Scand. J. Lab. Anim. Sci. No. 1. 1997. Vol. 24

The effect of oral corticosterone, prolactin and prolactin deprivation on weight gain and locomotor function in neonatal rats

by *Angela Kerton & Jann Hau**.
Department of Comparative Medicine, Uppsala University, BMC, Box 570, 751 23 Uppsala, Sweden
*Correspondence to Professor J. Hau.

Introduction

Approximately 10% of women suffer from non-psychotic depression during the first few months following childbirth (*Murray and Stein,* 1989). Post-Partum Depression (PPD) has been strongly linked to stress-factors in several studies (*Caplan et al,* 1989), with serum cortisol levels being significantly increased. Total, free cortisol levels and corticosteroid-binding globulin increase in the circulation and then fall precipitously within the first few days post-partum (*Hau et al,* 1983; *Cousins et al,* 1985). Ovarian steroid serum levels also fall dramatically post-partum. However, other hormones including prolactin and oxytocin are secreted in large bursts following parturition (*Wieck,* 1989).

Although the link between corticosteroids and stress is generally accepted, the link between PPD and cortisol is more contentious. Not all studies have demonstrated increased cortisol in women suffering from PPD (*Handley et al,* 1977; *Ballinger et al,* 1982; *Kueri et al,* 1983). There are several possible explanations for this inconsistency. Firstly, steroid levels in chronic stress are often normal due to feedback inhibition. In addition, in most of the above studies, only single samples were taken. Cortisol is released in a pulsatile manner and plasma levels are highest in the morning, decline throughout the day and rise again during sleep. This implies that serial samples over 24 hours is more appropriated to establish a reliable plasma corticosteroid profile. Finally, PPD could be caused by other hormonal imbalances or a combination of inappropriate hormone levels perhaps involving prolactin (PRL), ovarian hormones, their receptors in the brain and dopamine neurotransmission.

During pregnancy there is a gradual and progressive increase in PRL serum concentrations until term, when the levels are about ten times higher than during the menstrual cycle (*Tyson et al,* 1972). They remain remarkably high in the early puerperium, but non-breast-feeding mothers return to the prepregnant range by about the third week postpartum (*Tolis et al,* 1974). In regularly nursing mothers, basal PRL levels slowly decrease as lactation progresses, the rate of decline depending on the frequency of breast-feeding (*Howie et al,* 1981). *George et al* (1980) measured basal serum PRL levels in 38 women during the first post-partum week and reported a significant positive correlation with symptoms of depression, anxiety and tension as elicited by a standardized psychiatric interview. *Alder and Cox* (1983) reported that full breast feeding appeared to increase the risk of being depressed up to 3-5 months post-partum. The mothers who were least likely to be depressed were those considered to have normal levels of endogenous hormones i.e. the non-pill taking partial breast feeders. Mothers fully breast feeding would have high levels of prolactin and low levels of circulating oestrogen and progesterone. In contrast, *Harris et al* (1989), found significantly lower PRL levels in six breast-feeding mothers with depression, than in 12 breast-feeders who remained well. In this study sampling time was not controlled with regard to the last breast feed. This is important since suckling induced PRL secretion remains at a high level for at least 120 minutes after feeding has begun (*Noel et al,* 1974).

In lactating mammary epithelial cells, prolactin binds to its receptors, is endocytosed and carried to the milk (*Ollivier-Bousquet et al,* 1993). In women, work done in 1950s revealed that milk prolactin levels are approximately equal to serum

levels. The presence (or absence), of several hormones in milk occurring either by passive diffusion or by active transport can be of great importance to the neonate. There is good evidence for a link between depressive disorders in mothers and emotional disturbances in their children (*Billing & Moore,* 1983 and *Pound et al* 1985). This link is usually attributed to decreased quality of maternal care. There are reports on an increased frequency of psychiatric disturbance, greater insecurity in attachment relationships, impairments in attention and lowered IQ in offspring of depressed mothers (*Weissman et al,* 1972, 1984; *Gamer et al,* 1977; *Welner et al,* 1977; *Grunebaum et al,* 1978; *McKnew et al,* 1979; *Cox et al,* 1987; *Field,* 1984; *Field et al,* 1985, 1988). Babies are usually bottle fed once PPD is diagnosed because their mothers are treated with anti-depressants, but it often takes 6 months for a diagnosis to be made by psychological scoring systems. Were a hormonal link to be discovered it might be possible to diagnose PPD earlier and avoid possible harmful effects on the child.

