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### Birth, love, and fear: Physiological networks from pregnancy to parenthood



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Keywords: Dyad Mood Biological rhythm Mother Child Reproduction	Pregnancy and childbirth are among the most dramatic physiological and emotional transformations of a life- time. Despite their central importance to human survival, many gaps remain in our understanding of the tem- poral progression of and mechanisms underlying the transition to new parenthood. The goal of this paper is to outline the physiological and emotional development of the maternal-infant dyad from late pregnancy to the postpartum period, and to provide a framework to investigate this development using non-invasive timeseries. We focus on the interaction among neuroendocrine, emotional, and autonomic outputs in the context of late pregnancy, parturition, and post-partum. We then propose that coupled dynamics in these outputs can be leveraged to map both physiologic and pathologic pregnancy, parturition, and parenthood. This approach could address gaps in our knowledge and enable early detection or prediction of problems, with both personalized depth and broad population scale.

#### 1. Introduction & hypothesis

Few naturally occurring phenomena instill equal measures of fear and love as the experience of human childbirth. Throughout history, the documented dangers associated with pregnancy and birth stand alongside the narrative of the beauty, mystique, and reverence for giving birth as an act of love [1,2]. The idea that birth is a loving act likely stems from the notion that to do so risks one's own health and possibly life, and therefore could be seen as the ultimate sacrifice. Yet physical (e.g., endocrine and autonomic) processes enable parturition, as well as adaptation to caring for a newborn. How physiological and emotional states are linked in the context of reproduction and if such links can be measured through peripheral "surrogate markers" is a largely unanswered question. In this paper, we review how precisely coordinated fluctuations of steroid hormones, reproductive peptides, and autonomic nervous system (ANS) outputs within the maternal body integrate signals from the placenta, fetus (newborn), and environment. We propose that these coupled, that is, co-regulated, dynamics contribute to emotional experience and, potentially, peripheral biomarkers of these formative transitions [3,4].

Pregnancy, parturition, and parenting are enabled by hormonal and neural adaptations that influence behavior, permitting otherwise selfish humans to make themselves vulnerable. Human pregnancy has long been viewed from the perspective of life history evolution, with the mother and fetus in a tug-of-war for resources, driven by the extensive or invasive nature of hemochorial placentation and the demands of human brain development [5–7]. This conflict does not always culminate with the survival of parent *and* child, thereby infusing fear and uncertainty to the process of reproduction [8]. However, the process of pregnancy and birth may be viewed as cooperative rather than competitive or sacrificial; it is a well-timed physiologic dance between partners that usually results in a healthy newborn and a tired but accomplished mother ready to face the primal challenges of lactating and child care [9]. Parenting requires selflessness, creates vulnerabilities for the family, and requires a large investment of resources. Together, for humans to reproduce, fears of pregnancy, birth, and the work of parenting must be overcome by stronger forces: those of bonding, social motivation, and love [1,10, 11].

In this essay, we will highlight how the mother adapts to each of these phases of reproduction, and how these adaptations manifest across neuroendocrine, emotional, and autonomic networks. In section 1, we review the basis of interaction among these three systems. We will then discuss three parts of the transition to parenthood: section 2 on pregnancy, section 3 on childbirth, and section 4 on early postpartum. Within each part of this transition, we will briefly review a) physiological adaptations, b) emotional changes (with an emphasis on the balance of states of love and

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#### Table 1

Known Acute Hormonal Associations Among Body Temperature, HR, HRV, and Emotional State. Representative citations (reviews, where available, or primary literature) are included for each relationship in the context of female reproduction.

Hormone	Temperature	HR	HRV	Emotional State
Estrogens	lower [27]	lower [17]	elevate	mixed effects [29]
Oxytocin	lower [30]	lower [31]	[28] elevate [31]	love, bonding, anxiolytic [32,33]
Progesterone	elevate [34]	elevate [35]	lower [35]	fatigue [36]
Prolactin/ hCS	elevate [37]	elevate [38]	lower [38, 39]	love, bonding [40, 41]
Cortisol/ pCRH	lower [42]	elevate [16,43]	lower [44]	contextual arousal, fear [45]
hCS, human chorionic somatomammotropin; pCRH, placental corticotrophin releasing hormone				

fear), and c) examples of how autonomic timeseries can reflect these processes and, potentially, their pathology. These arguments rely on the existence of consistent temporal relationships among metrics that are difficult to measure (e.g., emotional and neuroendocrine timeseries) and autonomic metrics that are easier to measure (e.g., autonomic influence on skin temperature, heart rate (HR), and heart rate variability (HRV)) [12, 13]. We propose that such timeseries, measurable by wearable devices, may reflect the network reorganization that occurs during the transition to parenthood, and therefore offer non-invasive insights into the associated emotional and hormonal states. Due to the complexity of these processes and the number of systems discussed, this essay is intended to introduce a general framework for the study of becoming a parent, as opposed to providing a comprehensive review. Throughout, the reader will be referred to relevant reviews of each system and reproductive stage.

