human reproduction

ORIGINAL ARTICLE *Reproductive endocrinology*

Prolactin secretory rhythm in women: immediate and long-term alterations after sexual contact

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BACKGROUND: Prolactin (PRL) is one of the most versatile hormones in the mammalian body, affecting reproductive, sexual and other functions. In rats, mating or vaginocervical stimulation activates a characteristic PRL secretory pattern for several days, which is essential for successful reproduction. Although the underlying mechanisms appear to be different, PRL is also crucial for human fertility. We have detected a PRL increase in women induced by sexual intercourse. Extending these findings, the current study aimed at analyzing the PRL secretory rhythm after sexual contact, in order to elucidate whether human females also show long-term alterations of the PRL secretory pattern.

METHODS: In a pilot study, serial blood samples were taken from women ($n = 7$) in mid-cycle to assess changes in PRL secretory rhythm induced by sexual intercourse, during a period of 32 h.

RESULTS: Compared with control condition, sexual intercourse with orgasm induced not only the well-established immediate PRL increase of ~300% but also an additional PRL elevation around noon of the next day ($P < 0.05$). These fluctuations were measured on top of the regular circadian rhythm of PRL, manifested as a surge early in the morning.

CONCLUSIONS: We are able to demonstrate a long-term change in the PRL secretory rhythm after sexual intercourse with orgasm in females, suggesting memory effects. We hypothesize that the additionally secreted PRL could be beneficial for decidualization and implantation. Further studies with more participants are required to investigate in detail the implications of such effects on reproductive success in humans.

Key words: prolactin / reproduction / sexual intercourse / woman / mid-cycle

Introduction

Prolactin (PRL) is an extraordinary hormone in the mammalian body, involved in endocrine, reproductive and sexual functions. While in the case of rodents more than 300 biological functions have been described for PRL (Ben-Jonathan *et al.*, 2008; Grattan and Kokay, 2008), the physiological role of PRL in humans, particularly its role in the reproductive and sexual functions in females, is less well understood.

A pronounced PRL elevation after orgasm has been reported in healthy female volunteers (Exton *et al.*, 2001; Brody and Kruger, 2006). This experimental data led to the hypothesis that PRL may serve as a satiation hormone after sexual activity, modulating sexual

drive via feedback loops to dopaminergic neurons (Kruger *et al.*, 2002, 2003a,b). Similarly, the appearance of a pronounced PRL surge after receiving a copulomimetic stimulus applied to the uterine cervix during mating has been shown in animal studies (Freeman *et al.*, 2000). In rats, this mating stimulus changes the PRL secretion rhythm into an oscillatory pattern of two surges per day for 10 or 12 days (Smith *et al.*, 1975).

A crucial role in ovarian functions can be attributed to PRL in humans based on the clinical manifestations related to hyperprolactinemia (Egli *et al.*, 2010). It is known that high levels of circulating PRL causes disorders such as infertility, dysovulation and reproductive disturbances, but the precise mechanisms by which PRL causes theses

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pathological situations are yet to be revealed (Bouilly et al., 2011). In addition to the systemic effect, there is also increasing knowledge concerning the regulatory function of locally secreted PRL, for example, in the uterus. In vivo studies have shown that the human endometrial stroma is one of the major sites for PRL synthesis and secretion, in particular during decidualization (Maslar and Riddick, 1979). However, PRL synthesis is detectable in the non-pregnant uterus as well as between the mid-secretory phase and menses (Jabbour and Critchley, 2001). Owing to the temporal expression pattern of both PRL and its receptor in the human endometrium, a pivotal role for the hormone during pregnancy and a possible role in preparation of the endometrium for implantation of the trophoblast can be suggested (Jabbour et al., 1998; Jabbour and Critchley, 2001). The involvement of PRL in implantation may be realized through modifications of the immune environment of the endometrium at the time of implantation and/or in the regulation of factor(s) that may control trophoblast proliferation and/or invasion of the endometrium (Jabbour et al., 1998). Clinical manifestations of impaired PRL secretion during fertilization and implantation as well as decidualization are difficult to characterize because many of the involved mechanisms are poorly defined (Jabbour and Critchley, 2001). Nevertheless, a direct role of impaired decidualization in pregnancy is emphasized in women with recurrent miscarriages (Jabbour and Critchley, 2001) and the close link between the level of PRL gene expression and PRL production by individual decidual cells, which is directly related to the process of decidualization, has been shown (Wu et al., 1995). A study by Garzia et al. (2004) reports that alterations in PRL expression in patients suffering from unexplained infertility and with a history of miscarriages are related to defects of PRL secretion characteristics of the endometrium (Garzia et al., 2004).