In mammals, prolactin (PRL) is associated with learning, stimulation of the immune response, reduction of body temperature and the behavioural aspects of reproduction (*Sobrinho,* 1993). Accumulated evidence in human medicine suggests that certain immunoregulatory hormones including prolactin may play a role in the pathogenesis and disease expression of certain autoimmune diseases (*Jara et al,* 1994).

Animal studies have demonstrated that milk borne prolactin plays a role in neonatal immune cell maturation (*Grove et al,* 1991). Deprivation of the neonate of milk-PRL on days 2 -5 postpartum, reduced both thymocyte and splenocyte responsiveness to polyclonal mitogens. Milk borne PRL has also been shown to be important in the development of the neonatal neuroendocrine regulation of endogenous PRL secretion (*Grove et al,* 1991).

The permeability of the gut of the rat pup is very high in early postnatal life until 17 – 18 days of age when it decreases rapidly and *Grove et al* (1991) suggested that prolactin is able to cross the gut wall until day 21.

Rat pups born to stressed mothers have been reported to be of lower birth weight (*Benesova and Pavlik,* 1989), gain weight more slowly (*Kinsley and Svare,* 1988) and exhibit poorer locomotor control than pups born to non-stressed mothers (*Benesova and Pavlik,* 1989; *Pavlovska-Teglia et al,* 1995; *Young et al,* 1996). *Pavlovska-Teglia* (1995) and *Young et al* (1996) showed that even relatively low levels of corticosterone have a significant negative influence on the maturation and learning ability of the neonatal rat pup. This indicates that the glucocorticoid levels to which suckling neonates, such as children of PPD women, are exposed to in their early stages of neuronal development, may modify the normal development of the complex integrated neuromuscular adaptive mechanisms involved in the normal development of locomotor apparatus.

The aim of the present project was to investigate the effects of oral corticosterone and both lowered and increased milk-borne PRL concentrations on neuromuscular development (assessed by swim testing) and daily weight gains of offspring born to laboratory rats. To induce these conditions the lactating female was treated with bromocriptine, a dopamine agonist, to reduce PRL levels, or rat pups were dosed daily by gavage with PRL or corticosterone.

Materials & Methods

Animals

The progeny of primiparous females of the LEWIS inbred strain of rats were used. The females and their litters were maintained in a conventional animal facility. The lighting was 12h: 12h light-dark cycle. The temperature was 22 ± 1°C, and humidity was 55 ± 5%. All the animals were supplied with bedding, (Lignocel, UK, Grade 10). A diet for breeding mice (SDS, UK) and tap water was available *ad lib.* All females were housed singly.

On the day of parturition (designated day 0), the pups were weighed and marked (using Ofrex bullet-tip markers). Each pup was randomly allocated to one of two or three test groups within each litter. Total dose volume was 50 microliters for all groups; administered by gavage from day 2 to day 15. Weights were determined at 10.00 am each morning, prior to gavaging.

Bromocriptine and vehicle treatment of adult lactating females.
Two females (average weight 270 -300g) were treated from days 2 to 15 post-partum with either 0.1ml 1% ethanol subcutaneously or 2ug (0.1ml volume) bromocriptine(Sigma Chem. Co. batch no. 83H0799) subcutaneously from days 2 to 4 and subsequently increased to 4ug/rat/day bromocriptine from days 5 to 8 and then 12ug/rat/day for the remaining of the dosing period. Bromocriptine solutions were diluted daily from stock solution (4mg bromocriptine in 2ml 100% ethanol) using sterilised water as a vehicle. The dose of 2ug per rat was calculated as being 1/10th of the dose required to stop an adult female rat lactating based on the dose rate used in veterinary medicine for the treatment of pseudopregnant bitches. Previous work with rats (*Russel et al.* 1981; *Flint & Ensor,* 1979), reported doses between 2mg/kg and 4mg/kg effective in suppressing prolactin secretion (control serum prolactin 98ng/ml; treatment group 29ng/ml) and reducing or terminating milk secretion. The dose of 2ug to 12ug per rat per day lowers serum prolactin levels without interrupting lactation.