Additionally, we hypothesize that poor outcomes may be predicted or detected in HR, HRV, or temperature timeseries. Network disruption caused by abnormalities in pregnancy and postpartum physiology might allow us to better understand antecedents of preterm birth, preeclampsia, postpartum depression, or understand critical temporal and social influences (e.g., stress). If future studies support this hypothesis, then monitoring peripheral signals would create a unique opportunity to examine real-time neurobiological manifestations in humans. This knowledge could be integrated into personalized therapies for psychological or physiological conditions and inform the basic science of reproduction. Furthermore, the same methods could apply to studying the postnatal development of a newborn/mother dyad with important implications for early life.

### 2. Emotional, neuroendocrine, and autonomic co-regulation in women

#### 2.1. Synchrony in emotional, neuroendocrine, and autonomic regulation

Reproduction and the ANS are closely coordinated and have measurable associations with emotional state. Outputs of these systems, including reproductive steroid and peptide hormones, corticosteroids, body temperature, and cardiovascular output exhibit coupled oscillations within and across days (Table 1) [12,13]. Although the mechanisms underlying these interactions are incompletely understood, analysis of their synchronized, rhythmic change over time (i.e., *biological rhythms*) has enabled the development of tools for monitoring and making predictions about emotional and female reproductive state. At present, these include anticipating episodes of depression and mania [14,15], detecting stress [16], improving fertility awareness [17–19], optimizing substance use disorder treatment [20], and potentially providing early indications of pregnancy [21,22].

To date, physiological synchrony (e.g., temporal coupling among hormonal, emotional and autonomic systems) has been studied largely in non-pregnant contexts. However, synchrony across systems appears to be at least partially maintained during pregnancy and postpartum. This is remarkable, as gestation and parturition are associated with marked changes in emotional regulation, hypothalamic-pituitarygonadal feedback, the highest lifetime concentrations of sex and corticosteroids, and a rapid decline to a hypogonadal state after parturition [23,24]. If coupling across systems is sufficiently maintained during and after pregnancy, then continuous monitoring of peripheral outputs using a growing number of available wearable devices/monitors may reflect, and even be used to anticipate, the continuous dynamics of more difficult-to-assess hormonal or emotional states [25,26] with implications for understanding potential events (e.g., birth) or problems (e.g., depression, preterm birth).

### 2.2. Substrates for interactions between the reproductive and autonomic systems

Research on interactions between the ANS and the reproductive system has focused largely on the impact of sex steroids and peptides on skin and core temperature, HR, and HRV. Briefly, estradiol reduces core and skin temperature [27,46,47], promotes vasodilation, reduces HR [17,48-50] and increases parasympathetic tone (cholinergic activity)/HRV [17], (reviewed in: [51,52]). In cycling women, progesterone combined with estradiol raises core and skin body temperature and increases sympathetic tone and HR (adrenergic activity) [51-53], and lowers HRV [35,54,55]. These dynamics are more complicated in cases of exogenous hormone delivery, via hormonal contraceptive or hormone replacement therapy, or ovarian hyper stimulation (see: [28,56–58]). During most of pregnancy, progesterone dominance triggers nitric oxide production that, combined with elevated estriol (the dominant form of estrogen from placenta), leads to relaxation of maternal smooth muscle of the vasculature, venous distensibility and decreased systemic vascular resistance [59,60]. These adaptations likely reinforce the impact of high estrogen and progesterone to trigger higher cardiac output, HR, and reduced HRV [61].

Peptide hormones including prolactin and oxytocin also influence thermoregulation and autonomic tone. Oxytocin dose-dependently reduces body temperature and HR [30], and increases HRV [62]. Although less studied, prolactin appears to be relatively elevated during higher temperature states, including metabolic elevation to support milk production [63], exercise [37], and the luteal phase [64]. Moreover, prolactin opposes dopamine's temperature-lowering effects [65,66]. Accordingly, in rodents, the spike in prolactin (along with estradiol and progesterone) on estrous days is associated with a plateau of high core body temperature [67-69]. This phenomenon has also been observed in women following ovulation, along with increased HR and decreased HRV across the luteal phase [17,28,70]. Furthermore, elevation of basal body temperature during pregnancy, and its relationship to progesterone, has been recognized for about a century [71-73]. These changes are thought to be centrally mediated, likely via direct feedback of reproductive hormones and peptides on hypothalamic arcuate tuberoinfundibular dopaminergic, kisspeptin, neurokinin B, and dynorphin (KNDy) neurons that regulate pulsatile release of gonadotropin releasing hormone; via direct feedback medial preoptic populations regulating body temperature, HR, and vascular tone; and through direct synaptic coupling of the arcuate and medial preoptic area [27,46]. How these general principles of coordination among hormones and autonomic outputs are modified during pregnancy, parturition, and the early postpartum period are discussed in individual sections, below.

