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Nursing Behaviour of White New Zealand Rabbit Does. Effect of an Opioid Antagonist

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ABSTRACT: A group of does (n = 10) received 0.5 mg NX at 12 hr. intervals two days before and two days after mating, a control group (n = 10) was sham treated with saline injections. After kindling, kints born, nursing time and kint growth was studied. NX treated does nursed their kints for 235 ± 11.3 secs vs controls 220 ±16.2 secs (P<0.05). Milk yield and Kint weight was significantly higher in naloxone treated does.Kints born from control and naloxone treated does was 10.1 ± 1.1 and 12.13 ± 0.77 (P<0.05). Kints born live from naloxone treated and control dams was 11.3 ± 0.94 and 9.5 ± 0.9 (P<0.05). NX treated does weaned 10.0 ± 0.9 kints, controls 8.7 ± 1.05 (P<0.05). It was concluded that endogenous opioids are important modulators of nursing behavior in rabbit does favoring the development of their young.

I. INTRODUCTION

Rabbit does behavior during suckling their kints, is stereotyped, for the first minutes she crouches motionless over the feeding young, her expression is remote and she appears oblivious to peripheral events [1]. Thereafter they groom their young, licking and palpating their genitals to stimulate both defecation and urination. The viability of the suckling kint is highly dependent on the rabbit doe to behave maternally in order to ensure proper feeding of their young [12]. Several research teams report that spontaneous nursing in a variety of rabbit breeds occurs only once a day [3]. Exhaustive work has been made to relate nursing behavior of rabbit does with Central Nervous System neurotransmitters and metabolites[3-7-4-5-6], however, research related to the endogenous opioid system and nursing behavior in rabbit does, is limited, and justifies the objective of this study.

In domestic rabbits, pups display nipple search behavior immediately after being expelled, and they often succeed in gaining colostrum within minutes or even

seconds after birth, while the female is consuming the placentae and parturition is still
in progress [8]. Multiple and/or longer visits of the doe to the nest between birth and the first full nursing episode may interfere with the presumed energy saving strategy of the pups, compromising their survival regardless of their sucking success immediately after birth [2]. Milk production is a main factor for after birth growth rate of the young kints [9].
Maternal behavior is an important factor that determines survival of the young, there is substantial evidence that maternal behavior and lactation are physiological functions influenced by endogenous opioids [10].

In rats, it has been observed a decrease in the levels of hypothalamic β-endorphin during lactation, due to enhanced prolactin (PRL) secretion induced by pup-suckling behavior [10-11]. Indicating that through early lactation the endogenous opioid system influences both the termination of nursing bouts and the amount of time the dam spends in close proximity to her pups [10].

In ewes a close correlation between suckling bouts and portal beta endorphin and peripheral PRL concentrations suggest a hypothalamic effect of beta endorphin itself [12].
In human females, breast feeding is a pleasant sensation and sexually related satisfaction,pleasurable enough to ensure their frequent occurrence. [13-14-15].
In rabbit does it is possible to relate nursing with a possible analogy to coitus[16].
Rats, when treated with opioid antagonistsnursing and nesting bouts were increased in time, effect present only during early lactation[10]. It is possible to postulate that normal functioning of maternal behavior, maybe dependent on the fact that both endogenous Beta endorphin content and central opioid receptor presence are reduced during lactation [17].

Small doses of NX to male rabbits increased number of mounts and copulations [18],in male goats increased libido and testosterone levels [19], and decreased plasma prolactin (PRL) concentrations in the ewe [20]changes that suggest that small doses of naloxone have special affinity for μ opioid receptors [21].

Early work using naloxone in doses of 1 and 2 mg/kg to examine the interaction of endogenous opioids in the reproductive physiology of different species, they focused in changes in gonadotrophic hormones, and sexual behavior was not reported. Using high doses (1 mg/kg) of the opioid antagonist, the observed results show many differences between species; either significant changes are seen or there is no observed effect.

Fitzgerald and Perkins [22] reported that naloxone (1 mg/kg) did not stimulate courtship behavior of sexually inactive male rams. Furthermore, when naloxone is administered at a dose of 0.5 g/kg/h/24 h,Currie and Rawlings [23] observed a loss of responsiveness of LH pulse amplitude after the continuous administration of naloxone. It should be emphasized that, the effect of low doses of naloxone on hormone levels and behavior are not immediate; in rams and bucks it was observed that there was no change in testosterone levels during the first seven days of treatment, but after 7-15 days of treatment with the opioid antagonist, significant changes in plasma testosterone were observed [19].