There is no doubt that PRL plays an important role in human reproduction but the potential functions and the precise mechanisms of how PRL is exerting its effects have still to be fully elucidated. To further investigate the potential involvement of PRL in human reproduction, we have designed a pilot study based on the results from our animal and human studies. Our hypothesis is that some of the mechanisms of action of PRL in rodents apply to humans as well. In particular, the study was designed to determine whether sexual contact has similar effects on the PRL secretion pattern in women as has been shown in the animal study. We therefore investigated PRL secretion patterns in human females induced by sexual intercourse, using a 32 h sampling period.

Materials and Methods

Participants

A total of 32 heterosexual couples were screened to determine their eligibility for participation in the study. Twelve couples fulfilled the criteria as described below. However, further couples were excluded during or after the study owing to insufficient data quality or missing orgasm. In the end, valid data were obtained for seven females [mean age 25.71 $\pm$ 1.2 (SE) years; range 21–31 years]. The cycle length was on average 29.71 $\pm$ 1.31 days, (range 26–32 days). The body mass index was on average 19.7 $\pm$ 0.4 kg/m^2, and all women were of normal weight according to World Health Organization criteria.

The screening process for participants consisted of a general medical examination and a health questionnaire, which included gynecological history. Individuals on medication, abusing drugs/alcohol, or exhibiting endocrinological, gynecological, psychological, sexual or any other somatic dysfunctions/disorders were excluded from the study. All couples were sexually active and had been in a relationship for at least 12 months (mean 41.3 $\pm$ 8.1 months, range 19–84 months), which was considered to be important to avoid the confounding endocrine effects of romantic love (Marazziti and Canale, 2004). Only those women who had a regular menstrual cycle (as retrospectively observed over a period of at least 6 months) and who used non-hormonal contraception methods were included because of the side effects of hormonal contraception on endocrine and behavioral parameters (Alvergne and Lummaa, 2010).

Written informed consent was obtained from the couples after a thorough explanation of the study (oral and written). The protocol for the study was approved by the Ethics Committee for investigations involving human subjects in the canton of Zurich, Switzerland. Subjects were recruited via advertisements placed by ETH Zurich and the University of Zurich, Switzerland. Couples received 400 Swiss Francs for participating in the study.

Procedure

The investigation was performed using a controlled, counterbalanced crossover design in a naturalistic setting at home, thereby ensuring high external validity. A repeated measure design was used, with each subject participating in one experimental and one control condition after being informed of the sequence of the sessions prior to participation. The two sessions were 1 month apart. Owing to the importance of the cycle phase on sexual behavior and reproductive function (Alvergne and Lummaa, 2010), all investigations were timed at mid-cycle/ovulation. This was verified by using an LH-based ovulation test (Evial ovulations test strip, Inopharm, Bern, Switzerland). All investigations started at 17:00 h. In the experimental conditions, couples were asked to have sexual intercourse (penile vaginal intercourse) at home at 19:00 h $\pm$ 0.5 h, lasting ~0.5 h. In the control condition, the daily activity remained the same as in the experimental condition except that there was no sexual contact or activity during this period. Couples had to refrain from any kind of sexual activity for at least 96 h prior to the study. There was a debriefing tool during blood sampling after sexual intercourse to assess the occurrence of an orgasm and other parameters.