## 2.3. Reproductive and autonomic impacts on emotional regulation in women

Reproductive hormones and the ANS exhibit complex but predictable interactions with emotional state. Although absolute hormone levels do not exhibit consistent relationships with emotional regulation, direction of hormonal change reveals more consistent associations [74]. Broadly, rapid declines in estrogen and progesterone that occur in the late luteal phase of the ovulatory cycle [75], in cyclic hormone replacement therapy [76,77], and that follow birth [78], are associated with more variable emotional state and elevated amygdalar activity, including depressive/anxious symptoms, less suppression of stress, and potentially greater fear responses [79–81]).

Conversely, states of relatively elevated or rising estradiol (e.g., early-to mid-follicular phase) [82] or estradiol and progesterone (e.g., early to mid-luteal phase) may be associated with relatively elevated mood, and greater suppression of negative emotions [83]. These complex effects may be mediated through changes (largely increases) in serotonin (5-HT) receptor expression [82,84]. Perhaps the context in which the relationship among hormones, peripheral physiology, and mood has been most been studied is that of oxytocin and vasopressin in dyadic synchrony and bond formation (reviewed in: [85]), discussed later in Section 3. Briefly, oxytocin interacts with estrogen to facilitate bonding and onset of maternal behavior [86], increase parasympathetic activity [87,88] and coordinate "adaptive fear and stress responses" [89–91] (e.g., aggression toward intruders [92]). In contrast, maternal anxiety/hypervigilance (fear) may be linked to either variation in oxytocin function and/or in response to patterns of steroid hormone secretion [91,93,94]. Much remains to be learned about the relationship among reproductive hormones and emotional states, including the impacts of untimed, a static dose versus endogenous, naturally contextualized hormone fluctuations [82]. Further, more work has been devoted to negative affect and stress reactivity as opposed to resilience and love, providing broad opportunities for future research.

## 3. Physiological and emotional coordination in pregnancy: the power of the placenta

Interactions among neuroendocrine, emotional, and autonomic fluctuations have been largely studied in cycling humans and in experimental animal models. Pregnancy presents at least two important challenges in comparison to ovulatory cycles. First, the ovulatory cycles of the non-pregnant female are recurrent, relatively short, and internally controlled by an individual's hypothalamic axes via negative and positive feedback. By contrast, pregnancy is long, recurs relatively rarely, and requires significant remodeling of the HPG axis (reviewed in: [23]). Second, the placenta functions as both the conductor of and conduit between the developing fetus' metabolic, neuroendocrine, and autonomic state; and the maternal state [95]. We briefly review placentation to provide context regarding how pregnancy and parturition are influenced directly by the neuroendocrine processes of the placenta, in addition to the responses of the maternal body.

# 3.1. Placentation: physiological adaptation and cooperation between mother and fetus

Establishing the placenta is the primary task of early pregnancy, assuming fertilization and implantation occurred normally. Placentation is a complex and carefully regulated process which is influenced by paternally contributed genes and genetic imprints [96,97]. However, in principle, both maternal immune-tolerant factors within the decidua (transformed endometrium during the luteal phase) and the antigenic factors of the trophoblastic tissue (early placental tissue) cooperate to maintain ovarian progesterone production [98]. Luteal phase ovarian progesterone promotes uterine 'quiescence' or a lack of contractions. This allows the developing trophoblast tissue to produce  $\beta$ -hCG (human chorionic gonadotropin), which will further sustain production of maternal ovarian progesterone until the placenta assumes this task [99–101]. An overabundance of localized immune factors or thrombotic activity on the maternal side, or abnormal antigen expression by the trophoblast would lead to a failure of successful placentation and thus, pregnancy loss [102,103]. Mature placentation requires significant remodeling of maternal spiral arteries (removal of vasoconstrictive endothelial smooth muscle) located deep within the uterine lining and myometrium to support fetal development to term. The mother's uterus therefore must be tolerant of this process immunologically [104,105]. This conceptualization of placentation as an example of synchrony between maternal and embryonic features counters the dominant view that the placenta is dangerously invasive with tumor-like properties.

As the pregnancy progresses, the placenta primarily serves to maintain the pregnant state, producing high quantities of human chorionic somatomammotropin (HCS) (also known as human placental lactogen) and progesterone derived from maternal cholesterol [95,106]. This dominance of progesterone leads to significant reductions in reduced vascular resistance and proximal renal tubular reabsorption, permitting increased blood volume and cardiac output [61,107,108]. These critical adaptations necessarily occur very early in gestation and, if inadequate or absent, are thought to contribute to the early pathogenesis of inadequate fetal growth and some forms of preeclampsia [61] if the embryo survives. Later in pregnancy, the metabolic needs of the fetus are met as HCS prompts adaptation of the typical maternal response to insulin, causing relative insulin insensitivity leading to less maternal cellular uptake of nutrients and more nutrient availability for rapid fetal growth in the third trimester [106]. Progesterone dominance also leads to a shift toward Th2 (T Helper) cytokine profiles and responses, leading to a relatively anti-inflammatory state [109,110] and supporting pregnancy to full-term by suppressing contractile gene expression in the uterus. To initiate labor however, this progesterone dominance needs to be tempered, which is through the action of fetal maturation and rising placental estriol production (reviewed in section 3.1 below).

