

ISSWSH Master Journal Club 2016

Research Coming to Terms with Menstrual Cycling

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Disclosure of conflict of interest: J.R. Heiman

Nothing to declare

Many if not most biopsychosocial sexuality studies ignore menstrual cycle status for various reasons

- Prior research null findings
- Conviction that it is not important because other variables override
- Measurement complexity

..... And yet.....

- Lots of variability in results suggests addressing hormonal status makes sense
- Hormonal contraceptive use widespread

An example

Does neural activation change across the menstrual cycle when women evaluate men as potential sexual partners?

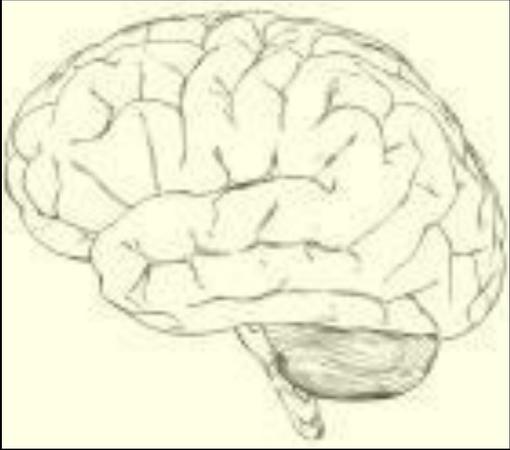
Rupp et al., Evolution and Human Behavior 30 (2009) 1–10

- 12 normal cycling heterosexual preference females aged 23-28.
- Tested at two phases of the menstrual cycle (follicular, days 10-12; luteal, days 19-23) in a counterbalanced order.
- Before each test session saliva and blood samples collected for assay of testosterone, estrogen, and progesterone.

Hormones



Sexual Stimulus



Sexual Interest

fMRI Methods

Participants viewed 224 pictures of morphed male faces (Rowland & Perrett, 1995) across 8 runs in an event related design while an fMRI (3T Seimens) measured brain activation.



30%



Pictures presented for 4 seconds with variable ISI (4-12 seconds).

Instructions

You are not in a committed relationship and are open to a sexual encounter. You and some friends are out Friday night. While out, you meet the man presented in the image for the first time. You two have a good time talking together and that continues into the evening. You and he end up back at his place to continue hanging out. It is clear to you that he would have sex with you if you want to.

Imagine that you are in this scenario and open to a sexual encounter. Based on the image and information presented, please indicate using the button box:

How likely would you be to have sex with him?

1 = Very Unlikely

2 = Unlikely

3 = Likely

4 = Very Likely

Subjective Evaluations

Participants' subjective evaluations of likelihood of having sex with the men presented did not differ by menstrual cycle phase or masculinity of the faces (Mean \pm SD=1.92 \pm .29).