Corticosterone treatment of pups.
Corticosterone (Sigma Chem. Co. Ltd. UK, batch no. 103H0660) solutions were diluted from stock solution (1.8mg corticosterone in 112.5ml of propylene glycol solvent) using almond oil as a vehicle. The doses were calculated on the basis that both human and rat milk have been reported to contain corticosteroid concentrations of around 200ng/ml (*Alexandrova & Machol,* 1983). *Pavlovska-Teglia et al.* (1995) showed that supplementing the pups with an extra 200ng of corticosteroid per ml of milk intake had the same retarding effect as a dose equivalent to 400ng/ml. The lower dose was therefore used in the present study. Both human babies and rat pups have a milk intake of about 0.15ml per g body weight each day, and the concentration of corticosterone solution required was calculated according to body weight.
Both *Pavlovska-Teglia et al.* (1995) and *Young et al.* (1996) reported no significant difference between vehicle treated pups dosed with 50 microliters of purified almond oil per day and the untreated control group. Consequently a vehicle treated pup group was not included in this study. Gavage tubes were made to fit the size of animal, by modifying 0.6 X 30mm; 0.9 X 40mm and 1.2 X 40mm hypodermic needles. The sharps were sanded off and epoxy-glue (Araldite) was used for making the bulbs, necessary for performing a safe intragastric administration.

Prolactin treatment of pups.
Ovine prolactin (Sigma Chem. Co. Ltd. UK, batch no.93H0467) was diluted from a stock solution (250 International Units ovine prolactin, presuming a mean activity of 8.5mg by bioassay, in 500ml sterilised water) using distilled water as vehicle. Each pup was supplemented with an extra 140ng/ml prolactin per ml milk intake, calculated as previously described for corticosterone, according to body weight and hence age. The dose of 140ng prolactin per ml milk intake, was based on previous work concerning serum levels of prolactin in breast-feeding women and lactating rats (*Amenomori et al,* 1970; *Caron et al,* 1994; *Flint & Ensor,* 1979; *Noel et al,*1974).
Noel et al. (1974) reported that in the first 6 weeks post-partum breast-feeding mothers had elevated serum prolactin levels of 29.6ng/ml (normal basal level <24ng/ml), 30 minutes before nursing commenced, rising to 252ng/ml (8.5 X normal basal level), during suckling and then gradually returning to the normal basal level over a 120-180 minute period after termination of feeding. A study by *Buckman & Kellner* (1984) found elevated levels (150.2ng/ml) of serum prolactin in women with signs of depression, hostility and anxiety. Female family practice patients with no psychological symptoms had serum prolactin levels between 4 to 27ng/ml. Serum levels in lactating rats are similar to those of women (*Amenomori et al,* 1970), with levels of 65.5ng/ml prolactin on the first day post-partum decreasing to 25.7ng/ml during the next 15-23 days. The maximum serum level recorded in this study was 130.3ng/ml after the lactating mother rat had been separated from her litter for 12 hours. Consequently, the dose of 140ng prolactin per ml milk intake used in this present study represents a mean value of serum prolactin recorded from lactating rats and a similar level would be recorded

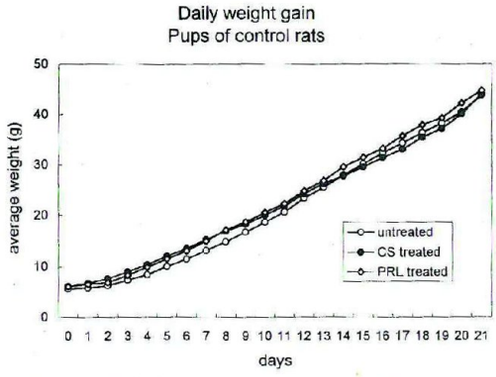

Figure 1a: Weight gain of rat pups in the three experimental groups: untreated, CS treated and PRL treated for the combined control and vehicle treated mother.