#### 3.2. Emotional regulation in pregnancy

Emotions associated with pregnancy are influenced by many interconnected factors (reviewed in: [111]). Individual life circumstances (e. g., unwanted pregnancy, unwanted single parenthood, social support, stress, presence of any pregnancy complications, and mental health history) as well as placenta-driven physiologic changes will influence pregnant individuals' emotional states and their vulnerability to mood disorders. Overall, depressive symptomatology across pregnancy has been shown to be stable or to generally improve [112]. This improvement may be attributed to a woman's anticipation of the newborn's arrival (particularly when pregnancy is a positive life circumstance) and/or the increased estriol signaling as the pregnancy advances [113. 114]. Despite this possible improvement in depression across pregnancy, several studies still demonstrate that around 20% or pregnant women do report depression and/or higher anxiety [112,115]. Importantly, poor mental health or emotional regulation during pregnancy is associated with altered immune pathways [116,117], promoting higher inflammation which can trigger spontaneous preterm birth [118]. The association of emotional regulation and mood disorder development with the early onset of labor exemplifies the connection between emotional state, endocrine changes, and possibly adverse birth outcomes.

### 3.3. Autonomic correlates of neuroendocrine and emotional adaptation in pregnancy

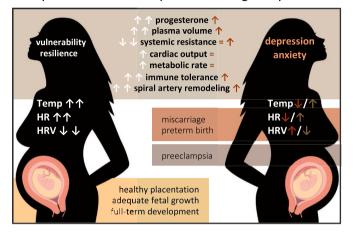
Wearable timeseries may aid the investigation of the full range of emotional and hormonal states in pregnancy. The value of timeseries is not only for observing the relationship between internal state and *levels* of autonomic output. Timeseries are particularly valuable in revealing synchronized *rhythmic patterning* [119], direction of change, and rate of change of hormones that uniquely characterize each stage of reproductive life and associated emotional experiences [120,121]. By the third trimester, for example, sex steroids [101], cortisol [122], prolactin, and HCS reach historically high levels [95]. The hormone changes result

#### Table 2

Hypothesized impacts of pregnancy adaptations and complications on autonomic metrics.

Physiologic or Pathologic Change in Pregnancy	Temperature	HR	HRV	Emotional State
1st Trimester rising progesterone	elevate [34]	elevate [35]	lower [35]	fatigue [36]
Suboptimal progesterone production prior to miscarriage [21]	relatively lower [137]	relatively lower, hypothesized [138]	relatively elevated, <i>hypothesized</i> [139]	?
Reduced plasma volume increase preceding preeclampsia [107]	relatively elevated, hypothesized	relatively elevated [16,43]	relatively lower [44]	anxiety [140]
Peripartum depression	circadian destabilization, reduced amplitude, <i>hypothesized</i>	relatively elevated, hypothesized	relatively lower, hypothesized	depressive symptom onset

#### Adaptation and Maladaptation in Pregnancy



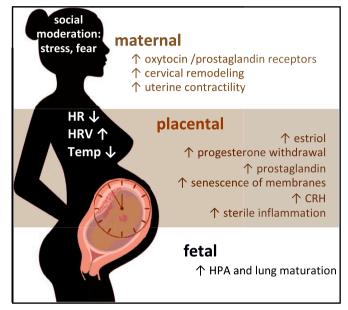
**Fig. 1.** Role of neuroendocrine hormones and associated mechanisms in the adaptation to pregnancy. Opportunities to monitor through timeseries and potential for observing maladaptation. Direction of hormonal, autonomic, and underlying physiological change during adaptation to pregnancy (left). Modifications to these changes in pregnancy complications (right). Arrows direction (up, down) indicates direction of change of the metric (increase, decrease).

in altered autonomic output [123] and are also associated with unique dynamics of emotional state [124]. Varied mechanisms enable these global hormonal elevations, including placental production of hypothalamic releasing hormones (e.g., placental corticotrophin releasing hormone (CRH)). Placental CRH overrides typical negative feedback [125] and increases burst frequency of arcuate and PVN populations regulating these hormones in the mother/fetus. We propose that the profound immunologic shifts [126] and changes in sex steroid production occurring in pregnancy (e.g., progesterone dominance) [127] should result in changes in peripheral outputs that reflect these adaptations (see: Table 2).

