i.e. the hypothalamus-pituitary-adrenal (HPA) response to stress, involves the release of many different hormones which circulates through the bloodstream to stimulate its target cells in the heart, the liver, the skeletal muscles, the adrenal glands, the adipose tissue and the brain (Brown 1994). Very simplified one could state that a perceived stress stimulus causes the hypothalamus to release corticotropin releasing factor, CRF (also called corticotropin releasing hormone, CRH) and vasopressin which enter the hypothalamic-pituitary portal circulation and triggers the pituitary gland to release adrenocorticotropic hormone (ACTH). ACTH then stimulates glucocorticoid release from the adrenal cortex and causes the adrenal medulla through sympathetic stimulations to release catecholamine known as adrenaline (epinephrine) and noradrenalin (norepinephrine) (Brown 1994). Glucocorticoids are different forms of steroids, of which cortisol is the dominant form in primates and most other mammals, whereas corticosterone is the equivalence in rodents and birds. Glucocorticoids and catecholamines together mediate most of the changes during the stress response (Sapolsky 2002).

The brain is hence an important target organ of stress hormones (i.e. cortisol, CRF and ACTH) and the brain is the key organ of stress processes. It determines what is to be considered a stressor to an
individual, it orchestrates which coping strategy an individual will use, and the brain changes both structurally and functionally as a result of stressful experiences. Within the brain, a distributed, dynamic, and plastic neural circuitry coordinates, monitors, and calibrates behavioral and physiological stress response systems to meet the demands imposed by particular stressors (McEwan and Gianaros 2010). The influence of stress hormones thus leads to changes of the molecular biology of the cell. This in turn leads to changes in neural connectivity and gene expression and as a consequence leading to changes in cognitive functioning, memory and learning processes but also to changed activity of the neuroendocrine system itself (Kloet et al. 2005). Empirical research on the relationship between stress and cognitive function e.g. the attention and memory processes reveals that excessively high or prolonged elevations of circulating glucocorticoids and catecholamines can lead to memory disruption, while low or moderate concentrations of these hormones can enhance memory formation (Mendl 1999).

**The nature and timing of stress**

Many mammalian species, including humans, live in social interactions with others. Disturbed social relations have been shown to be one of the strongest stressors. Studies in free-ranging social groups of animals indicate that the stability of the social environment is a very important factor in health and disease (Koolhaas et al. 2006). Crucial to survival in nature is also the predictability and controllability of for instance food availability and also the effort required to obtain food. Changes in food availability or in work load to obtain food are considered to be major stressor as well (Koolhaas et al. 2006). Other ways of inducing stress to an animal is by predation pressure or by human interaction where human interaction is not always considered a positive experience but a rather stressful one.

Apart from the nature of the stressors, its duration, the time it is issued, the intensity and frequency are also important factors. Several biological functions rely on critical timing to occur and acute stressors such as restraint, transportation or isolation have been found to disrupt for instance the events surrounding ovulation (Moberg 2000). Different individuals also possess individual coping styles and coping capacity including genotype, age, previous experiences etc. (Koolhaas et al. 1999). Stress can serve as an adaptive function and the stress response is likely to be a trade-off between benefits and costs in both short- and long term seen from the pathology and reduced evolutionary fitness point of view. A chronic state of stress can hence cause maladaptive behaviour and result in impaired cognitive ability and physical as well as psychological disorders (Kaiser and Sachser 2009). Allostasis is a concept described by for instance Korte et al. (2005), and which is used to explain the dynamic interaction between an organism and its environment. It can be described as the process by which homeostasis is achieved through behavioural or physiological change, and carried out for instance by means of alteration in the HPA axis as a response to stress. Natural selection has designed behaviour and physiology to meet the most common environmental demands plus a small safety margin and serve as an adaption to environmental changes. But elevated activation of the allostatic mechanism during long periods of time can produce a chronic deviation from the normal level of the regulatory system and different pathologies may develop (Koolhaas et al. 1999).

