SciMedCentral

JSM Anatomy & Physiology

Editorial

The South American Plains Vizcacha, *Lagostomus maximus*, as a Valuable Animal Model for Reproductive Studies

Verónica Berta Dorfman[1,2]*, Pablo Ignacio Felipe Inserra[1,2], Noelia Paola Leopardo[1,2], Julia Halperin[1,2], and Alfredo Daniel Vitullo[1,2]

[1]*Centro de Estudios Biomédicos, Biotecnológicos, Ambientales y Diagnóstico, Universidad Maimónides, Argentina*

[2]*Consejo Nacional de Investigaciones Científicas y Técnicas, Argentina*

***Corresponding author**

Verónica Berta Dorfman, Centro de Estudios Biomédicos, Biotecnológicos, Ambientales y Diagnóstico (CEBBAD), Universidad Maimónides, Hidalgo 775 6to piso, C1405BCK, Ciudad Autónoma de Buenos Aires, Argentina, Tel: 54 11 49051100; Email: dorfman.veronica@maimonides.edu

Submitted: 08 October 2016

Accepted: 11 October 2016

Published: 12 October 2016

INTRODUCTION

The vast majority of our understanding of the mammalian reproductive biology comes from investigations mainly performed in mice, rats and humans. However, evidence gathered from non-conventional laboratory models, farm and wild animals strongly suggests that reproductive mechanisms show a plethora of different strategies among species. For instance, studies developed in unconventional rodents such as guinea pigs and hamsters, that share with humans some endocrine and reproductive characters, have contributed to a better understanding of human physiology and disease [1,2]. A better knowledge on the variety of mechanisms that regulate reproduction could lead to improve early diagnosis, treatment, or novel strategies development to ameliorate fertility and guarantee a successful reproduction. In this letter, we briefly introduce *Lagostomus maximus*, an unconventional rodent whose neuroendocrinology and reproduction in general have attracted significant interest in recent years in view of its unusual reproductive traits.

Reproductive physiology and endocrinology of the plains vizcacha

The South American plains vizcacha, *L. maximus*, a hystricognathi fossorial rodent that inhabits the Pampean region of Argentina [3], exhibits certain peculiar reproductive features that stand out from most mammalian species. In the 70`s, this rodent was found to be the major poly-ovulatory species among mammals, with the ability to release up to 800 oocytes per estral cycle [4]. Despite the extreme poly-ovulatory rate, 8 to 10 oocytes are successfully fertilized and implanted in the uterus, and only one or two embryos are gestated to term [5]. This high ovulatory rate is closely related to several physiological aspects of the ovary: i) a greatly convoluted anatomy of the ovary that increases the surface for ovulation, ii) the small size of the ovulatory follicles [5], and iii) a preferential expression of the anti-apoptotic BCL-2 over the pro-apoptotic BAX protein which leads to a down-regulation of apoptotic pathways and promotes a continuous oocyte production [6,7]. Moreover, the inversion in the BAX/BCL-2 balance is expressed in embryonic ovaries throughout development, pinpointing this physiological aspect as a constitutive feature of the vizcacha´s ovary, which precludes massive intra-ovarian germ cell elimination. Massive intra-ovarian germ cell elimination through apoptosis during fetal life accounts for 66 to 85% loss at birth as recorded for human, mouse and rat [8]. On the contrary, female germ line in the vizcacha develops in the absence of germ cell attrition during fetal life and germ cell population rises continuously from colonization of the genital ridges until birth [9].

Other noteworthy features of the vizcachas' reproductive biology are the uninterrupted pre-ovulatory follicle formation throughout the 155-day lasting pregnancy and the pseudo-ovulatory process that takes place at mid-gestation and adds up numerous secondary corpora lutea with oocyte retention [10-11]. This latter event divides the vizcachas' gestation into two well defined phases: before and after pseudo-ovulation. During the first phase, from implantation until around day 70 of gestation, circulating progesterone gradually decreases as a result of decay in corpora lutea activity [12]; however, embryos are still too immature to be born. Approximately at gestation day 90, when circulating progesterone reaches its minimum level, only the two embryos nearest the cervix survive whereas most proximal embryos suffered a progressive elimination through a natural resorption process. At this point, a new wave of follicular recruitment, pseudo-ovulation and follicular luteinization is triggered. Consequently, progesterone released from the newly developed corpora lutea progressively increases throughout the second half of gestation saving distal embryos from degeneration and allowing their development to term [10-12]. As a secondary effect, the increased levels of progesterone favor a precocious development of the mammary gland, preparing females to face the nutritional demand of fully developed newborns [13].