Extrapolating from the non-pregnant literature, we would expect higher body temperatures and lower HRV due to the progesterone effects with healthy placental development during pregnancy. If true, what patterns of network outputs would correlate with abnormal adaptation or placentation? Fig. 1 demonstrates some of these possible adaptations and hypothesized timeseries with maladaptation. For example, could we predict a future miscarriage or preterm birth if suboptimal progesterone production were visible through body temperature monitoring? Could a lack of plasma volume increase in the second trimester [107] (with expected concomitant cardiac output increases and decreased HRV) be a reliable predictor of a future pregnancy complications like preeclampsia or fetal growth restriction? At present, these complications are only diagnosed once they manifest later in pregnancy, yet it is purported that these obstetric problems originate early in the process of placentation [128].

A growing number of wearable sensors offer non-invasive, continuous temperature, HR, and HRV data that may be used across the reproductive phases to investigate the relationship between emotional

### **Readiness for Parturition**



**Fig. 2.** Timing of parturition depends upon hormonal and autonomic mechanisms signaling readiness for labor and extrauterine life from maternal, placental and fetal compartments.

and physiological state [17–19,129]. Peripheral metrics generated from wearable devices, and in particular, metrics of biological rhythmic stability, are used to assess risk of depression and bipolar disorder [15, 130]. For example, reductions in stability and amplitude of daily (circadian) temperature and cortisol rhythms are associated with mood imbalances [14] and elevated risk of major depression in peripartum women [131]. Additionally, reduced circadian amplitude of temperature, reduced activity and HRV, and elevated HR are predictors of the onset depressive episodes [14,132–134]. Such timeseries, if appropriately measured and interpreted contextually [135,136], may provide a window onto potential problems with great temporal granularity, and create an opportunity for precise mapping of patterns of change in pregnancy and birth.

### 4. Parturition: maternal, fetal, and placental factors inform the timing and experience of birth

### 4.1. Neuroendocrine physiology of parturition: preparing the mother and fetus for birth

Progesterone inhibits the ability of the uterus to contract effectively and helps maintain the rigid collagen structure of the cervix [101]. This inhibition of labor persists for an average of 268 days in healthy gestations (estimated ovulation to birth) [141]. The body transitions away from the maintenance of pregnancy to actively giving birth via the phases of parturition [142]. This transition is necessarily tied to the processes of fetal maturation, representing the synchrony between the maternal and fetal networks [143]. Inhibition needs to be removed or counteracted to initiate the labor and birth process. The events characterized by the "activation phase" of labor likely occur prior to true labor symptoms being detected by the mother. In contrast to other mammals, human progesterone does not fall in absolute quantities [144]. Instead, the effects of progesterone are counteracted against by the measurable increases in estriol (also manufactured by the placenta). The production of estriol is directly influenced by fetal maturation of the hypothalamic-pituitary-adrenal (HPA) axis as the placenta requires a precursor (dehydroepiandrosterone sulfate; DHEA-S) from the maturing fetal adrenal gland/liver as a substrate [142].

In concert with rising estriol, and the *functional* progesterone withdrawal, the placenta, the maternal HPA system and fetal systems (again driven by adrenal and CNS maturation) all drive a surge in CRH production. This feed-forward system from maternal and fetal glucocorticoid production to placental CRH increase is associated with fetal lung maturation and upregulation of prostaglandin synthesis (which raises body temperature) and receptors important for uterine receptivity (oxytocin receptors, gap junctions) at the time of labor onset [145–147]. As such, activation of the processes of labor, when occurring in a healthy pregnancy, tend to occur when the fetus has achieved a level of maturation compatible with extrauterine viability (Fig. 2), both neurologically and for respiratory transition (glucocorticoids increase production of surfactant, which allows for alveolar expansion and gas exchange) [148–151].

A diminished role of progesterone as a protective 'anti-inflammatory' mediator and the rising role of estriol augments higher CRH, which further contributes to the rise in prostaglandin receptors, oxytocin receptors and connexin-43 (gap junctions) [101]. This cluster of *contraction-associated proteins* allow for the coordinated uterine contractions to finally occur with an expected and clinically measurable rhythm and pattern [146,152]. Other pro-inflammatory processes occur simultaneously with the rebalancing of steroid hormones and CRH surges. These include chorionic/amniotic and decidua cellular senescence as well as the presence of ascending inflammation as cervical softening and cervical smooth muscle apoptosis begins to occur [101,153]. Lastly, in the active stimulation of the labor itself (stimulation phase), we witness/experience the symptoms and observe the behaviors that accompany the complete expulsion of a fetus and placenta [154].