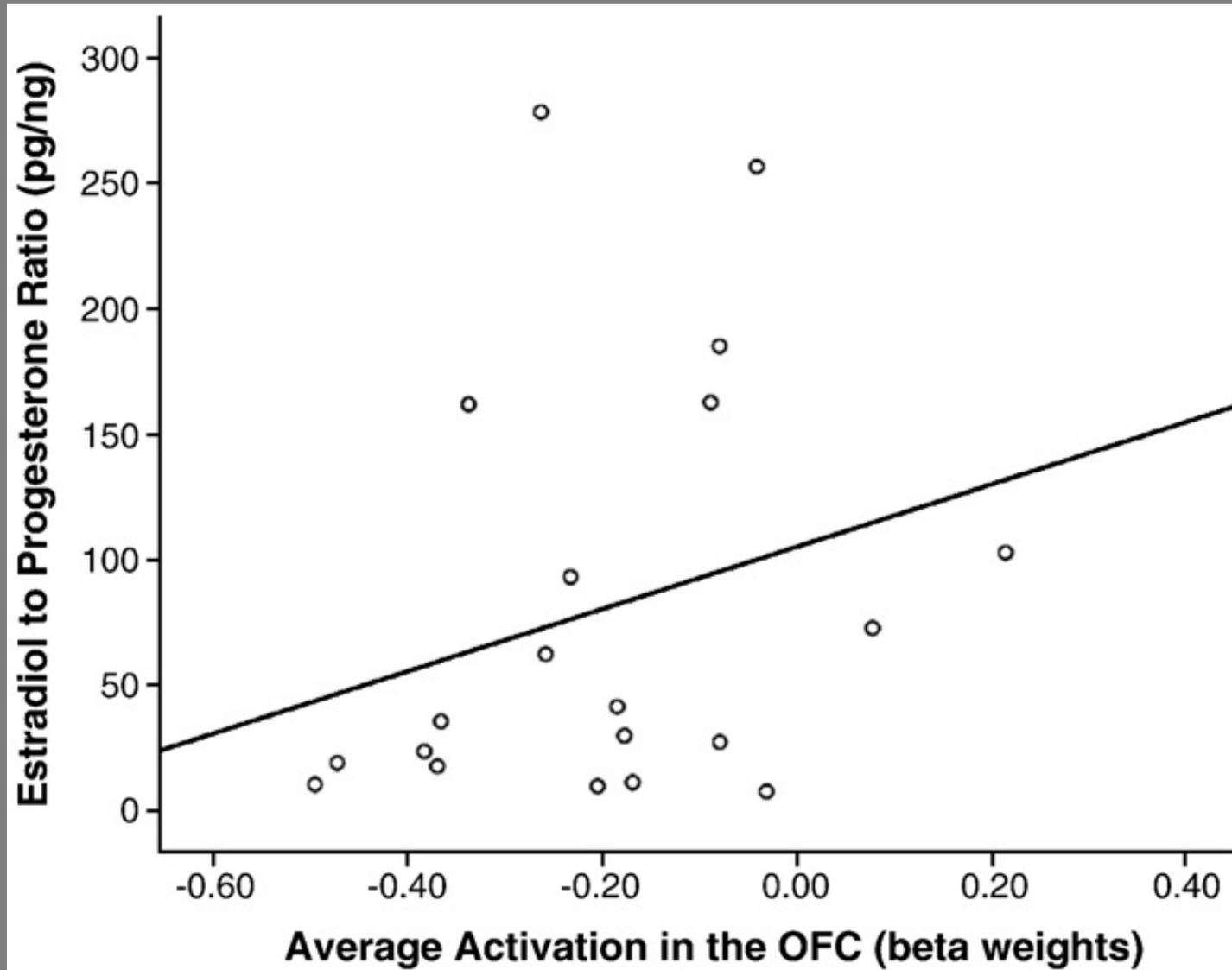
Subjective Evaluations—Hormonal Levels

r Subjective likelihood of having sex—Progesterone = -0.55 in Follicular

r Subjective likelihood of having sex—Estrogen/Progesterone = 0.54 in Luteal

Subjective ratings of both faces and houses were higher when either progesterone, or levels of progesterone in relation to levels of estradiol were lower, which is the characteristic hormone profile of the follicular phase.

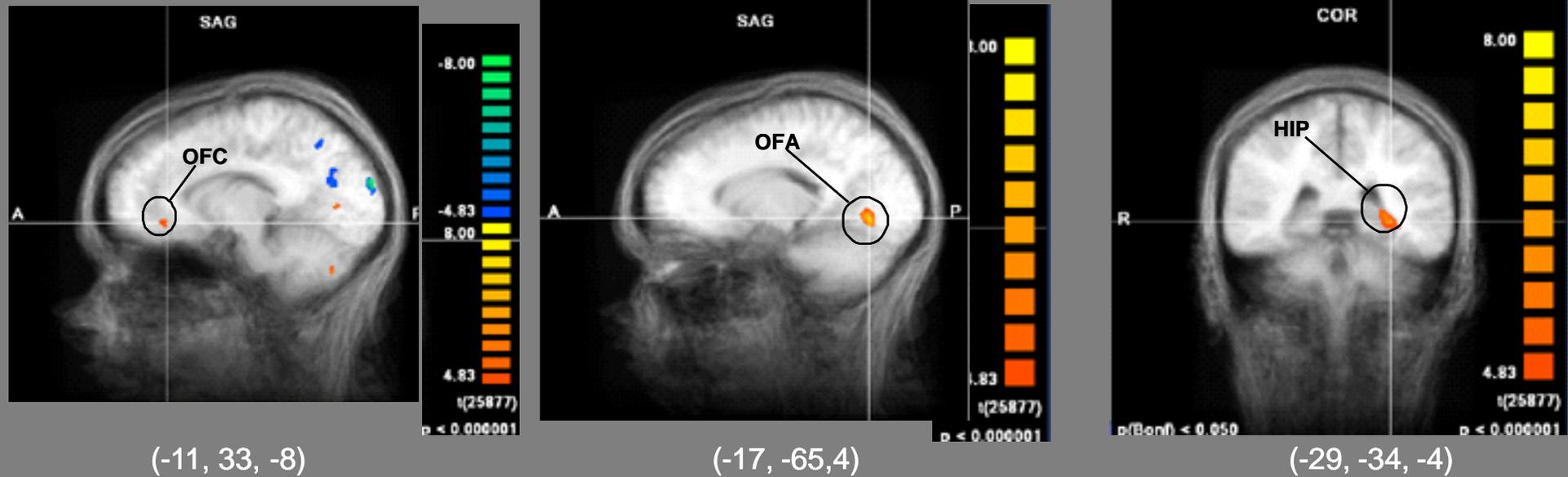
OFC activation and E/P Ratio



MORE ACTIVATION DURING THE FOLLICULAR PHASE IN BRAIN REGIONS ASSOCIATED WITH REWARD AND FACE PROCESSING

L Medial Orbitofrontal Cortex, L Occipital Face Area, L Hippocampus.

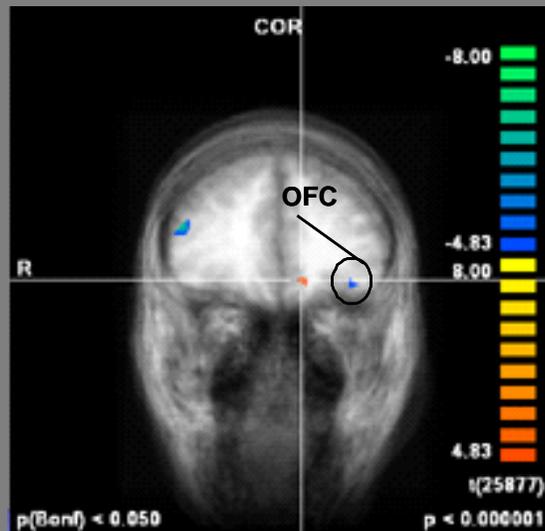
(Faces Follicular – Fixation) – (Faces Luteal – Fixation)