Serial blood sampling was initiated by a first blood withdrawal at 17:00 h. This was 1.5–2.5 h before sexual contact and the samples served as baseline. The 19:00 h sample was drawn within 30 min of sexual intercourse (the experimenter was called by the couple). Thereafter, blood samples were taken every 2 h, except during the sleeping period between 23:00 and 07:00 h when the blood sampling interval was set at 4 h (blood withdrawals at 21:00, 23:00, 03:00, 07:00, 09:00, 11:00, 13:00, 15:00, 17:00, 19:00, 21:00, 23:00 and 03:00). Blood sampling was continued until the early morning of the next day (01:00 h) in order to be able to detect the hypothesized afternoon surge and the next early morning PRL surge that mirrors the normal circadian PRL rhythm. This procedure represents a compromise between the aim of detecting altered PRL secretion patterns during a period of more than 24 h and that of avoiding the inconvenience to the couples of taking serial blood samples during their daily routine.

Blood collection and PRL assessment

Serial blood samples were taken via an i.v. cannula (Vasofix Braunüle 18G, Braun, Germany) inserted into a forearm vein of the non-dominant arm at least 30 min before the serial blood sampling was initiated at 17:00 h on the first day. Stylets (Vasofix-Mandrin, Braun, Germany) were used for

the closure of the indwelling cannula to inhibit blood coagulation. About 10 ml blood was collected in EDTA tubes (Sarstedt, Nümbrecht, Germany) at each point in time by a physician or other authorized person who visited the participants at home or other locations during their usual daily activities. Blood samples were immediately stored in ice until the samples were centrifuged, for 10 min at 7°C, at 2300g to separate plasma from blood cells. Plasma samples were then stored at −80°C until further analysis of the endocrine parameters. All samples from each participant were assayed in duplicate within the same assay. PRL plasma levels were measured using the Automated Chemiluminescence-Immunoassay-System 180 (ACS: Centaur; Chiron Diagnostics, Leverkusen, Germany). The intra- and inter-assay coefficients of variance were 2.5 and 3.6%, respectively.

Statistical analysis

Deviations from normal distribution were tested with the Kolmogorov–Smirnov test ($P > 0.1$ for all variables). Levene's test was used to verify the assumption that the samples had equal variances. Following statistical confirmation of normal distribution and variance, endocrine data from all subjects were analyzed by a two-way analysis of variance (condition × time) for repeated measures. Post hoc analyses were conducted via paired comparison t-test, with α adjusted for multiple comparisons. An α of 0.05 was considered statistically significant for all analyses. Data are expressed as mean ± SE.

Results

In the experimental condition, all couples had sexual intercourse within the given time frame. All females ($n = 7$) indicated having one or two orgasms during this period (mean 1.57 ± 0.20). The length of sexual activity was 36.4 min (± 5.64) on average.

Analysis of the PRL concentration in serial blood samples during the 32 h period revealed a first PRL surge in response to sexual intercourse. The PRL levels were still increased (by 300% above baseline) at 21:00 h (Fig. 1A and B). PRL plasma levels declined thereafter; however, they increased again at 01:00 h according to their circadian rhythm, with no significant differences between conditions. Afterwards PRL levels decreased during the morning hours. As hypothesized, a third elevation of nearly 100% was measured, beginning before noon. This increase in PRL fell soon after, reaching baseline levels again at 17:00 h. Analysis of PRL levels was continued until the detection of the next early morning surge at 01:00 h. In contrast, subjects during the control condition who refrained from any kind of sexual activity showed PRL plasma levels depicting only a single surge during early morning at 01:00 h and declining thereafter according to the circadian rhythm. Consequently, statistical analysis revealed condition effects ($F = 6.71$, $P = 0.041$), time effects ($F = 9.31$, $P = 0.000$) and condition × time effects ($F = 3.05$, $P = 0.001$). Post hoc analysis showed significant effects for the 19:00 h sample ($t = -2.50$, $P = 0.046$) and the 13:00 h sample ($t = -3.138$, $P = 0.020$) as well as borderline effects at 21:00 h ($t = -2.249$, $P = 0.066$) and 15:00 h ($t = -2.043$, $P = 0.087$; Fig. 1A).