Although inflammation and increased glucocorticoid production help transition the body away from quiescence, to prepare for the processes of parturition, mammalian parturition is best accomplished when the female is not under duress [155–157]. Parasympathetic activity dominates the process of parturition [158–160]. For example, transecting vagal nerves leading to the cervix results in delayed birth, compared to sham procedures in rats [160]. Studies from many species indicate that causing disruptions in the birthing environment, inducing stress or blocking parasympathetic nervous signaling leads to delayed or problematic parturition [159,161]. Further to this point, while many mammals give birth alone, humans tend to seek the companionship of other trusted humans.

#### 4.2. Love and fear: emotional state and support during parturition

The powers of the psychological state of the mother on labor progression are not well understood. The role of subjective experiences of stress on onset of labor has been a focus of research, with researchers noting higher CRH production either from the placenta or mother contributes to shorter gestational lengths or preterm birth [116,162,163]. It has also been noted that acute stress may initiate shorter gestation (preterm labor) and that individuals living in chronic stress conditions (physical and/or psychological) trend toward earlier gestation [116, 164,165]. The case of Black or African American individuals experiencing earlier onset of parturition than European-American/White counterparts in the United States speaks to the potential role for

#### Table 3

Hypothesized impacts of labor, delivery, and complications on autonomic metrics.

Physiologic or Pathologic Change around Birth	Temperature	HR	HRV	Emotional State
Functional progesterone withdrawal	relatively lower across third trimester [51,72,73]	relatively lower across third trimester [52]	relatively elevated across third trimester [52,197]	potential depressive symptoms [78]
Activation phase of parturition at term or preterm	relatively lower [127, 189–194]	relatively lower [197]	relative elevated [197]	variable and influenced by social support structures [78]
Labor	elevate [195]	elevate [197,200, 201]	decrease [197,200, 201]	fear/stress, joy, influenced by support structures and obstetric condition [78]

chronically higher glucocorticoids in triggering earlier maturation of the fetus and processes of labor as a consequence of racism, discrimination, or socio-economic or factors of the built environment [166–168].

Labor is both physically and emotionally intense, even under ideal social and environmental circumstances. Human birth is characterized by moving a relatively snug fitting fetal body through the pelvis [169–171], as well as by a highly vascularized placental attachment site (exposing one to possible hemorrhage) [5]. The challenges and fears that have historically accompanied childbirth are tempered by social support in the birthing process (family, midwives, physicians, doulas, partners) [172,173]. Fear results in higher levels of pain, may inhibit progression of labor, and can exacerbate postnatal depressive symptoms [174–177]. The absence of social support, even among healthy women, is associated with more problematic labor and birth [178–180]. Thus, supportive care could be an adaptive human strategy to help the labor to progress normally by countering sympathetic/adrenergic stimulation. This may be particularly important given that, birth, often occurs under distressing circumstances, for example, in the presence of obstetric violence (mistreatment or racism) [180-184]. Giving birth also happens in the context of an individual's life, which may not be overwhelmingly characterized by love [185,186] or a wanted child. Social support, therefore, confers protection through physiologic means (oxytocin expression and modulation of stress hormones) [187,188]. From this view, bonds between the support persons and the birthing parent could be viewed as being intertwined in the 'network physiology' of parturition itself and could be observed with autonomic output.

### 4.3. Observing parturition through autonomic correlates of neuroendocrine and emotional regulation

Physiological preparations for birth are associated with changes in autonomic output, including autonomic contributions to thermoregulation (See Table 3). In many mammalian species, females' core body temperature drops prior to the onset of parturition (orca, dog, cow, sheep, horse, rabbit, wolverine) [127,189–194], and rises during the active birthing process [195]. This decrease is likely due to diminished influence of progesterone, but may also be lowered by oxytocin secretion [30,144]. The span of time over which the temperature change occurs varies from species to species but may provide a forecast of impending birth in days [192,193]. If a similar phenomenon occurred in humans, it may be possible to utilize measurement of these signals via wearable devices to improve delivery planning for women in a multitude

of circumstances (workforce leave, high-risk delivery timing, travel required for delivery, induction of labor planning). In support of this hypothesis, lower than normal body temperatures were noted in a sample of laboring women upon hospital admission [195]. Not only was the mean temperature lower than normal in this study, but the distribution had a significant skew to the left, with nearly 80% falling under 98 °F.

Although low-temporal-resolution studies, or those done at the population level, have not consistently identified pregnancy-related patterns in HRV [196], within individual and continuous HRV data suggest that HRV is progressively more suppressed (effects of progesterone) and rises following birth [197] (likely oxytocin-mediated) [90]. Additionally, as body temperature, HR, and HRV levels and patterning broadly reflect reproductive hormone status, such a biomarker may help elucidate the underlying mechanisms of labor onset timing, or potentially preterm birth [198,199].