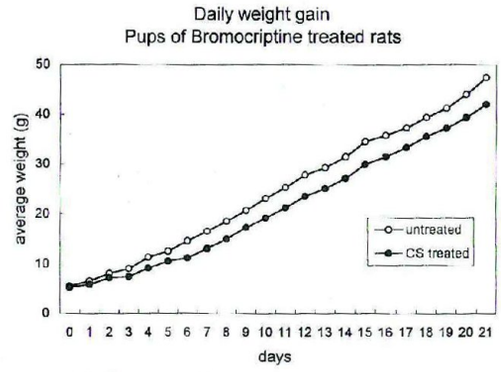

Figure 1b: Weight gain of rat pups in the two experimental groups: untreated (low PRL) and CS treated for the BrCRP treated mother.

in breast-feeding women during the gradual declining phase of prolactin secretion after termination of each nursing period.

Swim Test

Swim tests were carried out from day 7 to day 21 at 12pm as described by *Pavlovska-Teglia et al.* (1995). In brief, the test consisted of placing the pup into an aquarium for 5 to 15 seconds depending on age and ability. A 47x51x41cm aquarium was used. It was filled to a depth of 15cm and maintained at 35-37°C. Swimming ability was evaluated by a rating systems used by *Young et al.* (1996). The swim tests were recorded on video camera and scored by two different observers.

Collection of serum from lactating female rats

Individual blood samples (1.5ml) were taken on day 22 by cardiac puncture during euthanasia. The serum was stored at -20°C until assayed within 2 weeks.

Radioimmunoassay

Serum prolactin levels were measured by enzyme immunometric assay (Milenia Canine Prolactin, Hermann Biermann GmbH Diagnostica, Bad neuheim, Germany) designed for quantitative measurement of prolactin in canine serum.

Statistical methods

Statistical tests were carried out using the "MINITAB" statistics computer program. A Friedman test was used to compare the five pup treatment groups for each variable by way of a nonparametric two-way analysis of variance.

Results

Daily weight gain was found to be significantly ($p < 0.05$) greater in untreated pups than in treated pups (Figure 1). The progeny of both vehicle treated and control mothers were combined for analysis as there was no significant difference in locomotor development between the two control groups.

Rat pups exposed to various differing hormone levels (corticosterone treated, prolactin treated, prolactin deprived and prolactin deprived corticosterone treated) showed significant latency in varying aspects of locomotor development as recorded by swim tests.

Head score ratings were not significantly different between groups ($p = 0.106$).

Line of swimming ratings were significantly ($p = 0.026$) different between groups, the corticosterone treated pups were the most retarded followed by the prolactin treated and prolactin deprived corticosterone treated pups (Figure 2).

Front paw rating provided a more reliable set of data than the other parameters since the differences in limb usage were obvious and present at all times during swimming. The overall differences between groups were significant with a p-

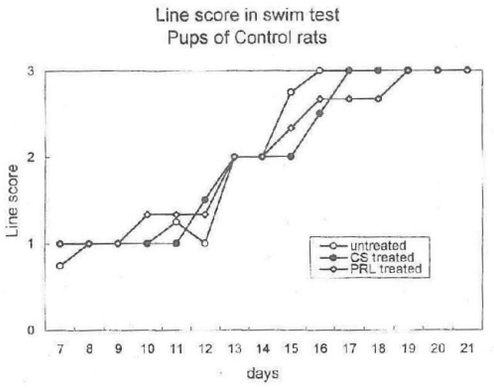

Figure 2a: Swim test Line score ratings in the three experimental groups: untreated, CS treated and PRL treated in 7-21 day old rat pups, for the combined control and vehicle treated mother.

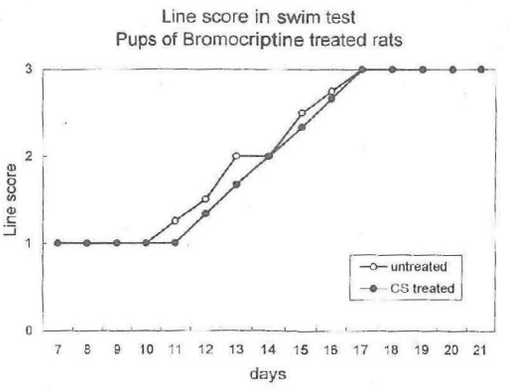

Figure 2b: Swim test Line score ratings in the two experimental groups: untreated (PRL deprived) and CS treated in 7-21 day old rat pups of the BrCRP treated mother.