Discussion

The role of PRL in human reproductive and sexual functions has not yet been fully elucidated. On the basis of our results from animal studies, we designed a pilot study to unveil potentially similar secretory
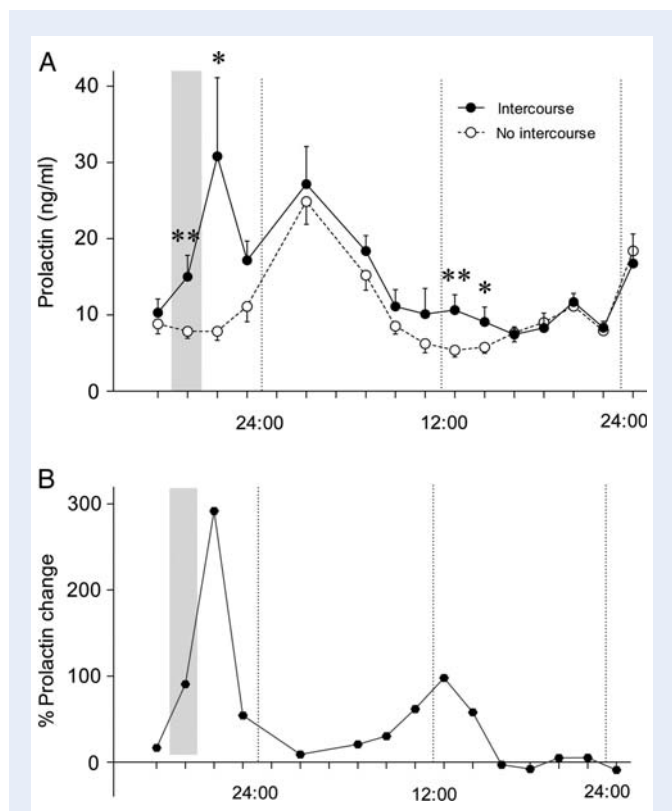

Figure 1 PRL secretory rhythm after sexual contact in women. (**A**) Mean ($\pm$ SE) plasma PRL concentrations following sexual intercourse (filled circle) and during a control condition (balanced crossover design) without sexual intercourse (open circle) in females ($n = 7$) during mid-cycle (ovulation) both starting at around 17:00 h. The sexual contact was time-phased around 19:00 h (indicated by gray bar). Blood samples were taken every 2 h, with the exception of the sleeping period between 23:00 and 07:00 h when the blood sampling interval was set at 4 h (*$P < 0.05$ and ** $P < 0.09$ versus control). (**B**) The percentage change in plasma PRL concentrations following sexual intercourse when compared with the control condition (no intercourse).

characteristics in women. In particular, we analyzed the PRL secretory rhythm after sexual contact in female volunteers over a period of 32 h. These data provide for the first time evidence of a prolonged alteration of the PRL secretory rhythm induced by sexual intercourse. In addition to the regular circadian rhythm-related fluctuation of the PRL concentration, a first transient PRL surge was measured immediately after sexual intercourse. The appearance of this surge has been reported previously (Exton et al., 2001; Kruger et al., 2003a,b; Brody and Kruger, 2006). Surprisingly, our data revealed an additional PRL elevation that appeared on the next day around noon (Fig. 1). To our knowledge, this is the first time a secondary PRL surge has been shown in humans that has been induced by sexual contact only. As our study focused roughly on the 24 h following sexual contact, we have no data concerning a third or even a fourth surge. One can only speculate that sexual intercourse induces an oscillatory PRL secretion pattern, similar to the secretory rhythm measured in rodents leading to a third, fourth and further surges. Further studies are necessary to elucidate the appearance of additional surges in

women. Moreover, supplementary studies are needed to detect potential correlation between the length of couple's relationship and the extent of PRL surge, verifying habituation effects to mating partners (Coolidge effect).

