Asynchrony of mother–infant hypothalamic–pituitary–adrenal axis activity following extinction of infant crying responses induced during the transition to sleep

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A B S T R A C T

This study examines change in the synchrony between mothers' and infants' physiology as 25 infants (11 males; 4 to 10 months of age) participate in a 5-day inpatient sleep training program in which they learn to self-settle through extinction of crying responses during the transition to sleep. The mothers' and infants' experience during the extinction protocol was “yoked” by the infants' behavioral signaling during the sleep transition period. Saliva was sampled for mothers and infants at initiation of infants' nighttime sleep and following infants' falling to sleep on two program days and later assayed for cortisol. As expected on the first day of the program, mothers' and infants' cortisol levels were positively associated at initiation of nighttime sleep following a day of shared activities. Also, when infants expressed distress in response to the sleep transition, mother and infant cortisol responses were again positively associated. On the third day of the program, however, results showed that infants' physiological and behavioral responses were dissociated. They no longer expressed behavioral distress during the sleep transition but their cortisol levels were elevated. Without the infants' distress cue, mothers' cortisol levels decreased. The dissociation between infants' behavioral and physiological responses resulted in asynchrony in mothers' and infants' cortisol levels. The findings are discussed in relation to understanding the determinants and implications of maternal–infant physiological synchrony in early childhood.

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1. Introduction

Synchronous mother–infant interactions are characterized by temporal, patterned coordination of behavior, affective states, and biological rhythms of both mother and infant [1]. Infants' abilities to organize biorhythms, such as sleep–wake cycles and cardiac vagal tone, as well as modulate arousal contribute significantly to co-regulation of synchronous interactions from an early age [2]. Thus, infants' rhythmicity influences synchronicity as does maternal sensitivity and appropriate responsiveness to infant states. When the infant is 2 to 3 months old, mother–infant interactions involve repeated, rhythmic cycles [1,3] in which infants typically alternate between states of neutral and low arousal [4]. By the age of 9 months, infants' ability to respond to changes in their mothers' affect results in the establishment of mutual synchrony [5]. According to Feldman [6], mutually synchronous interaction may occur as concurrent, co-occurrences of behavioral interactions between mothers and infants, sequential chains of changes of behavior, and patterned shifts in mother–infant affective involvement. The concept of mutual synchrony is unique in its focus on the timing of interactions, rather than on such specific behaviors as sensitivity or responsivity [1].

Both members of a synchronous dyad must adapt to one another's cycles of affective involvement and attention vs. inattention in order to establish coordinated responsiveness [1]. Moreover, synchronous interactions follow a lead–lag structure, where either the infant or the mother leads and the other member of the dyad responds. Infants can lead interactions through change in attention state either by changing from social attention to averting gaze; mothers can initiate interactions by engaging infants' attention for social interaction [1]. The establishment of synchrony is affected by infants' physiological development [2], and can be disrupted by presence of stress in either mother or infant, including presence of maternal depression or infant prematurity and delay development of age-appropriate biorhythms [1,3].

Mother–infant behavioral synchrony is foundational in the development of the infant's cognitive, social–emotional, and self-regulatory skills [2]. Synchronous interactions are also foundational to the development and maintenance of a secure mother–infant attachment [1,7]. For example, Isabella and Belsky [7] found that synchronous interactions when infants were 3 and 9 months of age were predictive of secure attachments when infants were 1 year of age, while asynchrony interactions were predictive of insecure attachments. Notably,
specific types of insecure attachments were related to different inter-
actional asynchronies. Avoidant attachments were fostered by nonre-
sponsive, intrusive maternal behaviors, while resistant attachments stemmed from poorly coordinated mother and infant behavior and limited maternal involvement.

Although the role of behavioral synchrony has been studied and found to play a salient role in maintaining positive mother–infant inter-
action and promoting healthy infant development, less attention has been directed toward the potential role of physiological synchro-
nity between mothers and infants. Mother and infant physiological at-
tunement represents a parallel process to the behavioral synchrony be-
tween mothers and children that has been studied extensively in animals and humans for the past 50 years. In principle, synchronized interaction between mothers and their offspring is considered adap-
tive, facilitative, and as having a positive impact on developmental outcomes. It is tempting to assume that physiological synchrony be-
tween mothers and infants is adaptive and has positive effects on children’s development. This seems obvious for sleep–wake behaviors and feeding cycles [9], but less obvious for the activity of the psycho-
biology of the stress response [10].