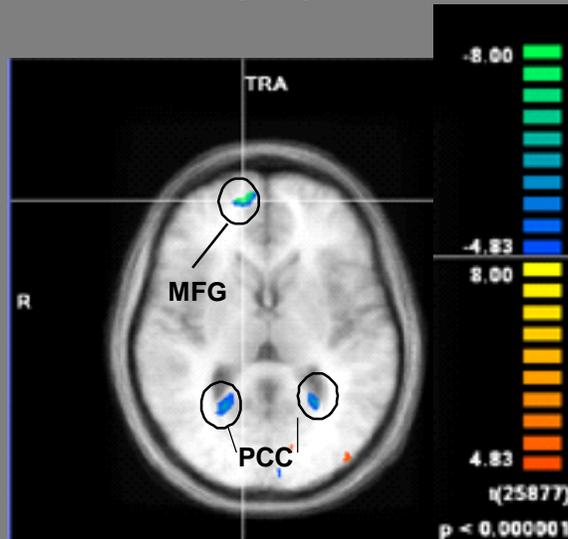
MORE ACTIVATION DURING THE LUTEAL PHASE IN BRAIN REGIONS ASSOCIATED WITH COGNITIVE CONTROL AND RISK

L Lateral Orbitofrontal Cortex, *R* Medial Frontal Gyrus, Bilateral *I* Posterior Cingulate, *R* Dorsal Lateral Prefrontal Cortex

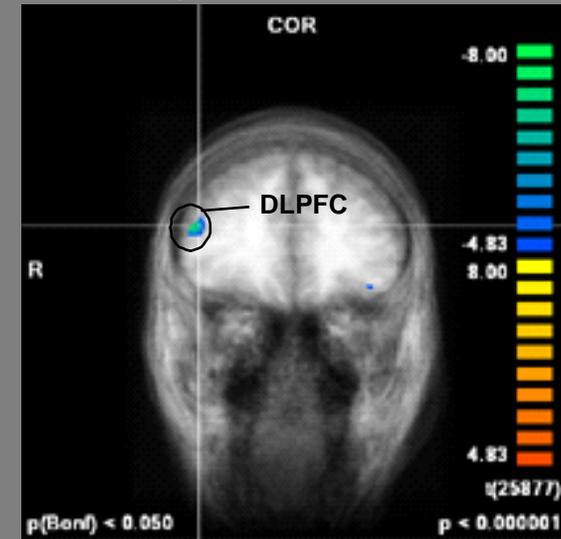
(Faces Luteal– Fixation) – (Faces Follicular– Fixation)



(-33, 34, -8)



(12,53,7)

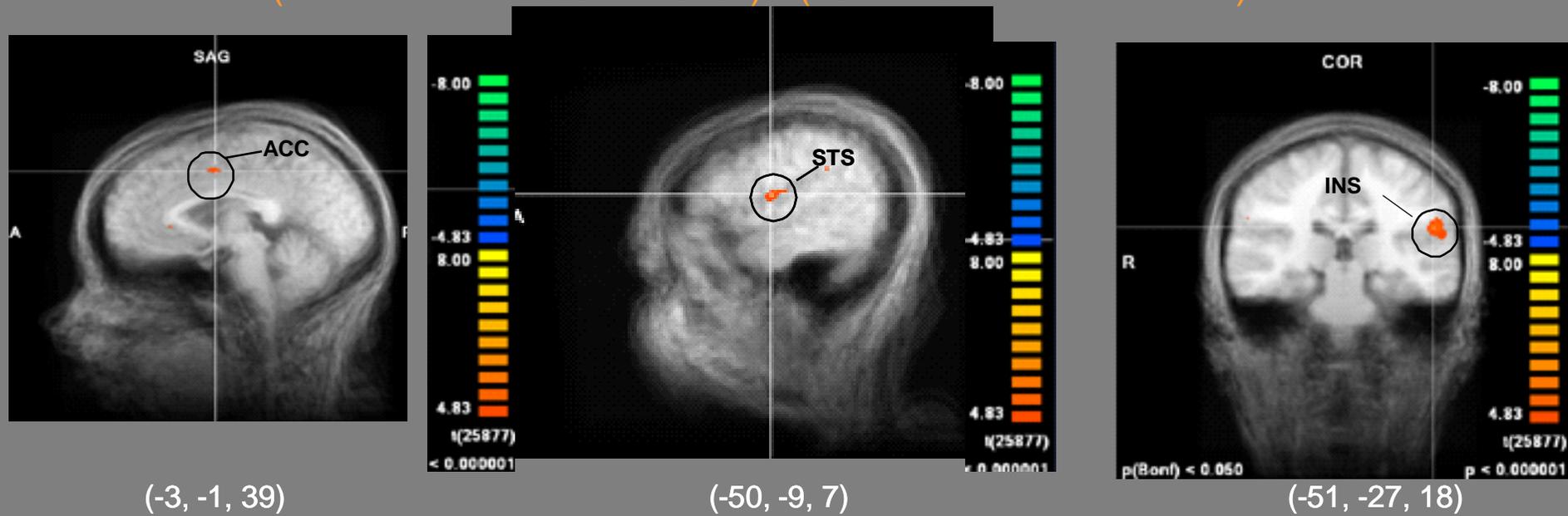


(44, 30, 20)