The PRL secretory pattern observed here resembles the oscillatory fluctuation of PRL levels measured in pregnant or pseudo-pregnant rats, where mating-induced PRL surges fulfill important reproductive, endocrine and behavioral functions (Grattan and Kokay, 2008; Egli et al., 2010). The oscillatory secretion pattern in rats consists of a diurnal (around 15:00 h) and a nocturnal (around 03:00 h) surge (Freeman et al., 2000). One of the major purposes of the additionally secreted PRL is to maintain the functional and structural integrity of the corpus luteum (luteotrophic function), ensuring progesterone secretion during early pregnancy. Owing to the persistence of the PRL surges for about 10 days, a 'memory'—characterized by short-term neural activity resulting in long-term neuroendocrine response—has been proposed in the literature (Egli et al., 2006; Grattan and Kokay, 2008). During mid- and late-pregnancy, this function is taken over by placental lactogens that terminate the diurnal PRL rhythm in rodents (Grattan et al., 2008). To generate such a secretion pattern, a complicated interplay of PRL stimulatory and inhibitory factors, released in a precise chronological order within the anterior lobe of the pituitary gland, is necessary to orchestrate PRL secretion by lactotrophs. We have proposed a neuro-endocrinological mechanism that is able to generate such a secretory pattern upon stimulation (Egli et al., 2004, 2006). In this mechanism, oxytocin serves as an inducer of the changed PRL secretory rhythm. Oxytocin is a potent PRL-releasing factor and it is secreted in response to the mating stimulus in rats (Egli et al., 2004) and sexual contact in humans (Kruger et al., 2003a,b; Levin, 2011). It is therefore possible that oxytocin triggers a neuroendocrine reflex leading to an altered PRL secretion pattern (Egli et al., 2006). As a response to the changed secretion rhythm, the additional PRL circulating would favor successful conception and pregnancy (Kruger et al., 2002; Egli et al., 2010).

The physiological role of PRL in human gestation is less well understood, although hypo- and hyperprolactinemia have been linked to impaired oocyte quality and luteal function deficiency (Egli et al., 2010). Indeed, it has been shown that PRL inhibits catabolism in the corpus luteum. Furthermore, PRL is responsible for maintaining a large number of LH and estrogen receptors (Leroy-Martin et al., 1989) and it demonstrates potent antiapoptotic properties on granulosa cells (Perks et al., 2003). Additionally, on a local level, PRL has been shown to play a crucial role in implantation and subsequent placentation in the human endometrium (Jabbour and Critchley, 2001), while a lack of endometrial PRL is involved in reproductive failure (Garzia et al., 2004). Interestingly, the PRL receptor has been detected in endometrial tissue and its concentration is particularly high during the secretory phase of the menstrual cycle (Jabbour and Critchley, 2001). In contrast, during the proliferative state, the PRL receptor concentration of the same tissue is negligible (Jabbour and Critchley, 2001). Thus, PRL secretion during the secretory phase of the cycle is likely to have a bigger influence on the endometrium than during the proliferative phase because of the expression pattern of the PRL receptor. It is thus reasonable to assume that the regulatory influence of PRL on PRL receptor expression in the endometrium, which has been suggested earlier (Jabbour and Critchley, 2001) and demonstrated in the mammary gland (Djiane and Durand, 1977), plays a

more important role during the secretory phase. One can further presume that sexual contact during the proliferative phase initiates PRL surges such as we have shown in Fig. 1 but because of low PRL receptor expression, the endometrium would not respond accordingly. In contrast, a stronger response of the endometrium can be assumed when the sexual contact takes place during the early secretory phase. Within that period of time, the demonstrated positive role of PRL in the implantation process (Negami and Tominaga, 1991) would be executed more effectively. The role of a longer lasting change in the PRL secretory rhythm induced by intercourse may be for keeping the PRL concentration higher from the moment of fertilization until PRL synthesis and secretion is established in the endometrium, around Day 20–24 (mid-secretory phase) of the menstrual cycle (Bryant-Greenwood et al., 1993) which is about 6–10 days post-fertilization.