Stress can be executed either as prenatal induced stress or postnatal stress. In both cases the effect on the animals can be subscribed to both the mother and the offspring. As for prenatal stress in rats, females exposed to gestational stress during pregnancy showed increased retrieval latencies (Kinsley
Foyer, P: Early experiences and adult behaviour

and Bridges 1988). And Champagne et al. (2003) examined how gestational stress effected maternal behaviour in previously defined High and Low LG-ABN mothers (i.e. mothers that performs relatively high or low levels of licking and grooming and arch-backed nursing). They found that High LG-ABN mothers exposed to restraint stress during the last half of gestation decreased the frequency of maternal licking/grooming and arched-back nursing, but that the Low LG-ABN mothers did not. Further they found that the effects were fully evident also in the third litter even in the absence of any further stress, reflecting a potent and transgenerational effect. These results suggest that stress increases anxiety and fearfulness in the mother and thus decrease maternal responsiveness, which in turn influence the development of stress response in the offspring. As for the offspring, the development of different behaviours and the neural systems mediating these behaviours remains highly plastic during the early developmental phase. Many complex traits are probably shaped both by genetic, epigenetic and environmental factors. These factors interact dynamically at different periods of time in life, including the prenatal period via intra-uterine mechanisms, the early postnatal period via maternal factors and post weaning period through physical (e.g. environmental enrichment) and social factors (Holmes et al. 2005). Studies have shown that offspring to High and Low LG-ABN mothers also differs in behavioural responses to novelty (Caldji et al. 1998). As adults, offspring of Low LG-ABN mothers showed an increased startle response, decreased open-field exploratory behaviour and a longer latency to eat food provided in a novel environment. Results from cross fostering studies (i.e. biological offspring of High LG-ABN mothers reared by Low LG-ABN mothers were significantly more fearful under novel condition than offspring reared by High LG-ABN mothers) have shown that individual differences in fearfulness or maternal behaviour mapped onto those of the rearing mother rather than to the biological mother (Meaney 2001).

One disputable but interesting theory is the possible occurrence of parental programming of the fetus. Particular maternal hormonal responses to different environmental stimuli can alter the phenotype of the offspring (Kaiser and Sachser 2009). The results on intergenerational transmission via maternal behaviour could serve an adaptive approach to development (Meaney 2001), since the offspring usually inhabit a niche that is similar to their parents. Groothuis et al. (2005) have shown that maternal androgen deposition in avian eggs provides a flexible mechanism of non-genetic inheritance, by which the mother can favour some offspring over others, and adjust their developmental course to present environmental conditions, producing different phenotypes. Under conditions of increased environmental demand, it is utterly important for the animal to enhance its behavioural (e.g. vigilance, fearfulness) and endocrine (HPA and metabolic/cardiovascular) responsivity to stress. These responses are essential under increased demands of the stressor, as they promote detection of potential threat and avoidance learning. This process of transmission across generation is also known as the epigenetic factor.

Handling

Human-animal interactions can involve visual, olfactory, auditory perception or tactile human contact. The interaction may be perceived as negative, neutral or positive by the animal (Waiblinger et al. 2006). In some cases, when the animal does not perceive the contact as positive it can cause a stress response that in turn can influence the neurobiological development and later behaviour of the animal. However, a number of studies have shown that visual contact and regular handling by humans can be effective methods in reducing fear of human in many domestic species such as poultry, cattle, sheep, pigs, horses, rabbits and silver foxes (for review, see Jones, 1996).
The human-animal interaction can also be performed in an experimental process known as neonatal handling. Neonatal handling involves daily short (i.e. 3-15min) periods of separation of the pup from the mother for the first few weeks of life and already in 1967 Levine et al. demonstrated that such brief separation of rats from their mother had long-term positive effects on the offspring’s as adult, where the separated rats were less reactive, more explorative and more emotionally stable compared to controls. Levine later hypothesized that, for rodents, early handling followed by an increase in maternal care was responsible for this behavioural response and later studies by Liu et al. (1997) and Macrí et al. (2004) support this hypothesis and showed that the consequence of neonatal handling is associated with elevated levels of active maternal care and reduced behavioural and HPA responses to stress in the adult offspring.

Longer periods (3-6h) of daily separation from the mother does on the contrary increase fear and stress responses in the adult offspring (Plotsky and Meaney 1993); (Macrí et al. 2004). Macrí and Würbel (2007) have shown that small changes of maternal environment (food location) without direct human interaction, as in ordinary neonatal handling studies, are able to modify the pattern of maternal behaviour and nest attendance, and that this environment-dependent variation in maternal behaviour also resulted in altered behavioural and HPA responses to stressors in the adult offspring. As a rule however, neonatal handling and mildly stressful stimulation in rodents favorably changed their behaviour as adults, as they became less susceptible to stress (Valleé et al. 1997) and further, in stressful situations, they showed a lower activation of the HPA axis compared to control (Levine et al. 1967); (Plotsky and Meaney 1993).