Several independent studies report that cortisol levels are moder-
ately positively associated between mothers and their children and can be affected by mothers’ behavioral sensitivity to her child [11,12]. This research indicated that infants whose mothers showed more behavioral synchrony had significantly correlated cortisol levels prior to initiation of a separation/learning task. However, cortisol change scores for mothers and infants were not correlated across a challenge task, suggesting that infants must display behaviors, such as a cry or sad facial expression, to trigger an attuned response from the mother. It is important to explore the biological underpinnings of synchronous interaction to determine underlying mechanisms that support such connections.

Further evidence for a link between behavioral synchrony and the psychobiology of stress can be extrapolated from the attachment re-
search. To the extent that an insecure attachment is reflective of asyn-
chronous interaction, these types of attachments are linked to less adaptive cortisol responses [7]. Higher levels of salivary cortisol have been shown to be significantly correlated with insecure attach-
ment styles as assessed in the Strange Situation Procedure [13–15].
Moreover, infants with a disorganized attachment style do not demo-
strate typical diurnal variation in cortisol levels [15]. Additionally, insecure attachment status interacts with infant temperament in pre-
dicting elevated cortisol levels in comparison to infants with secure attachment status [16]. In this research, cortisol levels were found to be significantly elevated after a stressful mother–child interaction only for inhibited, insecurely attached infants [16]. In sum, research has supported a link between insecure attachment patterns and in-
creased cortisol levels in response to threat and challenge.

Although genetic contributions to synchrony in HPA axis activity have been reported [17], Schreiber and colleagues [18] note the greater contributions made by shared environmental demands as contributing to synchrony in afternoon cortisol levels across family members. Other studies suggest that the synchrony in mothers’ and children’s cortisol levels is partially explained by maternal sensitivity [11,19]. For example, mother–preschooler dyads characterized by higher maternal sensitivity showed synchronicity in cortisol levels in response to the child’s perform-
ance of a stressful, novel task [11]. Mothers’ ability to accurately per-
ceive distress in their infants was partially responsible for cortisol attunement in these dyads [11,19]. Mothers’ psychological health, e.g., presence of maternal depression and the stressfulness of the care envi-
ronment have also been found to influence the synchrony of cortisol levels between mothers and children, as both variables limit the mother’s ability to perceive and respond appropriately to her child’s needs [20].

Synchrony in cortisol levels is operationalized by a correlation be-
tween members of dyadic pairs. That association does not distinguish whether: (1) the correlation is due to both members of the dyad shar-
ing a common experience that activates their HPA axis individually—
in this case the coordination is a coincidence; (2) whether the mother is driving the association by being attuned to her child’s behavioral cues (i.e., asymmetrical synchrony type I); (3) whether the infant is driving the association by being attuned to his/her mother’s behav-
ioral cues (i.e., asymmetrical synchrony type II), or (4) reciprocal regard and attunement between both members of the dyad (i.e., symmetrical synchrony) [21]. Several assumptions about signal senders and receivers underlie physiological synchrony. One assump-
tion that is essential to set the stage for physiological synchrony is that there must be a behavioral signal that enables one member of the dyad to communicate/transmit their state to the other. A second assumption is that the behavioral signaler must be capable of coordi-
nating his/her physiological and behavioral responses to the environ-
ment. A third assumption is that the receiver must be capable of perceiving that signal, and the signaler’s and receiver’s behavioral and physiological states are capable of coordinating.

At present, there are no studies that have addressed how synchrony between mother and infant HPA axis activity is established or main-
tained. This lack of research stems in part from the challenge of estab-
lishing a condition in which the questions of relative influence of mothers’ and infants’ behavioral signaling of distress can be examined.