MORE ACTIVATION IN RESPONSE TO MASCULINIZED FACES IN BRAIN REGIONS ASSOCIATED WITH RISK, SENSORY PROCESSING, AND EMOTION

L Anterior Cingulate Cortex, Bilateral Superior Temporal Sulcus, And L Insula

(Masculinized Faces – Fixation) – (Feminized Faces – Fixation)



DISCUSSION

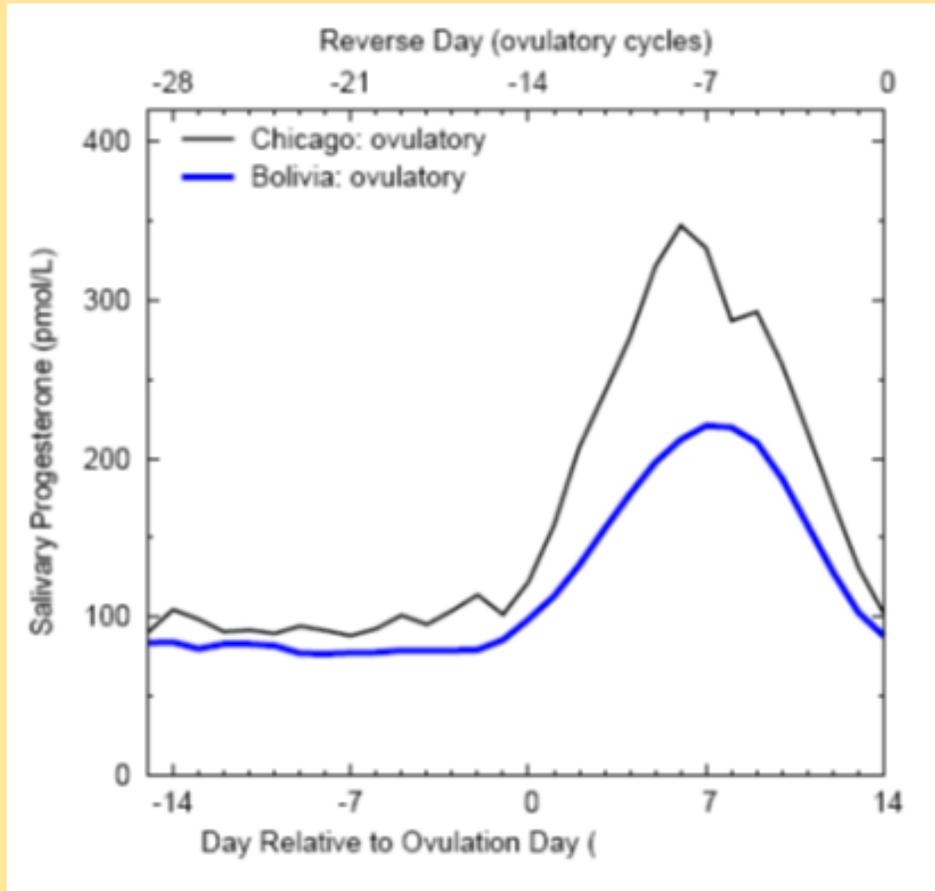
- Women's patterns of neural activation were phase dependent.
- During the follicular phase, women exhibited more neural activation in response to male faces in areas related to reward and face processing, and less activation in brain regions associated with executive and cognitive control.
- Women showed increased activation in response to masculinized faces in brain areas associated with risk, including the ACC, suggesting that masculinized faces are perceived to be more risky than feminized faces. Women also appeared to engage more complex sensory processing systems when viewing masculinized faces.
- This patterns of activation observed here may promote increased risk aversion later in the menstrual cycle, which may contribute to previously reported decreases in sexual behavior and preferences for less masculine men later in the cycle.

CONCLUSIONS

- Subjective ratings, response times, and neural activation may be differentially influenced by menstrual cycle phase.
- Cyclic variation in neural activity in the absence of robust differences in subjective ratings suggests a subtle hormonal effect in the brain on the cognitive processing of stimuli that may bias, but not dictate, women's sexual behavior.