Information related to the importance of endogenous opioids on rabbit doe milk production, kint nursing and growth is limited, therefore, we considered of interest to study milk production,nursing time and kint growth of White New Zealand Rabbit does treated with small doses of naloxone two days before and two days after mating.

II. Materials and Methods

Rabbit does (n = 20) were selected, with a history of two normal kindling's, and mated with sexually active males; each doereceived two ejaculations. Thereafter, they were divided at random in to two groups of ten. Kept in individual wire mesh cages (90 cm long X 60 cm wide X 40 cm high) under natural light (19ºN August 2013)

and housed in separated pens, treated and control does were separated by at least 100 meters to prevent bio stimulation. Water and food (Purina rabbit pellets) were provided*ad libitum.*

A wooden box (50 cm long X 30 cm wide X 32 cm high) with a round opening on one side (diameter: 22 cm) which could be opened and closed by a sliding door, was attached to the doe cage entrance. to be used as the maternal nest. This box was left in place for the entire duration of the experiment. The top of the box was hinged, to be opened and kint weight noted, before and after the doe nursed their kints.
Welfare of both rabbit groups were handled according to the bioethical animal welfare procedures of the animal research facilities at the Centro Universitario de los Altos, Universidad de Guadalajara, Mexico.

One technician injected, cleaned and fed each group of rabbit does and kints,furthermore an observer was appointed for each group, to avoid handling stress of the kints during the duration of the experiment. While handling and feeding control and treated does, the observer noted all behavioral signs during nursing; kint weightwas carried out three times a week, till weaning as recommended byFernández-Carmona et al. [24] and Fortun-Lamothe and Sabater[25].

Rabbit does (n = 10) were medicated with 0.5 mg naloxone at 12 hr. intervals two days before and two days after mating, the control group was sham treated with saline injections. Once mated, gestation was continued and the study initiated on kindling day.

After kindling, does were allowed to suckle their kints by opening the sliding door at 8:00 h for 20 minutes, and the period of suckling noted, suckling was defined as the period of time that the pups were attached to the nipple, was recorded to the second. The young attached themselves to the nipple within 5 - 30 sec of entering their mother's cage, event favored by the mammary pheromone [26-27]; suckling was terminated by the abrupt departure of the mother from her suckling young[1]. The kints were then gently weighed, milk yield noted. Weight losses during this brief period in urine and feces are negligible.
A Two Sample T test and the Analysis of Variance were used to evaluate the resulting data from this experiment.

III. Results

Rabbit does treated with naloxone, were extremely calm, when allowed to enter to nurse their kints, without hesitation or delay they proceeded to nurse their kints. Control does show certain degree of curiosity for few seconds and thereafter, entered to nurse their young. This behavior was consistent for the duration of the experiment.

Nursing time in naloxone treated does was longer, 235 ± 11.3 secs compared with controls 220 ±16.2 secs ($P<0.05$). Nursing time and milk yield decreased continually until weaning when treated does nursed their kint for 175 ± 3.3 secs. Control does nursed their kints for 160 ± 3.3 secs ($P<0.05$). From kindling to weaning, treated does nursed their kints significantly more time than non-treated does (table I). Milk yield and Kint weight was significantly higher in naloxone treated does as compared with controls.

In naloxone treated doesnumber ofkints born, live and weaned was larger vs control does (kints born Control l1.0 vs NX 12.13 $P<0.05$), (live kints Control 9.5 vs NX 11.3 $P<0.05$) (weaned kints: Control 8.7 vs NX 10 $P<0.05$) (Weight at weaning: NX treated 612 g vs controls 530 g)(table I).

Table I. Nursing time, milk yield and weight gain of kints from control and naloxone treated rabbit does. Mean ± Standard deviation. With a significance level of 0.05. A -t