Although there are essential differences between the regulation of the corpus luteum in humans and that of rodents, our results reveal the possibility that PRL has a regulatory function in the steroidogenesis of human luteal tissues, with substantial implications for successful conception and early pregnancy. Before integrating this knowledge into the assessment of patients with reproductive failure, this study needs to be replicated using a larger sample size and an extended blood sampling period. Furthermore, by administrating a single dose of oxytocin to human females during mid-cycle, the role of oxytocin as a lactotrophic PRL-releasing hormone and initiator of altered PRL rhythm could be verified, as shown in rats (Egli et al., 2006; McKee et al., 2007). This approach may further extend our limited understanding of the function of PRL in human endocrinology and reproduction.

Acknowledgements

Authors' roles

The first two authors designed the study. They were also involved in the analysis of the data as well as in the writing process. They have both contributed equally to the manuscript. E.N. and S.S. carried out the study which included acquiring the volunteers and guiding them through the study process. Furthermore, they were engaged in the blood sampling activities (supervised by T.H.C.K., B.L. and M.E.). The scientific support was provided by U.H. and M.S.. In addition, M.S. was engaged in analyzing the blood samples. M.E. came up with the idea and the concept of the research project and he was involved in the design of the study. He also provided scientific support and participated in writing the manuscript.

Funding

Conflict of interest

There is no conflict of interest for any of the authors.

References

Alvergne A, Lummaa V. Does the contraceptive pill alter mate choice in humans? *Trends Ecol Evol* 2010;**25**:171–179.

Ben-Jonathan N, LaPensee CR, LaPensee EW. What can we learn from rodents about prolactin in humans? *Endocr Rev* 2008;**29**:1–41.

Bouilly J, Sonigo C, Auffret J, Gibori G, Binart N. Prolactin signaling mechanisms in ovary. *Mol Cell Endocrinol* 2011; [Epub ahead of print].

Brody S, Kruger TH. The post-orgasmic prolactin increase following intercourse is greater than following masturbation and suggests greater satiety. *Biol Psychol* 2006;**71**:312–315.

Bryant-Greenwood GD, Rutanen EM, Partanen S, Coelho TK, Yamamoto SY. Sequential appearance of relaxin, prolactin and IGFBP-1 during growth and differentiation of the human endometrium. *Mol Cell Endocrinol* 1993;**95**:23–29.

Djiane J, Durand P. Prolactin-progesterone antagonism in self regulation of prolactin receptors in the mammary gland. *Nature* 1977;**266**:641–643.

Egli M, Bertram R, Sellix MT, Freeman ME. Rhythmic secretion of prolactin in rats: action of oxytocin coordinated by vasoactive intestinal polypeptide of suprachiasmatic nucleus origin. *Endocrinology* 2004;**145**:3386–3394.

Egli M, Bertram R, Toporikova N, Sellix MT, Blanco W, Freeman ME. Prolactin secretory rhythm of mated rats induced by a single injection of oxytocin. *Am J Physiol Endocrinol Metab* 2006;**290**:E566–E572.

Egli M, Leeners B, Kruger TH. Prolactin secretion patterns: basic mechanisms and clinical implications for reproduction. *Reproduction* 2010;**140**:643–654.

Exton MS, Kruger TH, Koch M, Paulson E, Knapp W, Hartmann U, Schedlowski M. Coitus-induced orgasm stimulates prolactin secretion in healthy subjects. *Psychoneuroendocrinology* 2001;**26**:287–294.