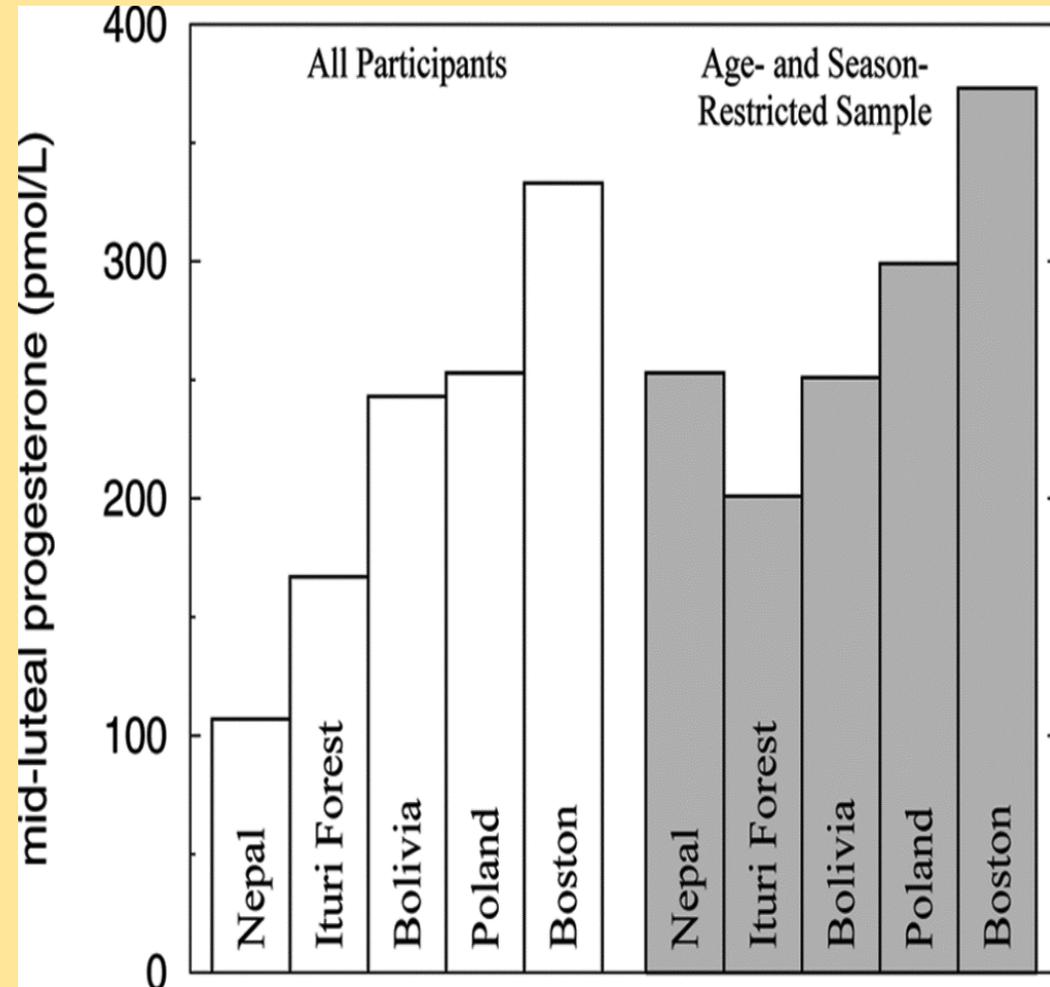
Other Menstrual Cycle Knowledge

Cross cultural differences in Hormone Levels



In Bolivian women, P4 concentrations in ovulatory cycles averaged about 70% of those in a sample of Chicago women.

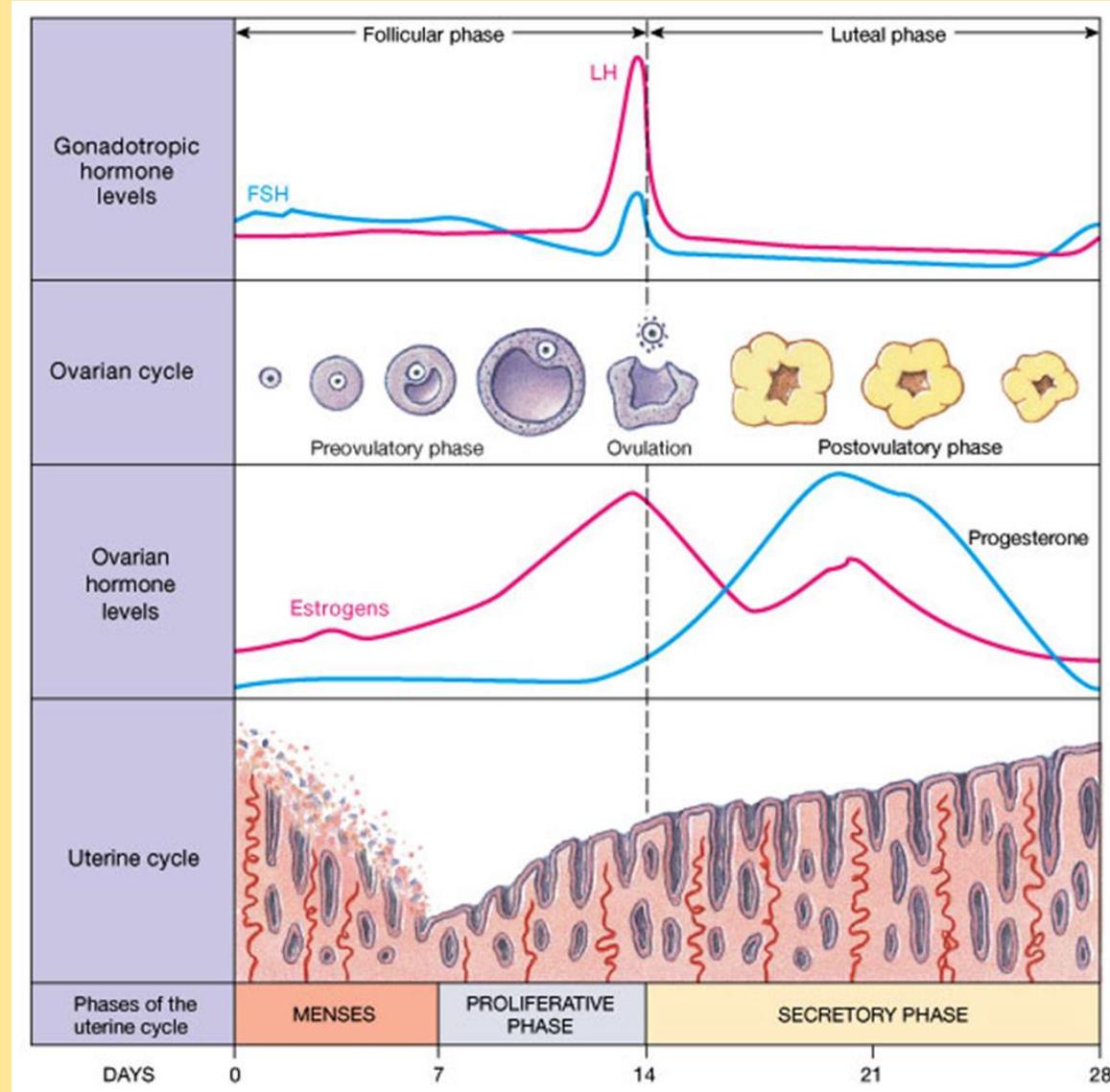
Vitzthum & Ringheim 2005. *Stud. Fam. Plan.* 36:13-32.