As for rodents, neonatal handling seems to affect dogs as well. Puppies are born in a state of large neuronal immaturity, but the nervous system rapidly develops via an intense synaptogenesis in which external stimulation plays an important role (Gazzano et al. 2008). This study on early handling in dogs by Gazzano et al. (2008) also support the existence of a positive effect of neonatal handling on emotional stability of puppies, but additionally it also suggests that this effect is influenced by the environment. It is also however uncertain if the difference seen in the puppies is consistent to adulthood since the puppy test was performed only on 8-week-old puppies. Wilsson and Sundgren (1997) found that the correspondence between puppy test result and performance at adult age was negligible. If handling have the same effect in dogs as in rats it is likely that the effect is mediated not by the handling procedure itself but by the fact that handled puppies achieve more maternal attention. If that would be the case we would assume that increased maternal attention might be mediated also by other factors. Welker (1959) found that the behaviour of neonate puppies changed according to the temperature in the whelping box. Low temperature not only made puppies aggregate in order to decrease heat loss, it also made them more sensitive to tactile stimulation. Wilson and Sundgren (1998), also found that puppies born in the winter and resting on corrugated cardboard had 15% lower 50 day weight than puppies born in the summer and during a period when soft-pile blankets were used in the nest, winter puppies were 5% heavier (p<0.01). Puppies raised on corrugated cardboard also scored higher in “nerve stability” at 15-18 month of age when tested. The general opinion in the breeding kennel was that puppies resting on soft-pile blankets were less active and slept more and achieved less maternal attention than puppies resting on corrugated cardboard.

The timing of handling and maternal deprivation is crucial for the long-term effect as well. Results from studies in pigs suggest that a sensitive period in postnatal development exists when environmental manipulations can cause long lasting changes in behavior, and likely in underlying
neural correlates (Siegford et al. 2008). van Oers et al. (1998) showed that in rats, maternal separation at the beginning of the stress hypo-responsive period (SHRP) e.g. a period of low stress system activity in rodents that lasts for about the first two weeks post partum (Sapolsky and Meaney 1986) may have very different long term consequences as the same treatment towards the end of the SHRP. In a study with a single 24-h mother pup separation period van Oers et al. (1998) got results that indicated that especially at the beginning of the SHRP the stress system of the pups is vulnerable to external disturbance and the separated pups showed a persistent alteration of the HPA axis. Besides neonatal handling, which is one of two different models historically used when studying stress and maternal care, prolonged maternal separation (Kloet et al. 2005) is another commonly used technique. In research that use prolonged maternal separation the stress response seems to be activated via metabolic signals due to the lack of nutrition and that the initial activation of the HPA axis occurs during the first 8 h of maternal absence (Kloet et al. 2005). (2006) have shown that prolonged maternal separation causes an up regulating effect of the stress response in the offspring due to environmental stressors, and repeated prolonged neonatal mother offspring separation is a technique used to increase susceptibility to mood and anxiety disorders in rodent models for human psychiatric conditions (Newberry and Swanson 2008).

**Mother-offspring Interaction**

In mammals the neonatal period is a time of significant social interaction. This is true even in solitary species as females spend a significant amount of time nursing and caring for their offspring. In social species interactions may also include the father, older siblings and extended family members (Cushing and Kramer 2005). The development of social behaviour is hence influenced by the social environment and begins shortly after conception and proceeds throughout an individual’s life. Although behaviour may be somewhat plastic, some periods seems to be more critical to when an individual is susceptible to long-term alteration of behaviour (Cushing and Kramer 2005). The early postnatal period is considered to be such a critical period in the development of social behaviour sustained as adult (Francis et al. 1999). One classical example of infant-mother attachment is the visual imprinting shown by newly hatched goslings. Within a discrete developmental window the young goslings respond to a particular stimulus normally provided by the parent and this becomes permanently associated with a particular response (i.e. when seeing a large moving object the gosling learns to recognize and follow its mother). The same goes for rodents, primates and even guinea pigs, where there appears to be a strong maternal influence of subsequent social behaviour of their offspring (Cushing and Kramer 2005).