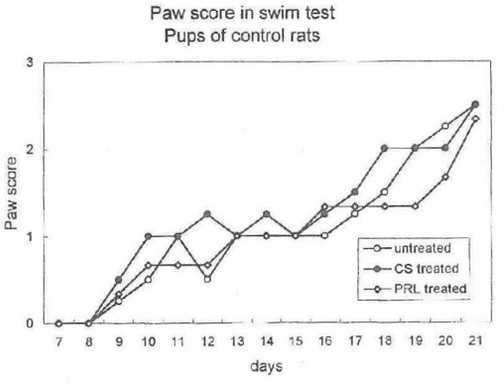

Figure 3a: Swim test Front paw ratings in the three groups days 7-21. Details as in text to Figure 2a.

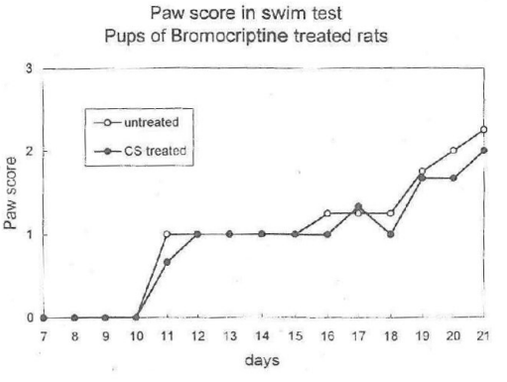

Figure 3b: Swim test Front paw ratings in the two groups days 7-21. Details as in text to Figure 2b.

value of 0.013. The untreated pups performed significantly better ($p = 0.028$) than both prolactin and corticosterone treated pups. The prolactin deprived corticosterone treated pups were the most retarded in their development followed by the prolactin treated pups (Figure 3).

Tail movement scores were also significantly different between groups ($p = 0.039$) with the untreated control pups developing more rapidly than the treated pups, the prolactin deprived corticosterone treated pups being the most retarded.

The serum prolactin levels of mother rats at day 22 of lactation treated with bromocriptine were below the detection limit of the assay (0.5 ng/ml). The serum prolactin levels in the untreated rats varied from 1.75 ng/ml to 2.90 ng/ml..

Discussion

There was a significant difference in body weight gains between treatment groups, the greatest negative effect on gain was observed in the prolactin deprived/corticosterone treated group.

Findings of previous studies (*Pavlovska-Teglia et al,* 1995; *Young et al,* 1996) did not demonstrate a negative effect on weight gain with corticosterone administration. This demonstrates that the prolactin deprivation/corticosterone administrated combination may influence growth rate. However, factors other than fluctuating hormone levels are involved in the retardation of juvenile growth associated with maternal stress. No difference was observed in the physical appearance and behaviour between pups of various treatment groups.

Swimming requires the smooth integrated organisation of coordinated series of reflex responses including the righting reflex, vestibular reflexes and extensor reflexes. This makes it suitable for assessing functional and behavioral development of the central nervous system in the neonate (*Pavlovska-Teglia et al,* 1995; *Young et al,* 1996). Several studies have demonstrated the retardation of locomotor development using swimming patterns (*Pavlovska-Teglia et al,* 1995; *Young et al,* 1996) poor post-weaning maturation and performance in adulthood (3 months of age) (*Benesova & Pavlik,* 1989) in rats treated with corticosterone orally or subcutaneously at an early age. *Scharpiro et al* (1970), administered a single dose of cortisol acetate (0.50mg) intraperitoneally on the first postnatal day to rat pups which on swim testing exhibited delay in biochemical, neurophysiological and behavioral development of the CNS. *Pavlovska-Teglia et al* (1995) and *Young et al* (1996) found significantly poor achievements on swim testing by corticosterone treated pups. Corticosterone treatment groups showed latency in the development of the normal juvenile head position, maintaining nose and face and forehead well above water surface, line and tail scores and the development of full forelimb inhibition whilst swimming. The present study confirmed a significant difference associated with treatment and front limb inhibition and retardation in the line of swimming score and tail movement ratings.

Adult rats do not use the forelimbs while swimming, but hold them in hyperextension. *Pavlovska-Teglia et al* (1995) found that pups in the control group achieved this by day 22, whilst it was not achieved by any of the corticosterone dosed groups at this time. Very few pups in this present study achieved full forelimb inhibition by day 22, the end of the study period. There was a significant difference between treatment groups on latency and final forelimb swim test score. The prolactin deprived corticosterone treated groups showed the greatest degree of retardation.