day	Nursig time scs control	Nursing time scs NX	t	Milk yield g control	Milk yield g NX	t	Kint weight control	Kint weight NX	t
Birth	220±16.2	235±11.3	-2.41	145±3.3	165±3.3	-13.4	58±4.6	59±2.7	o.59
1	215±8.8	225±4.7	-3.16	140±5,7	150±6.2	-3.72	62±2.1	65±2.3	-3.0
3	200±4.7	230±2.3	-17.9	160±6.2	155±7.4	1.62	71±2.0	74±1.5	-3.67
6	180±3.3	200±9.4	2.10	180±8.8	180±5.2	0	90±3.4	96±3.7	-3.72
9	170±4.7	200±9.2	-9.23	195±3.3	200±6.2	-2.23	140±4.7	152±3.1	-6.7
12	160±4.0	175±7.0	-5.80	200±9.1	210±9.1	-2.44	186±3,6	195±4	-5.19
15	165±3.9	175±4.0	-6.12	1756.1	215±7.7	-12.7	245±6.2	320±12	-16.7
18	160±2.3	170±4.8	-5.93	195±7.2	195±5.2	0	330±6.6	362±4.7	-12.3
21	150±3.3	175±4.0	-14.9	180±4.8	200±3.3	-10.7	392±2.6	440±8.8	-16.4
23	140±4.7	145±4.7	-2.37	180±4.3	200±10.2	-5-52	415±9.4	435±7.4	-5.26
25	135±3.3	145±3.3	-6.70	165±7.4	175±4.1	-3.91	475±4.0	525±6.2	-21.2
28	160±3.3	175±3.3	-10.0	165±7.0	180±3.8	-5.88	530±8.1	612±8.2	-22.3

value denoted a significance of 0.005.

IV. Discussion

Naloxone has early history of promoting LH release in different species[28-29-30-31]and rabbits[32_33-34-35], Small doses of naloxone facilitated the release of LH an increased ovulation rate. LH secretion will favor ovulation and higher prolificacy in NX treated does [36]. In this work rabbit does received small doses of naloxone since two days before mating and continued for two days after, therefore, LH release was facilitated by the administration of the opioid antagonist. The latter effect can be considered a factor that increased ovulation rate, reflected in the higher number of kints born as compared with control does. Also the higher number of live kints born, might be due to the behavior of the rabbit doe fostering their young after birth. Nursing is a rewarding maternal behavior that enhances survival of the new born providing nutrients and warmth, promoting maternal behavior and bonding[37].

During nursing β endorphin levels increase, activating endogenous μ opioid receptors shortening nursing time[10], when naloxone is present, prolonged nursing timeswere observed[10-38-39]. Furthermore,

Endorphins increase during lactation, therefore nursing bouts will decrease continually through lactation[40]. The latter gives way to postulate that naloxone, in low doses inhibits the action of endorphins at the μ receptor level[41], increasing nursing time of NX treated does, permitting nursing kints to attach themselves rapidly to the mother's nipples and suckling more milk. Naloxone as previously stated made rabbit does more calm during nursing. Similar findings reported in rats, in which administration of naloxone before parturition in pregnant dams, during the last two weeks of gestation, had pups that grew faster and exhibited faster development[35]. The latter report is consistent with others that a daily dose of naltrexone produces the same pattern of increased development [42-43]. In this work weight gain of kints from naloxone treated and control does show [37]an arched chart, similar to the report of Rao *et al*. [44], observation also reported in rats, results attributed to longer nursing times after naloxone treatment The survival rate of kits is in close correlation with their birth weight and milk supply[45]. Results here reported make possible to postulate that naloxone isolates nursing dams from environmental stimuli favoring nursing behavior.

V. Conclusions

It was concluded that endogenous opioids facilitate nursing behavior in rabbit does favoring the development of their young.

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Conflict of interest

The author declares no conflict of interest.

References

[1] Lincoln D W. (1974). Suckling: a time constant in the Nursing behavior of the rabbit. Physiol. Behav. 13: 711 – 714

[2] Coureaud, G; Schaal B; Coudert P; Rideaud P; Fortun-Lamothe L; Hudson R and Orgeur P. 2000. Immediate postnatal sucking in the rabbit: Its influence on pup survival and growth. Reprod. Nutr. Dev. 40 (2000) 19–32

[3] Gabriela González-Mariscal. Mother rabbits and their offspring: Timing is everything. 2006 https://doi.org/10.1002/dev.20196

[4] Gonzalez-Mariscal, G. (2001). Neuroendocrinology of maternal behavior in the rabbit. Hormones and Behavior, 40, 125– 132

[5] Caba M, González-Mariscal G and Meza E. 2018 Circadian Rhythms and Clock Genes in Reproduction: insights: From Behavior and the Female Rabbit's Brain. Frontiers in endocrinology 9:1 – 7 Article 106

[6] Meza E, Aguirre J, Waliszewski S, Caba M. 2014. Suckling induces a daily rhythm in the preoptic area and lateral septum but not in the bed nucleus of the striaterminalis in lactating rabbit does. European Journal of NeuroscienceVolume 41, Issue 2 p. 196-204

[7] Loutfi; M. A. Ayoub; H. A. Khalil and I. M. M. Assaf. Effect of l-tyrosine administration on milk yield and some blood parameters in new zealand white rabbits does. Egyptian Journal of Rabbit Science, 28 (1): 157 -171(2018)

[8] Hudson R; Cruz Y; Lucio RA; Ninomiya J and Martínez-Gómez M., (1999). Temporal and behavioral patterning of parturition in rabbits and rats, Physiol. Behav. 599–604.