During gestation of most mammals, increased ovarian steroid levels induce a negative feedback over the hypothalamic-hypophyseal-ovary (HHO) axis keeping it inhibited till the end of pregnancy [14-16]. The pseudo-ovulatory event at mid-gestation exhibited by *L. maximus* is only possible with a reactivation of the HHO axis. We have already demonstrated HHO axis activity throughout the second half of gestation in spite of high hormone levels. Particularly, gonadotropin-releasing hormone (GnRH) and luteinizing hormone (LH) significantly increase their expression around gestational day 100-120, together with ovarian progesterone and estradiol [10].

The distribution of GnRH in the hypothalamus of the vizcacha shows similarities with other mammals. In addition, GnRH neurons are also localized in the supraoptic nucleus (SON) [17]. This localization of GnRH neurons has been reported only in the domestic pig, another recognized poly-ovulatory mammal [18]. The co-localization of progesterone receptor or estrogen receptor alpha with GnRH in neurons of the medial preoptic area and SON suggests a direct regulation of GnRH expression by progesterone and estradiol in opposition to the indirect model of GnRH regulation by ovarian hormones classically described [10,19].

This particular strategy developed by vizcacha, allows a greater sensitivity of GnRH neurons to sense changes in steroid levels which eventually trigger ovulation during pregnancy. Female vizcachas also exhibit a significant increase in serum LH at mid-gestation, although oocyte extrusion is rarely observed. Instead, follicular luteinization with oocyte retention is mostly detected and the morphological evidence of such event is the ovulatory stigmata [10,11].

CONCLUSION

The peculiar reproductive features mentioned above situate vizcacha as a valuable animal model for the development of studies in reproductive biology. In this sense, vizcacha is positioned as a mammal with a unique strategy that warrants reproductive success. Such a different strategy, far from being an oddity, offers a useful possibility To explore other expression patterns in conserved gene networks and to identify molecular markers that can be evaluated as potential targets of therapeutic interest. This may help to develop novel treatments against female infertility conditions such as premature menopause, hypothalamic amenorrhea and oligomenorrhea, and vulnerability to diseases such as polycystic ovary syndrome, or complications during pregnancy.

ACKNOWLEDGEMENTS

This work was supported by CONICET (PIP Nº 110/14), PICT 2014-1281 and by Fundación Científica Felipe Fiorellino, Universidad Maimónides, Argentina. We are especially grateful to the Ministerio de Asuntos Agrarios, Dirección de Flora y Fauna, Buenos Aires Province for authorizing animal capture at the Estación de Cría de Animales Silvestres (ECAS) and to the personnel of ECAS for their invaluable help in trapping and handling of animals.