The neonatal period is also a time of significant development of the brain, including organization of the central nervous system (CNS), and therefore a time when the degree and type of social interaction influences the development and expression of social behavior (Cushing and Kramer 2005), as well as the stress response (Liu et al. 1997) in adulthood. The social attachment, as described by Insel and Young (2001), is a behavioural process that involves multi-sensory processing (predominantly olfactory in rodents and visual in primates and birds) and complex motor responses (for example, proximity seeking, nurturing responses and defensive behaviours). Other factors than neurobiological that could influence normal maternal behaviour are as already discussed stress. But also litter composition, litter size, earlier maternal experiences, housing and management routines in the laboratory animal facilities, which are often standardized and designed for hygiene and does not always take the animals need for natural behaviour into consideration (Weber and Olsson 2008) as
well as other environmental and genomic factors (Kikusui et al. 2008) could all have an effect on maternal behaviour. Studies with mice have shown that females nursing mixed litters spent more time on maternal behaviours and seemed to wean later (Mendl and Paul 1990). Priestnall (1972) found that females rearing large litters spent less time on maternal behaviour and (Brown et al. 1999) found that survival rate and weight gain improved as mothers became more experienced.

Other biological functions such as the release of a number of neuropeptides (e.g. oxytocin and arginine vasopressin) and gonadal steroids (e.g. estrogen) opioids and other neurotransmitters released at parturition and during suckling, promote the development and maintenance of maternal bonding and maternal care and further influence the expression of behaviours such as affiliation, aggression, sociosexual behaviour and responses to stress (Cushing and Kramer 2005); (Keverne and Curley 2004). It seems for instance like oxytocin released during lactation, mediates the activation of the reward system involving dopamine and opioids as a direct response to the social contact during the act of maternal care (Insel and Young 2001); (Insel 2003). Oxytocin also facilitates learning in rat pups when the association is to social cues, such as the mother, but it fails to alter learning associated with non-social stimuli (Insel and Young 2001). And further, in rodents so called High LG-ABN mothers produce daughters with elevated production of oxytocin and increased expression of oxytocin receptors, while their sons have an elevated production of vasopressin and vasopressin receptors. The offspring of High LG-ABN mothers also show a more modest HPA response to stress as adults (Liu et al. 1997). In addition these changes have long term effects on the following social and sexual behaviour, producing daughters that display less anxiety-related behaviours and higher level of maternal care as adults and sons that exhibit more aggression towards other males as adults (Cushing and Kramer 2005). Rats from High LG-ABN mothers also display a higher spatial learning and memory ability compared to the offspring of low grooming mothers (Liu et al. 2000). Other studies by Champagne et al. (2001) and Francis et al. (2000) also suggest that oxytocin receptor levels are functionally related to differences in licking/grooming. They have shown that central infusion of an oxytocin receptor antagonist (OTA) on day 3 post partum significantly reduces licking/grooming in high, but not low LG dams. Variations in hormonal levels appear to have an especially important influence on brain development during the fetal period. This so-called programming from the early hormonal effects influences the structure of the brain and their effects can be long lasting if not permanent (Weerth et al. 2005).

The social bond between the mother and the offspring are developed within hours after parturition (Newberry and Swanson 2008) and it is a neurobiological mechanism that underlies this mother-young bonding. The onset, maintenance and termination of maternal care are also tightly linked to maternal physiology and synchronized with the mother’s ability to provide nutrient until the offspring is able to fend for itself (Keverne and Curley 2004). As a response to the close proximity following tactile contact, food sharing and allogrooming between bonded individuals is a reduction in heart rate and endogenous opioids (Keverne et al 1989). The maintenance of this close proximity between mother and offspring also provides opportunities for social transmission of information about predators and food sources (Mateo and Holmes 1997). Variations in strength and duration of mother offspring attachment are observed across as well as within species, but in general, these differences are predicted to reflect differences in life history strategies and local selection pressures (i.e. r- and K-selection theory) (Newberry and Swanson 2008). The quality of maternal care during the neonatal and lactating period is also important. The famous social deprivation study with the use
of surrogate mothers in rhesus monkeys by Harlow (1958) demonstrated that a young rhesus needs social experience to develop normal social behaviour. But he also showed that if maternal deprived rhesus infants were allowed to interact with other such infants for 15 minutes each day, they developed nearly normal social behaviours as adults. Maestripieri (2005) has shown that female rhesus monkeys reared with inadequate maternal care display more aggression, are more likely to withdrawn from novel social interactions and are more likely to neglect or abuse their own offspring as adults.