Endogenous ovarian steroid levels are lower in several non-industrialized populations, including Bolivia

Harris & Vitzthum, 2013

Why menstruate?



Theories

- Margie Profet, UC Berkeley, suggested in 1993 that menstruation's function is to "defend against pathogens transported to the uterus by sperm". Data did not support this.
- Beverly Strassmann, U Michigan, argued in 1996 that costs a lot of energy to maintain a thick, blood-filled layer inside the womb all the time. Thus breakdown of tissue was energetically economical. Menstruation is a by-product, rather than something evolution had specifically favored.
- Colin Finn, U Liverpool in the UK, proposed 1998 that menstruation is a necessary consequence of the way the womb evolved. Embryos have pushed deeply into the mother's tissue, and the womb lining has defended itself against the embryo by thickening and forming layers.

Theories

Emera et al., 2011 focused on how spontaneous decidualization evolved

Conflict at the maternal-fetal interface has driven the evolution of spontaneous decidualization (SD) in menstruating species, either:

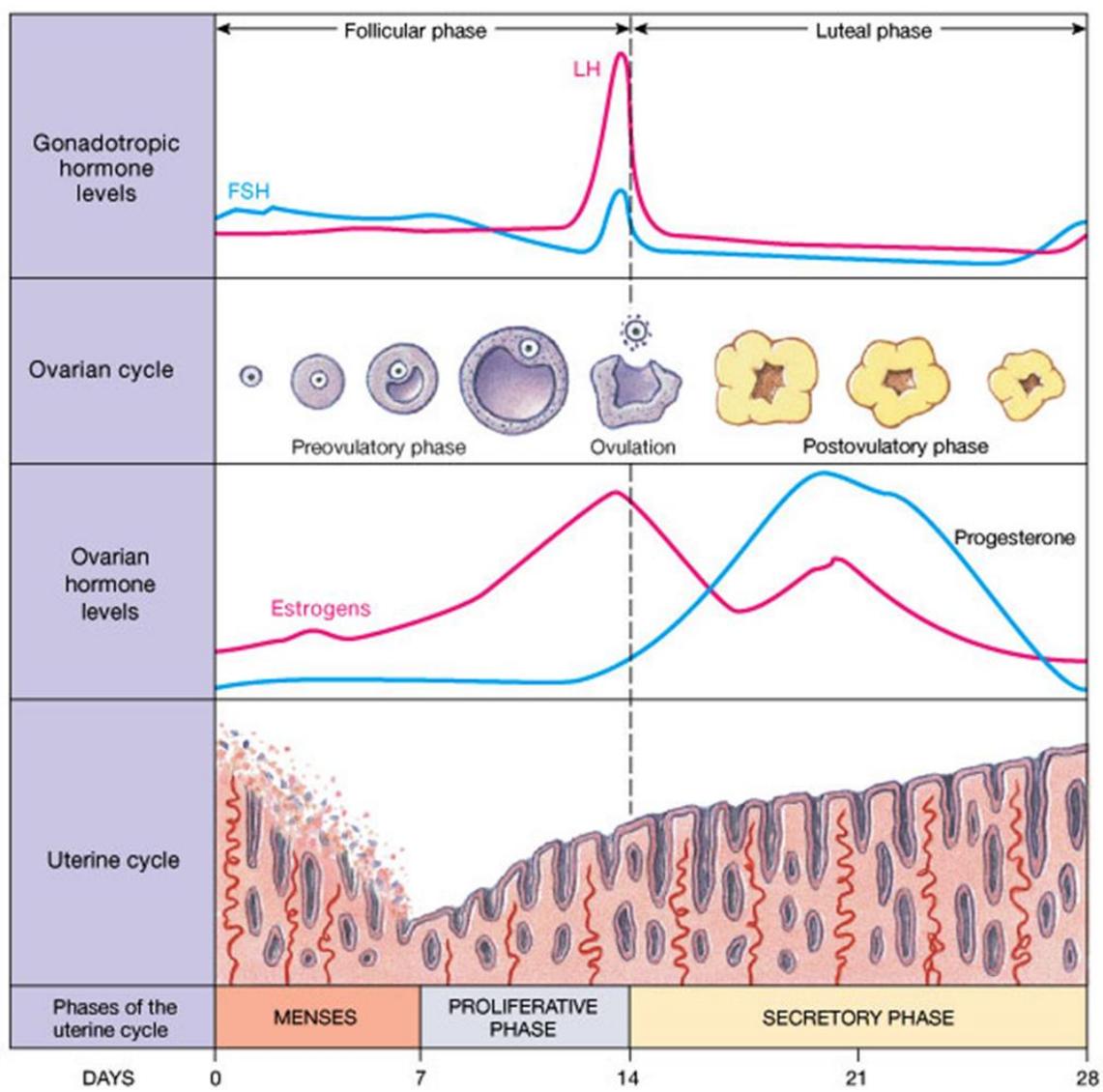
- for early protection against invasive fetal tissues, and/or
- for embryo selection (SD allows the mother to sense embryo quality)