Bromocriptine had a significant effect on lowering serum prolactin in the treated females using the dose rage 2 ug – 12 ug/rat/day. No previous work has focused on the effect of prolactin on neonatal neuromuscular development, although recent medical research has indicated several "new" possible roles for this hormone, including a vital function in immunological development. Swim test results from this study have demonstrated significant statistical evidence for a detrimental effect of prolactin administration on neuromuscular development. Prolactin administration resulted in a latency to achieve the ability to swim in a straight line, an extra 2 days was observed in these groups compared to controls. It also resulted in a significant retardation in the development of front limb inhibition. Tail movement scores were also lower in prolactin treated and deprived groups. Retardation of neuromuscular development was marked in the prolactin deprived corticosterone treated group, but prolactin deprivation alone did not significantly affect development.

Puerperal psychosis has been suggested to be triggered by the sudden effects of oestrogen withdrawal upon central Dopamine (DA) systems (*Wieck* 1989). Hypothalamic DA is a potent inhibitor of prolactin and it seems likely that the poor development of adult swimming pattern observed in the prolactin treated pups, may be due to a lowered DA concentration in the neural tissue. Further work is required to test the hypothesis that the link between altered prolactin levels and neuromuscular development in rat pups involves DA concentration changes and/or changes in DA receptor sensitivity.

Summary

In order to simulate the elevated corticosteroid and prolactin levels that offspring of stressed mothers may be subjected during breast feeding, rat pups were treated daily with oral corticosterone (200ng/ml milk intake) or prolactin (140ng/

ml milk intake) from the 2nd to the 15th postnatal day. To investigate the potential influence of reduced prolactin intake, the mothers were either treated with bromocriptine (2ug-12ug/rat/day) or 1% ethanol (vehicle). The rat pups were subjected to swim tests from their 8th postnatal day to examine their neuromuscular development. Results from swim tests showed latency in development in the prolactin, corticosterone and prolactin deprived/corticosterone administered groups, compared with the controls. There was decreased daily weight gains in the treatment groups compared to the control. This study demonstrates that increased prolactin and corticosterone and decreased prolactin combined with elevated corticosterone levels to which suckling neonates were exposed to, had a significant negative effect on their neuromuscular adaptive mechanism involved in the normal development of the locomotor system.

Acknowledgements

Thanks are due to Dr. G. England, Royal Veterinary College (RVC), University of London and Dr. J. Verstegen (Belgium) for their assistance with the analysis of the prolactin assays and to Mr G. Stodulski (RVC) for his help with the statistical analyses.

References

Alder E. M., Cook A., Davidson D., West C., Bancroft J. (1986) Hormones, mood and sexuality in lactating women. *British Journal Psychiatry 148*, 74-79.

Alder E. M. & Cox J. L. (1983) Breast feeding and Post-natal Depression. *Journal Psychosomatic Research 27*, (2), 139-44.

Alexandrova M., Macho L. (1983) Gluçocorticoids in human, cow and rat milk. *Endocrinologica Experimentalis 17*, 183-189.

Altman J., Sudarshan K (1975) Post-natal development of locomotion in the laboratory rat. *Animal Behaviour 23*, 896-920.

Amenomori Y., Chen C. L., Meites J. (1970) Serum prolactin levels in rats during different reproductive states. *Endocrinology 86*, 506-510.

Ballinger C. B., Kay D. S. G., Naylor G. J., Smith A. H. W. (1982) Some biochemical findings during pregnancy and after delivery in relation to mood change. *Psychological Medicine 12*, 549-556.

Benesova O, Pavlik A (1989) Perinatal treatment with glucocorticoids and the risk of maldevelopment of the brain. *Neuropharmacology 28*, 89-97.

Buckman M. T. & Kellner R. (1985) Reduction of distress in hyperprolactinemia with bromocriptine. *American Journal Psychiatry 142*, 242-244.

Caplan H. L., Coghill S. R., Alexandra H., Robson K. M., Katz R., Kumar R. (1989) Maternal depression and the emotional development of the child. *British Journal Psychiatry 154*, 818-22.