Freeman ME, Kanyicska B, Lerant A, Nagy G. Prolactin: structure, function, and regulation of secretion. *Physiol Rev* 2000;**80**:1523–1631.

Garzia E, Borgato S, Cozzi V, Doi P, Bulfamante G, Persani L, Cetin I. Lack of expression of endometrial prolactin in early implantation failure: a pilot study. *Hum Reprod* 2004;**19**:1911–1916.

Grattan DR, Kokay IC. Prolactin: a pleiotropic neuroendocrine hormone. *J Neuroendocrinol* 2008;**20**:752–763.

Grattan DR, Steyn FJ, Kokay IC, Anderson GM, Bunn SJ. Pregnancy induced adaptation in the neuroendocrine control of prolactin secretion. *J Neuroendocrinol* 2008;**20**:497–507.

Jabbour HN, Critchley HO. Potential roles of decidual prolactin in early pregnancy. *Reproduction* 2001;**121**:197–205.

Jabbour HN, Critchley HO, Boddy SC. Expression of functional prolactin receptors in nonpregnant human endometrium: janus kinase-2, signal transducer and activator of transcription-1 (STAT1), and STAT5 proteins are phosphorylated after stimulation with prolactin. *J Clin Endocrinol Metab* 1998;**83**:2545–2553.

Kruger TH, Haake P, Hartmann U, Schedlowski M, Exton MS. Orgasm-induced prolactin secretion: feedback control of sexual drive? *Neurosci Biobehav Rev* 2002;**26**:31–44.

Kruger TH, Haake P, Chereath D, Knapp W, Janssen OE, Schedlowski M, Hartmann U. Specificity of the neuroendocrine response to orgasm during sexual arousal in men. *J Endocrinol* 2003a;**177**:57–64.

Kruger TH, Haake P, Haverkamp J, Kramer M, Exton MS, Saller B, Leygraf N, Hartmann U, Schedlowski M. Effects of acute prolactin manipulation on sexual drive and function in males. *J Endocrinol* 2003b;**179**:357–365.

Leroy-Martin B, Bouhdiba M, Saint Pol P, Peyrat JP. Peripheral effects of prolactin in reproduc-tive function. II. Female reproductive function. *J Gynecol Obstet Biol Reprod (Paris)* 1989;**18**:288–294.

Levin RJ. Can the controversy about the putative role of the human female orgasm in sperm transport be settled with our current physiological knowledge of coitus? *J Sex Med* 2011;**8**:1566–1578.

Marazziti D, Canale D. Hormonal changes when falling in love. *Psychoneuroendocrinology* 2004;**29**:931–936.

Maslar IA, Riddick DH. Prolactin production by human endometrium during the normal menstrual cycle. *Am J Obstet Gynecol* 1979;**135**:751–754.

McKee DT, Poletini MO, Bertram R, Freeman ME. Oxytocin action at the lactotroph is required for prolactin surges in cervically stimulated ovariectomized rats. *Endocrinology* 2007;**148**:4649–4657.

Negami AI, Tominaga T. (1991) Effects of prolactin on cultured human endometrial cells. *Horm Res* 1991;**35**:50–57.

Perks CM, Newcomb PV, Grohmann M, Wright RJ, Mason HD, Holly JM. Prolactin acts as a potent survival factor against C2-ceramide-induced apoptosis in human granulosa cells. *Hum Reprod* 2003;**18**:2672–2677.

Smith MS, Freeman ME, Neill JD. The control of progesterone secretion during the estrous cycle and early pseudopregnancy in the rat: prolactin, gonadotropin and steroid levels associated with rescue of the corpus luteum of pseudopregnancy. *Endocrinology* 1975;**96**:219–226.

Wu WX, Brooks J, Glasier AF, McNeilly AS. The relationship between decidualization and prolactin mRNA and production at different stages of human pregnancy. *J Mol Endocrinol* 1995;**14**:255–261.