Autonomic physiology during active phases of labor has not been described in detail in humans, although vagally-mediated activity mirroring that observed in other animals has been reported [200,201]. The metabolic work of labor, coping with pain, and increased ventilation will be reflected in increased body temperature as the duration of labor lengthens, alongside inflammation as assessed by white blood cell count [195]. Heart rate increases are seen as a physiologic adaptation but may also be visible relative to levels of coping, anxiety, fear, or other physical effects of labor complications (i.e., infection). How a person's subjective birth experience could be monitored within the timeseries is a compelling area for research as it may reflect not only the physiologic manifestations of fear (or love/support) but also a possible key connection to understanding the connection between labor dysfunction, intrauterine infection, and autonomic physiology.

For pregnant individuals and their families, the uncertainty of when labor could begin can be complex and anxiety-provoking [202–204]. Future labor prediction could be informative and valuable to individuals and families. Advance knowledge of the onset of parturition could lead to a fundamental shift in the way in which we approach birth care. This is partly because it would allow families to gather the necessary social support for the birth process or move closer to medical facilities, if necessary. Not only would this ensure that appropriate medical care is available but having additional preparation time may help alleviate anxiety and promote parasympathetic activation.

## 5. Dyadic synchrony: neuroendocrine and autonomic markers of bonding and maternal-infant coordination

#### 5.1. Neuroendocrine adaptations in early parenthood

The immediate postpartum state (particularly following vaginal birth or physiologic labor) is dominated by steroid hormone withdrawal and a significant surge of pulsatile prolactin and oxytocin secretion. Oxytocin facilitates involution of the uterus [205], prevents hemorrhage [146], promotes prolactin secretion, and coordinates lactation with milk-ejection [40]. Furthermore, oxytocin plays a significant role in modulating stress reactivity and contributes to mood regulation, given sex-steroid suppression and the potential for provoking depressive or anxious symptoms [32,206,207].

Temporal coordination between the mother and a new infant is influenced by numerous factors. The most salient of these factors is that the infant inhabits a world physically distinct from the mother. The nervous and hormonal connection of the placenta is removed and is replaced by endocrine, autonomic, and emotional cues from intermittent breast feeding, touch, and other sensory inputs. Despite physical separation, mothers and infants can maintain a high degree of behavioral, emotional, and physiological coordination. This coordination is influenced by numerous factors, including physical contact, stress, medical interventions, light exposure, and feeding practices (reviewed in: [26,208,209]). Absence of (or overly tight) synchrony between

### Early Parenthood and Dyadic Synchrony

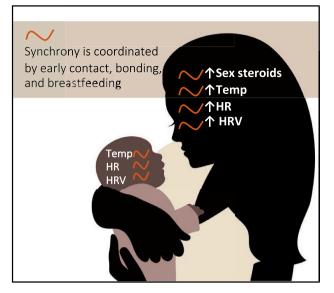


Fig. 3. Synchrony between mother/infant, role of neuroendocrine systems and autonomic physiology observable via timeseries.

parent-infant dyads leads to pronounced impacts on bonding and development.

#### 5.2. The emotional process of synchrony and bonding

Dyadic or biobehavioral synchrony here refers to the temporal coordination of physiology and behavior during interactions between mothers and children (e.g., Ref. [210]). Dyadic synchrony was historically assessed behaviorally via observation and coding of dyads' touch, gaze, attention, and vocalization [211-213]. These investigations consistently report that "detectable" synchrony leads to better emotional regulation in toddlers, including greater empathy and longer attention spans in childhood [214], and greater social bonding within dyads [215,216]. These findings, as well as studies of dyadic synchrony in couples, led to the theory that human physiology benefits from the loving presence of another human regulator, and that synchrony promotes bonding and survival [217,218]. Although these studies might lead one to assume that greater synchrony is linearly associated with better outcomes, an inverse-U-curve of the benefits of synchrony has since been proposed for mothers and infants [26]. In this hypothesized framework, both lack of synchrony and perfect synchrony are associated with inferior emotional and cognitive outcomes in comparison to an intermediate amount described as "appropriate maternal responsiveness to the infant's needs" [26,219], or a "cooperative" vs. "controlling" dyadic interaction [220]. This "some is more" concept may enable children and parents to develop awareness of, and practice refining the anticipation of one another's needs.

#### 5.3. Autonomic correlates of dyadic synchrony

Neuroendocrine and autonomic synchrony may be initiated by skinto-skin contact and breastfeeding and maintained through maternal and infant interactions and familial support (Fig. 3). Behavioral synchrony has been observed at approximately two to three months of age [221–223], and may both arise from and reinforce underlying physiological synchrony. Hormonal and autonomic synchrony are facilitated via skin-to-skin contact, and breastfeeding [224]. Dyadic synchrony has been recorded across myriad physiological outputs including melatonin

Table 4

Hypothesized impacts of dyadic synchrony formation on autonomic outputs in mothers and infants.