Caron R. W., Jahn G. A., Deis R. P. (1994) Lactogenic actions of different growth hormone preparations in pregnant and lactating rats. *Journal Endocrinology 142*, 535-545.

Coghill S. R., Caplan H. L., Alexandra H., Robson K. M., Kumar R. (1986) Impact of maternal postnatal depression on cognitive development of young children. *British Medical Journal 292*, 1165-1167.

Cousins L., Hollingsworth D. et al. (1983) Qualitative and quantitative assessment of the circadian rhythm of cortisol in pregnancy. *American Journal of Obstetrics and Gynecology 145*, 411-416.

Cox A. D., Puckering C., Pound A., Mills M. (1987) The impact of maternal depression on young children. *Journal of Child Psychology and Psychiatry and Allied Disciplines 28*, 917-928.

Dobie S. A., Walker E. A. (1992) Depression after childbirth. *Journal of the American Board Family Practitioners 5*, 303-11.

Field T. M. (1984) Early interactions between infants and their postpartum depressed mothers. *Infant Behaviour and Development 7*, 517-522.

Field T. M., Healy B., Goldstein S., Perry S., Bendell D. (1988) Infants of depressed mothers show "depressed" behaviour even with nondepressed adults. *Child Development 59*, 1569-1579.

Flint D. J. & Ensor D. M. (1979) Effects of ergocryptine on prolactin secretion during concurrent pregnancy and lactation in the rat. *Journal Reproduction and Fertility 56*, 691-696.

Gamer E., Gallant D., Grunebaum H. U., Cohler B. J. (1977) Children of psychotic mothers. *Archives of General Psychiatry 34*, 592-97.

Gard C, Hard E, Larsson K, Petersson V. A. (1967) The relationship between sensory stimulation and locomotor behaviour during post-natal development in the rat. *Animal Behaviour 15*, 563- 567.

George A. J., Copelaqnd J. R. M., Wilson K. C. M. (1980) Prolactin secretion and the postpartum blues syndrome. *Proceedings of the B.P.S.* 9th-11th April, 102.

Grove D. S., Bour B., Kacsoh B., Mastro A. M. (1991) Effect of neonatal milk-prolactin deprivation on the ontogeny of the immune system of the rat. *Endocr. Regul. 25*, (1-2), 11-119.

Grunebaum H. U., Cohler B. J., Kauffman C., Gallant D. (1978) Children of depressed and schizophrenic mothers. *Child Psychiatry and Human Development 8*, 219-228.

Handley S. L., Dunn T. L., Baker J. M., Cockshoff C., Gould S. (1977) Mood changes in puerperium and plasma tryptophan and cortisol concentrations. *British Medical Journal 2*, 18- 22.

Handley S. l., Dunn T. L., Waldron G., Baker J. M. (1977) Tryptophan, cortisol and puerperal mood. *British Journal Psychiatry 136*, 498-508.

Harris B., Johns S., Fung H., Thomas R., Walker R., Read G., Riad-Fahmy D. (1989) The hormonal environment of post-natal depression. *British Journal Psychiatry 154*, 660-667.

Hau J., Westergaard J. G., Svendsen p. & Grudzinskas J. G. (1983) Quantification of corticosteroid binding globulin by electroimmunoassay during human pregnancy. *Arch. Gynecol., 233*, 217-223.

Kellner R., Buckman M. T., Fava G. A., Pathak D. (1984) Hyperprolactinaemia, distress and hostility. *American Journal of Psychiatry 141*, 759-763.

Kinsley C. & Svare B. (1988) Prenatal stress alters maternal behaviour in mice. *Physiology and Behaviour 42*, 7-13.

Kuevi V., Causon R., Dixson A. F. (1983) Plasma amine and hormone changes in "post- partum blues". *Clinical Endocrinology 19*, 39-46.

Lorenzaza-Jimenez M. & Salas M. (1980) *Neurobehavioural Toxicology 2*, 31-36.

McKnew P. H., Cytryn L., Efron A. M., Gershon E. S., Bunney W. E. (1979) The offspring of parents with affective disorders. *British Journal of Psychiatry 134*, 148-152.