How? Uncertain but authors suggest three models of evolution of SD by genetic assimilation

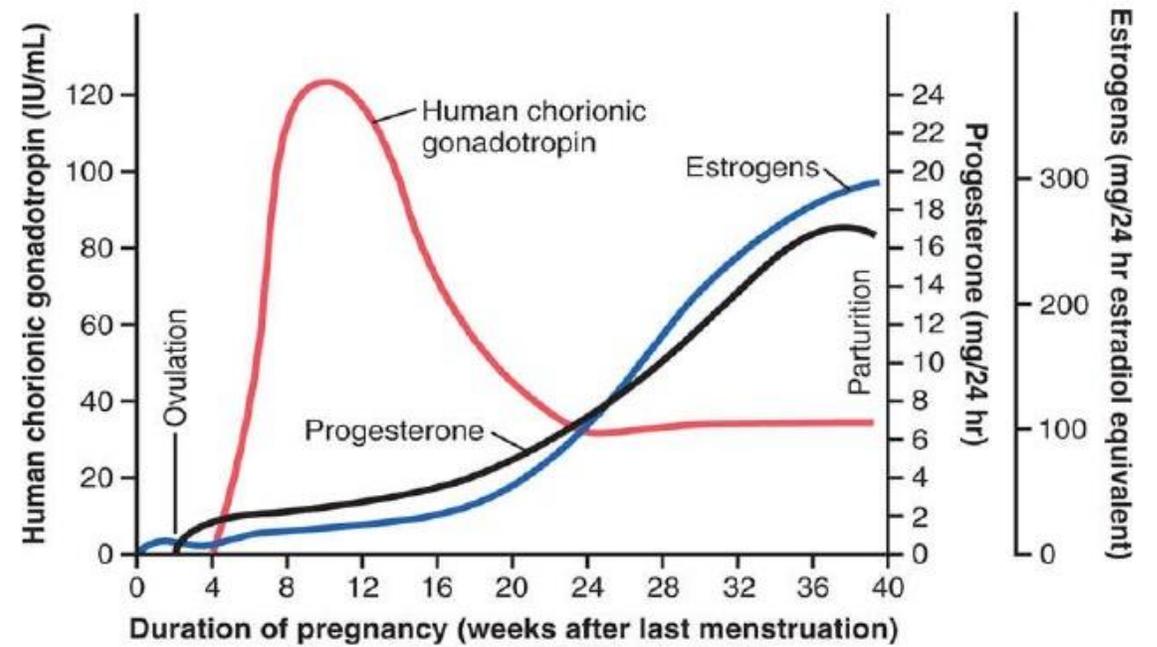
A role for menstruation in preconditioning the uterus for successful pregnancy

Jan J. Brosens, MD, PhD; Malcolm G. Parker, PhD; Angus McIndoe, MD, PhD; Robert Pijnenborg, PhD; Ivo A. Brosens, MD, PhD

Am J Obstet Gynecol 2009;200:615.e1-615.e6.



Rates of secretion of estrogen and progesterone and concentration of hCG at different stages of pregnancy