Physiologic or Pathologic Change in Early Parenthood	Temperature	HR	HRV	Emotional State
Skin-to-skin contact and family nurturing	decrease; oscillation with breast- feeding	Lower [247]; synchronized oscillation with breast-feeding	elevate [248]; synchronized oscillation with breast feeding	fatigue, relaxation, bonding, love
Early postpartum maternal-infant separation, formula use, short maternity leave	attenuated decrease, reduced synchrony of oscillation	attenuated decrease, reduced synchrony of oscillation	attenuated elevation, reduced synchrony of oscillation	fatigue, stress, attenuated bonding
Development of healthy dyadic synchrony	appropriate oscillatory synchrony	appropriate oscillatory synchrony	appropriate oscillatory synchrony	fatigue, stress, relaxation, bonding, love
Postpartum depression	circadian destabilization, reduced amplitude, decreased oscillatory synchrony	elevate	decrease	depressive symptom onset

(immediately post-partum) [225–227], oxytocin (4–6 months) [228], cortisol (4–11 months) [208,210,229], various measures and correlates of neural activity [230,231], and sleep and circadian rhythms (reviewed in: [232,233]). Additionally, coupled patterns of HR and HRV emerge by about six months of age [210,234–236], apparently coordinated via gaze and vocalizations [218]. Finally, the presence or absence, and degree of this coupling appears to be influenced by a) the presence of breastfeeding [227,229], b) whether breast milk is fresh or previously collected [237] and c) environmental light [238,239] and d) touch [26].

There are several common cases of intentional or unintentional disruption of maternal-infant synchrony that may be observable through peripheral autonomic metrics. These include routine separation of mothers and infants during the critical window after delivery (e.g., for cleaning, weighing of infant), which is associated with increased maternal-infant stress, reduced metrics of maternal-infant bonding (reviewed in: [240,241]) and, we hypothesize, reduced physiological synchrony. Additional disruptors of synchrony include cases in which formula is used, either due to the choice, feeding difficulties (i.e., hypotonia or ankyloglossia) or an inability to lactate [242]; these are especially likely to occur in a neonatal intensive care unit (NICU) [243] as well as cases in which mothers must work outside the home early in the child's life [244]. In each of these cases, a degree of additional separation is placed between the intrinsic physiological, emotional, and behavioral rhythms of the mother and those of the child. Use of real-time physiological monitoring to understand relationships among these types of separation on dyadic synchrony, short term bonding, and long-term outcomes has the potential to inform our understanding of both mechanisms underlying bonding, and for early detection and intervention to promote healthier dyadic relationships.

These factors also reinforce the role of the environment on dyads; especially in cases of early maternal-infant separation, a triadic framework of parent-infant-environmental monitoring may prove useful for deciphering outcomes [245,246]. Parent-infant-environment interactions are a powerful example of how external inputs can "train" and "reinforce" an individual's physiological networks, and how physiological networks appear to be key for forming bonds and facilitating emotional communication. Much remains to be learned about the association among physiological, behavioral, and emotional correlates of synchrony under different parenting conditions, as well as their long-term outcomes for maternal mood and child development/interactions, which have implications for shaping the emotional perceptions (love and fear).

Leveraging knowledge of the physiological networks described above may allow for development of new tools to study variability, structure, and temporal progression of dyadic synchrony and its connection to health outcomes (See Table 4). Numerous wearable devices [17,18] and smart phone application-based platforms have recently been developed for pregnancy, birth, parent, and infant monitoring. They include smart bassinets [249], sock-based infant monitors [250,251], and sleep tracking apps. Challenges of data access, device safety, and data-interpretation standards for infants [26] may limit the speed of investigations into the dynamics of maternal-infant health. Moreover, the complex temporal disruptions of the modern world (e.g., light-at-night) likely hinder the coordination across systems and may make autonomic signal interpretation more difficult. However, the array of powerful tools may allow us to address these questions at scale, in a wide variety of individuals, and in participants' home environments. Combining these powerful sensor platforms with signal-processing and questions targeted at mapping maternal and maternal-infant dynamics may reveal peripheral markers of healthy or pathological pregnancy, birth and bonding, and eventually enable objective, continuous assessment of interventions [252].

#### 6. Conclusions

Maternal physiology and mental state adapt dynamically across pregnancy, parturition, and postpartum. These adaptations integrate across systems and environmental conditions and, remarkably, may do so in a coordinated manner. Such coordination may enable information about internal systems to be gleaned from peripheral autonomic timeseries. These measures may lend insight into the etiology of physiologic and pathologic reproduction, from miscarriage to pre-term labor, healthy pregnancy adaptation to maternal-infant bonding. Observing the development of new life in real-time will help us address the uncertainties and fears surrounding birth and promote loving interactions around the time of birth and between parents and children.

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#### Author contributions

Elise N. Erickson: Conceptualization, Investigation, Writing, Visualization, Funding acquisition, Project Administration. Azure D. Grant: Investigation, Methodology, Writing, Visualization.

#### **Declaration of interests**

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