The mother-offspring relationship during the neonatal phase is likewise an important factor in the so called HPA stress response (Liu et al. 1997). In rodents, the strategies animals use to cope with stress as adults are affected by the amount of maternal care received during their early development. Neonatal handled rat pups received more maternal care than non handled pups and the handled pups responded less intensely and for shorter periods of time to restraint stress as adults compared to non handled pups (Liu et al. 1997); (Macrí et al. 2004). The mother offspring bonding that occurs shortly after birth is typically succeeded by the gradually development of independence of the young from the mother’s milk supply and associated maternal care (Newberry and Swanson 2008). In nature, weaning is one of the most important events that occur in developing animals and the timing of natural weaning is largely dependent on environmental resources during the nursing period and some conflict between mother and offspring usually occurs about the timing of weaning, where the mother is attempting to terminate it while the young attempts to extend it. In the domestic dog, the nursing frequency usually declines from 2 to 7 weeks post partum and a tendency for increased aggression from the mother to her pups (Malm and Jensen, 1997). Under human management, the young mammalian species in laboratory or production are typically separated abruptly and permanent from their mother earlier than the timing for weaning in nature (Newberry and Swanson 2008). The disruption of mother-infant bonding can induce an increased neuroendocrine stress response as well as behavioural responses (Kikusui et al. 2008).

Epigenetics
Parental effects are a major source of phenotypic plasticity and may in concert with environmental demands influence offspring phenotype. There is evidence for parental effects on multiple phenotypic outcomes, including growth, reproductive tactics and defensive responses (Kappeler and Meaney 2010). The hypothesis that intergenerational transmission via maternal behaviour could serve to be adaptive also take into account that various levels of environmental demand require different traits in the offspring. For example, in cases where the threats experienced by the parents predict those likely to be encountered by the offspring, the parental behaviour should function in the direction of endowing the offspring with an appropriate level of defensive responses (Meaney 2001). As such, licking and grooming in the rat may serve to transmit information regarding the quality of the maternal environment to the offspring and further to help regulate the expression of defensive responses in a manner that provides a certain measure of “preparedness” relevant to face that environment (Champagne, Francis et al. 2003). This non-genomic mechanism that underlies the transmission of behaviour across generation and that refers to a functional change to the genome that does not involve an alteration in nucleotide sequence in known as the epigenetic factor (Kappeler and Meaney 2010).
Foyer, P: Early experiences and adult behaviour

Epigenetics on the molecule level is an alteration of the expression of genes via DNA modifications without changing their coding sequence (Holmes, Guisquet et al. 2005). Two processes have been indicated that could be involved in that process, methylation of promoter regions on specific genes and deacetylation of related histone (Weaver, Cervoni et al. 2004).

(Weaver, Cervoni et al. 2004) found that maternal behaviour permanently alters the development of HPA responses to stress through tissue-specific effects on gene expression in the rat. Their result showed that offspring to High LG-ABN mothers had differences in DNA methylation of the exon 1, promoter of the GR gene in the hippocampus compared to offspring of Low LG-ABN mothers. In rats, offspring to Low LG ABN mothers had reduced GR expression in the hippocampus, indicating a decreased negative feedback loop by glucocorticoids and an elevated HPA axis activation in response to stress. These findings along with results from a cross fostering study suggests that the group difference in DNA methylation occurs as a direct function of maternal behaviour in the first week of life. Thus, maternal effects could result in the transmission of adaptive responses across generations and among mammals natural selection may have shaped offspring to respond to such subtle variations in parental behaviour as a cue to the future environmental conditions they will experience (Meaney 2001).

Summary
Taken together data from several tests in the above shortly described topics show that the postnatal period is a sensitive period of the organization and development of the brain and also that changes in the environment could alter the development and expression of various behaviour in the adult offspring. It has also been emphasized that maternal care matters and that alterations of maternal care during the development affect the function of the individual during adulthood. Further has it been suggested that variations in maternal behaviour serves as a mechanism for the non-genomic transmission of individual differences in stress reactivity across generations and that this may have an adaptive value.

References


Foyer, P: Early experiences and adult behaviour


Foyer, P: Early experiences and adult behaviour