Maes M., Claes M., Schotte C. (1992) Disturbances in dexamethasone suppression test and lower availability of L-tryptophan and tyrosine in early puerperium and in women under contraceptive therapy. *Journal Psychosomatic Research 36*, 191-7.

Manser C. E. (1992) The assessment of stress in laboratory animals, RSPCA.

Martignoni E., Costa A., Sinforiani E. (1992) The brain as a target for adrenocortical steroids; cognitive implications. *Psychoneuroendocrinology 17*, 343-54.

Murphy B. E. P. (1991) Steroids and depression. *Journal Steroid Biochem. and Molec. Biology 38*, 537-559.

Murray L & Stein A. (1989) The effects of postnatal depression on the infant. *Bailliere's Clinical Obstetrics and Gynaecology 3*, (4), 921-933.

Noel G. L., Suh H. K., Frantz A. G. (1974) Prolactin release during nursing and breast stimulation in postpartum and nonpostpartum subjects. *Journal Clinical Endocrinology 38*, 413- 423.

Nott P. N., Franklin M., Armitage C., Gelder M. G. (1974) Hormonal changes in the puerperium. *British Journal of Psychiatry 128*, 379-383.

Ollivier-Bousquet M., Kann G., Durand G. (1993) Prolactin transit through mammary epithelial cells and appearance in milk. *Endocrinology-Regul. 27*, (3) 115-24.

Olpe H. R. & McEwen B. S. (1976) Glucocorticoid binding to receptor-like proteins in rat brain and pituitary: Ontogenic and experimentally induced changes. *Brain Research 14*, 121-128.

Pavlovska-Teglia G., Stodulski G., Svendsen L., Dalton K., Hau J. (1995) Effect of oral administration of corticosterone on neonatal and juvenile rat locomotor development. Experimental Physiology 80, 469-475.

Porter J. K. & Thompson F. N. (1992) Effects of fescue toxicosis on reproduction in livestock. *Journal of Animal Science 70*, (5): 1594-603.

Rupprecht R. M. C., Sofic E., Barocka A., Beck G., Noder M. (1989) Effects of glucocorticoids on the regulation of the hypothalamus-pituitary-somatotropic system in depression. *Journal Affective Disorders 17*, 9-16.

Russel J. A., Harrison D. J., McNeilly A. S. (1981) Bromocriptine and ergocryptine do not inhibit oxytocin secretion in the lactating rat. *Journal Endocrinology 89*, 91-98.

Scharpiro S., Salas M., Vukovich K. (1970) Hormonal effects ontogeny of swimming ability in the rat: Assessment of CNS development. *Science 168*, 147-150.

Sobrinho L. G. (1993) The psychogenic effects of prolactin. *Acta-Endocrinol-Copenh. 129*, (1): 38-40.

Stein A., Gath D. H., Bucher J., Bond A., Day A., Cooper P. J. (1991) The relationship between post-natal depression and the mother-child interaction. *British Journal Psychiatry 158*, 46-52.

Tolis G., Guyda H., Pillorger R. & Friesen H. G. (1972) Breast-feeding: effects on the hypothalamic pituitary gonadal axis. *Endocrine Research Communication 1*, 283-303.

Tyson J. E., Hwang P., Guyda H. & Friesen H. G. (1972) Studies of prolactin secretion in human pregnancy. *American Journal of Obstetrics and Gynecology 113*, 14-20.

Weissman M. M., Paykel E. S., Klerman G. L. (1972) The depressed woman as a mother. *Social Psychiatry 7*, 98-108.

Weissman M. M., Prusoff B. A., Gammon G. D., Merinkangas K. R., Leckman J. F., Kid K. K. (1984) Psychopathology in children (6-18) of depressed and normal parents. *Journal of the American Academy of Child Psychiatry 23*, 78-84.

Welner Z., Welner A., Donald M., McCraney B. A., Leonard M. A. (1977) Psychopathology in children of inpatients with depression. *Journal of Nervous and Mental Disease 164*, 408-413.

Wieck A. (1989) Endocrine aspects of post-natal disorders. *Baillieres Clinical Obstetrics And Gynaecology 3*, 857-77.

Young L. A., Pavlovska-Teglia G., Stoudulski G., Hau J. (1996) Effect of oral corticosterone administration and group housing on weight gain and locomotor development in neonatal rats. *Animal Welfare 5*, 167-176.