Brosens et al., 2009

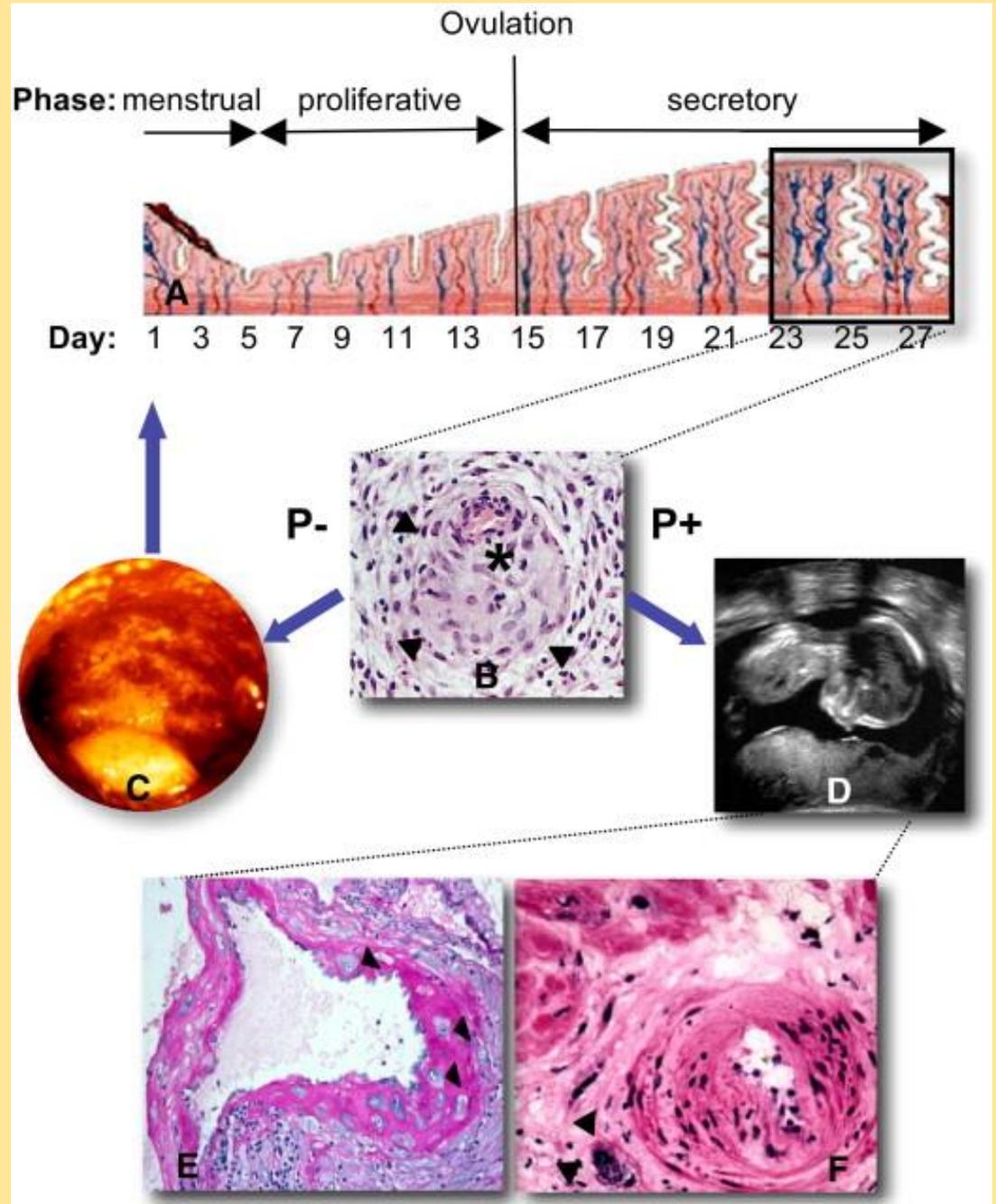
Simian primates (Old World monkeys, apes, and human beings) possess invasive hemochorial placentae and typically exhibit some form of menstruation.

Menstruation in humans “not only extraordinarily heavy but placentation is also exceptionally deep, with trophoblast invading not only the decidual endometrium but also the inner third of the myometrium..” (p 615)

Brosens et al., 2009

“One unifying feature of the endometrium of menstruating species, including bats, appears to be the profound progesterone-driven remodeling of the stromal compartment, a process termed ‘decidualization’” (p 615).

Brosens et al., 2009



Cyclic menstruation
and deep placentation

Brosens et al., 2009

Human reproduction has evolved in ways that limit the likelihood of pregnancy while maximizing the frequency of menstruation.

Human beings: do not exhibit overt estrous behavior, have a limited and variable fertile window and concealed ovulation and have a high incidence of pre-implantation embryo wastage. Moreover, 90% of all menstrual cycles in very young adolescent girls are anovulatory.

“The reciprocal relationship between fecundity and menstruation suggests that repeated menstrual priming or preconditioning of uterine tissues and its vasculature during nonconception cycles could be instrumental for successful deep placentation.”

Neonatal uterine bleeding as antecedent of pelvic endometriosis

Ivo Brosens, Jan Brosens, and Giuseppe Benagiano

Human Reproduction, 2013, 28, 2893–2897

doi:10.1093/humrep/det359

Data source for NUB

Table I Prevalence of overt and occult NUB.

Clinical presentation	Incidence (%)	References
Visible	4.7	Levy et al. (1964)
	5.3	Kaiser and Grassel (1974)
	3.3	Huber and Zechmann (1974)
Occult ^a	61.3	Kaiser and Grassel (1974)
	25.4	Huber and Zechmann (1974)

^aBased on blood detection test.

Brosens, et al., 2013

“Endometrial stem cells may become disseminated in the pelvis at the time of neonatal uterine bleeding (NUB). These neonatal endometrial stem cells may in turn be responsible, through a variety of mechanisms, for early-onset endometriosis.” (Brosens et al, 2013, p 2893)

Occult vaginal bleeding occurs in a majority of neonates, although overt bleeding is estimated to occur in only 5% of neonates.

Does NUB have a role in the pathogenesis of endometriosis?

Existing data, though limited, “support the hypothesis that retrograde bleeding in the neonate lies at the roots of pelvic endometriosis, thus extending Sampson’s theory (Sampson, 1927) to include the pathogenesis of pre-menarcheal and adolescent disease. There is unequivocal evidence that the neonatal endometrium can mount a decidual response”(Brosens et al., 2013)

Summary re hypothesized function of menstrual cycling

“The concepts of “ontogenetic progesterone resistance” and “menstrual preconditioning” infer that the human uterus starts out as an immature organ that acquires competence in response to dynamic remodeling events triggered by neonatal uterine bleeding, anovulatory bleeding, menstruation, miscarriage or parturition. In fact, the term “uterine plasticity” has been coined to describe the ability of this organ to constantly adapt throughout the reproductive years.” (Brosens et al., 2015, p 4.)



Seba's short-tailed bat (*Carollia perspicillata*) menstruates (Credit: Visuals Unlimited)



Rufous elephant shrews (*E. rufescens*) also menstruate (Credit: Mark MacEwen/NPL)



Wild Fulvous Fruit Bats



Douc langur