REFERENCES

1. Mitchell BF, Taggart MJ. Are animal models relevant to key aspects of human parturition? Am J Physiol Regul Integr Comp Physiol. 2009; 297: 525-545.
2. Keightley MC, Fuller PJ. Anomalies in the endocrine axes of the guinea pig: relevance to human physiology and disease. Endocr Rev. 1996; 17: 30-44.
3. Jackson JE, Branch LC, Villarreal D. *Lagostomus maximus*. Mammalian Species. 1996; 543: 1-6.
4. Weir BJ. The reproductive organs of the female plains viscacha, *Lagostomus maximus*. J Reprod Fertil. 1971; 25: 365-373,
5. Weir BJ. The reproductive physiology of the plains viscacha, *Lagostomus maximus*. J Reprod Fertil. 1971; 25: 355-363.
6. Jensen F, Willis MA, Albamonte MS, Espinosa MB, Vitullo AD. Naturally suppressed apoptosis prevents follicular atresia and oocyte reserve decline in the adult ovary of *Lagostomus maximus* (Rodentia, Caviomorpha). Reproduction. 2006; 132: 301-308.
7. Leopardo NP, Jensen F, Willis MA, Espinosa MB, Vitullo AD. The developing ovary of the South American plains vizcacha, *Lagostomus maximus* (Mammalia, Rodentia): massive proliferation with no sign of apoptosis-mediated germ cell attrition. Reproduction. 2011; 141; 633-641.
8. Forabosco A, Sforza C, De Pol A, Vizzotto L, Marzona L, Ferrario VF. Morphometric study of the human neonatal ovary. Anat Rec. 1991; 231: 201-208.
9. Inserra PIF, Leopardo NP, Willis MA, Freysselinard AL, Vitullo AD. Quantification of healthy and atretic germ cells and follicles in the developing and post-natal ovary of the South American plains vizcacha, *Lagostomus maximus*: evidence of continuous rise of the germinal reserve. Reproduction. 2014; 147; 199-209.
10. Dorfman VB, Saucedo L, Di Giorgio NP, Inserra PIF, Fraunhoffer N, Leopardo NP, et al. Variation in progesterone receptors and GnRH expression in the hypothalamus of the pregnant South American plains vizcacha, *Lagostomus maximus* (Mammalia, Rodentia). Biol Reprod. 2013; 89: 115-125.
11. Jensen F, Willis MA, Leopardo NP, Espinosa MB, Vitullo AD. The ovary of the gestating South American plains vizcacha (*Lagostomus maximus*): suppressed apoptosis and corpora lutea persistence. Biol Reprod. 2008; 79: 240-246.
12. Fraunhoffer N. Renovación de masa germinal ovárica en un modelo animal poliovulatorio (*Lagostomus maximus*) y en la Endometriosis ovárica humana. PhD Thesis. Facultad de Medicina, Universidad de Buenos Aires. 2014.
13. Halperin J, Dorfman VB, Fraunhoffer N, Vitullo AD. Estradiol, progesterone and prolactin modulate mammary gland morphogenesis in adult female plains vizcacha (*Lagostomus maximus*). J Mol Histol. 2013; 44: 299-310.
14. Goodman RL, Bittman EL, Foster DL, Karsch FJ. The endocrine basis of the synergistic suppression of luteinizing hormone by estradiol and progesterone. Endocrinol. 1981; 109: 1414-1417.
15. Scaramuzzi RJ, Tillson SA, Thorneycroft IH, Caldwell BV. Action of exogenous progesterone and estrogen on behavioral estrus and luteinizing hormone levels in the ovariectomized ewe. Endocrinol. 1971; 88: 1184-1189.
16. Skinner DC, Evans NP, Delaleu B, Goodman RL, Bouchard P, Caraty A. The negative feedback actions of progesterone on gonadotropin releasing hormone secretion are transduced by the classical progesterone receptor. Proc Nat Acad Sci. 1998; 95: 10978-10983.

17. Dorfman VB, Fraunhoffer N, Inserra PIF, Loidl CF, Vitullo AD. Histological characterization of gonadotropin-releasing hormone (GnRH) in the hypothalamus of the South American plains vizcacha (*Lagostomus maximus*). J Mol Histol. 2011; 42: 311-321.

18. Kineman RD, Leshin LS, Crim JW, Rampacek GB, Kraeling RR. Localization of luteinizing hormone-releasing hormone in the forebrain of the pig. Biol Reprod. 1988; 39: 665-672.

19. Inserra, PIF, Charif SE, Rey-Funes M, Saucedo L, Di Giorgio NP, Lux-Lantos V, et al. Hypothalamic - Hypophyseal - Gonadal axis activity in the South American plains vizcacha during gestation. Histology and Histopathology, Cellular and Molecular Biology. 2014; 28: 87.

Cite this article

Dorfman VB, Felipe Inserra PI, Leopardo NP, Halperin J, Vitullo AD (2016) The South American Plains Vizcacha, Lagostomus maximus, as a Valuable Animal Model for Reproductive Studies. JSM Anat Physiol 1(1): 1004.