[9] Baselga M; Blasco A and Garcia F. (1982). Parametrosgeneticos de caracteres economicos en poblaciones de conejo. In Proc.: 2º Congreso Mundial de Genética Aplicada a la produccion Ganadera, VI. Madrid. Ed, Garci. p: 472.

[10] Byrnes EM; Rigeiro BA and Bridges RS. 2000. Opioid receptor antagonism during early lacatton results in the increased duration of nursing bouts Physiol. Behav. 70: 211 - 216Circadian Rhythms and Clock

[11] Riskind P N; Millard EJ and Martin JB. (1984). Opiate modulation of the anterior pititary hormone response during suckling in the rat. Endocrinology 114: 1232 – 1237

[12] Gordon K; Renfree MB; Short R. V; and Clarke IJ. 1987. Hypothalamopituitry portl blood concentration of beta endorphin during suclking in the ewe. J Reprod. Fertil. 79: 397 - 408

[13] Newton, N and Newton, M (1967). Psychologic aspects of lactation. New England Journal of Medicine, 277:1179--1188.

[14] AlderE M; Cook A; Davidson D; West C and Bancroft J. 1986. Hormones, mood and sexuality in lactting women. Br. J. Psychiatry. 148: 75 – 79

[15] Small EC. (1994) Psychosocial – Sexual issues. ObstetGynecolClin North Am. 21: 773 – 780

[16] Findlay ALR. and Rorrr. L. L, Long-term dissociation of nursing behavior and the condition of the mammary gland in the rabbit. Journal of Comparative and Physiological Psychology, 1970,72,341-344.

[17] Hammer RP. and Bridges R S. (1987). Preoptic area opioids ad opiate receptors increase during pregnancy and decrease during lactation. Brain Research. 420: 48 – 56

[18] Fuentes V O, C.Villagran C, Navarro J, Fuentes P I. Effect of small doses of naloxone on sexual exhaustion in White New Zealand male rabbits- Animal Reproduction Science Volume 90, Issues 3–4, December 2005, Pages 341-346

[19] Fuentes V O, Fuentes P, Garcia A. The effect of naloxone on plasma concentrations of testosterone in male goats- Small Ruminant Research Volume 27, Issue 2, February 1998, Pages 173-176

[20] Fuentes V O, Gonzalez H, Sanchez V M, Fuentes P I. Effect of small doses of naloxone on the pulsatile secretion of prolactin in the crossbreed ewe during the non-breeding season. Animal Reproduction Science Volume 100, Issues 1– 2, July 2007, Pages 44-50

[21] Halperin J. Devi S.Y. Elizur S. Stocco C. Shehu A. Rebourcet D. Unterman T.G. Leslie N.D. Le J. Binart N. Gibori G. 2006 Prolactin signaling through the short form of its receptor represses forkhead transcription factor FOXO3 and its target gene galt causing a severe ovarian defect Mol. Endocrinol 22 513 522 [Crossref], [Google Scholar]

[22] Fitzgerald J A, Perkins A. Effect of morphine and naloxone on LH response and sexual behavior of rams (Ovisaries). Domestic Animal Endocrinology Volume 11, Issue 3, July 1994, Pages 271-279

[23] Currie W D and Rawlings N C. Fluctuation in responsiveness of LH and lack of responsiveness of FSH to prolonged infusion of morphine and naloxone in the ewe. Reproduction 1986 86:359 – 396 https://doi.org/10.1530/jrf.0.0860359

[24] Fernández-Carmona J., Blas E., Cervera C., Pascual J.J., 2006. The measure of milk rabbit. World Rabbit Sci., 14(sp), 58.

[25] Fortun-Lamothe L., Sabater F., 2003. Estimation de la productionlaitière à partir de la croissance des lapereaux. In Proc.: 10èmes Journ. Rech. Cunicole, Paris, ITAVI Ed., Paris, 69-72.

[26] Hudson, R., &Distel, H. (1983). Nipple location by newborn rabbits: Behavioral evidence for pheromonal guidance. Behaviour, 85, 260–275

[27] MélanieJouhanneauBenoistSchaalGérardCoureaud. Mammary pheromone-induced odour learning influences sucking behaviour and milk intake in the newborn rabbit. Animal Behaviour 111: 2016, 1-11

[28] Brooks AN; Lamming GF and Haynes NB. (1986). Endogenous opioid peptides and the control of gonadotrophin secretion. Res Vet. Sci. 41: 285 – 289)

[29] Donham RS; Sarafidis E.H and Stetson MH. 1986. Naloxone administration to female hamsters advances puberty by enhancing luteinizing hormone release. Proc. Soc. Exp. Biol. Med. 182: 291-295.

[30] Ieri T; Chen H.T; Campbell GA and Meites J. (1980). Effects of naloxone and morphine on the proestrous surge of prolactin and gonadotrophins in the rat. Endocrinology 106:1568 – 1570

[31] NandaA.S. WardW.R. DobsonH. 1989 Opioid modulation of tonic luteinizing hormone release in ovariectomized dairy cows J. Vet. Pharmacol. Ther 12 397 403 [Crossref], [PubMed], [Google Scholar]

[32] Alexander SL; Irvine CH; Sand N and Turner J. (2000). The role of endogenous opioids in the ovulatory LH surge in mares. J ReprodFertil Suppl. 56:217-26.

[33] Lamb I.C; Strachan W; Henderson G; Partridge GG; Fuller MF and Racey PA. (1993). Effects of naloxone, metaclopramide and domperidone on plasma levels of prolactin and Lh following suckling in the female rabbit. Theriogenology 39: 1193 – 1200

[34] Rebollar PG; Alvariño J. M; Illera JC and Silván G. (1997). Effect of gonadoreline and naloxone on induction of ovulation and plasma LH in rabbit. Revistaespañola de fisiología. 53(2):205-10.

[35] Vorhees, CJ. (1981). Effects of prenatal naloxone exposure on postnantal behavioral development of rats. NeurobehavToxicolTeratol 3: 295 – 301

[36] Fuentes VO, Bernal-Canseco A, Fuentes-Castro PI and Sanchez-Parra VM, 2009. The Effect of High and Low Doses of Naloxone on Estrous Display and Ovulation Rate in Creole Ewes During the Mating Season. J. Biol. Sci. 9: 621-624.

[37] Drewett RF; Kendrick KM; Sanders DJ; Trew AM. 1982. A quantitative analysis of the feeding behavior of suckling rabbits. Develop. Psychobiol. 15: 25–32,

[38] Ferris CF; Kulkarni P; Sullivan Jr JM; Harder JA; Messenger TL and Febo M. 2005. Pup Suckling Is More Rewarding Than Cocaine: Evidence from Functional Magnetic Resonance Imaging and Three-Dimensional Computational Analysis. J. Neurosci. 25(1):149 –156 • 149

[39] Sukikara MH; Platero M. D; Canteras N. S and Felicio LF. (2007). Opiate regulation of behavioral selection during lactation. PharmacolBiochemBehav 87: 325 – 320

[40] Teodorov E; Tomita AT; Banon GPR; IGil L. G; Bernardi MM. and, Felício L.F. (2008). Behavioral effects of acute stimulation of κ-opioid receptors during lactation. Pharmacol. Biochem. Behavior 90: 534–539,

[41] Sobor M; Timár J; Riba P; Friedmann T; Király KP; Gyarmati S; Al- Khrasani M; and Fürst S. (2011). Effects of opioid agonist and antagonist in dams exposed to morphine during the perinatal period. Brain Research Bulletin 84: 53–60

[42] Zagon IS and McLaughlin PJ. (1983). Increased brain size and celular content in infant rats treated with an opiate antagonist. Science 221: 1179 – 1180

[43] Zagon IS. and McLaughlin PJ. (1984). Naltrexone modulates body and brain development in rats: A role for endogenous opioid systems in growth. Life Sci. 35: 2057 – 2064

[44] Rao DR; Sunki GR; Johnson WM and Chen CP. (1977). Postnatal Growth of New Zealand White Rabbit (OryctolagusCuniculus) J Anim Sci. 44:1021 –1025

[45] SzendroZs. 2008 Improving of reproductive performance of rabbit does in small and medium scale rabbit farms. Recommendations for developing countries. ActaAgrariaKaposváriensis (2008) Vol 12 No 1, 1-23