2. Present study and hypotheses

This research begins to address this question by examining phys-
iological and behavioral components of mother–infant interactions across a natural experiment—participation in a 5-day residential sleep training program in New Zealand. The sleep training program involves separation of the infant and mother during the sleep routine, and the extinction of the infants crying across days in treatment as the infant learns to self-settle. For multiple reasons, this program is a unique setting in which to study this phenomenon. The infant di-
rectly experiences the novel challenge of independently self-settling and the lack of maternal responsiveness to their distress signaling. The mother is located in a nearby room where she can hear the infant’s distress signals, but is asked not to intervene. Thus, the infant and mother are “yoked” in the experience by their separation and the degree of the infant’s vocal signaling. Communication between the dyad is restricted to be uni-directional. The mother can only tell the infant’s affective state via the infant distress signals.

3. Hypotheses

3.1. Synchrony at bedtime initiation

At baseline (i.e., the first day of the sleep training program at the ini-
tiation of preparing infants for nighttime sleep), synchrony in mothers’ and infants’ salivary cortisol levels was expected. This expectation is based on the fact that mothers and infants would have spent the day to-
gether in positively focused reciprocally-oriented shared activities [6,22].

Following the nighttime sleep training routine on the first day of the program, after infants had fallen asleep, mothers’ and infants’ cortisol levels were expected to continue to be positively correlated, but abso-
lute levels of cortisol were expected to be significantly higher than be-
fore the initiation of the sleep routine. Both the expectation for synchrony in mothers’ and infants’ cortisol levels and the higher abso-
lute levels of cortisol anticipated reflect that both mothers and infants were experiencing the stressor of infants’ transition to sleep, character-
ized by presence of infants’ vocal distress without parental intervention.

3.2. After training program established self-settling

On the third treatment day, mothers’ and infants’ pre-sleep-routine cortisol levels were expected to continue to be positively
correlated based on shared activities during the daytime. On this day, the level of the infants’ vocal distress is expected to be low during transition to sleep. The diminished expressed distress is expected because the infant has “learned” that crying is not effective in soliciting support behavior from the immediate care-giving environment [23]. By contrast, we did not expect the infants’ physiological response to extinguish. That is, similar to the first day of the training program, we expected that infants’ cortisol levels would be elevated after falling asleep in response to the continued challenge of the sleep training program. Given the dissociation between infants’ physiological response and behavioral signaling of distress on this the third day, we expected that mothers’ and infants’ cortisol levels would not be synchronized. Mothers’ cortisol levels were expected to decrease post-sleep on this day because of the absence of distress signals from the infant.

4. Method

4.1. Participants

Participants in this study were 25 mother–infant dyads (infants aged 4 to 10 months, $M = 6.5$ months, $SD = 1.7$ months; 11 boys) attending a 4-day, in-residence, hospital-based program in the Northern Y District of New Zealand. Mothers’ ages ranged from 17 to 40 years ($M = 28.1$ years, $SD = 5.9$ years). In terms of ethnicity, 55.2% identified themselves as Pakeha, i.e., non-indigenous New Zealanders of European ancestry; 17.2% identified Maori ancestry, i.e., first inhabitants of New Zealand; 3.4% were European or Canadian, 3.4% Middle Eastern, and 3.4% African. Of the participating mothers, 34.5% had completed high school; 20.7% had technical training; and 27.6% had at least some university. Family income ranged from NZ$11,000 to NZ$71,000 or above, with 51.0% of parents stating annual income of $71,000 or more.

The residential, hospital-based unit engaged mothers and infants in a behaviorally-based sleep training program. All mothers on the program wait list received a written and verbal invitation to participate at the scheduling of their participation in the hospital-based program. Typically, mothers are referred to the program by their midwives, doctors, or other medical-based practitioners following reported difficulties either with infants’ sleep routine and ability to self-settle or expressed concerns regarding infants’ feeding and physical growth. Many of the mothers reported a lack of support in caring for their infants at home. No mothers in the study were receiving medical treatment for postnatal depression because antidepressants affect cortisol. In addition, to participate in the study, mothers could not be smoking or using anti-inflammatory steroid-based medications because these also affect cortisol levels study [24]. The project received approval by ethics committees at all involved institutions.

4.2. Sleep training program protocol

The program was designed to extinguish infants’ signaling for attention during transition to nighttime sleep and to increase infants’ self-settling both at initial nighttime sleep and when waking during the night. Mother–infant dyads attended the sleep training program following referral by their or their infants’ medical providers or through other health-based organizations addressing issues of infant sleep, feeding, or development. Goals of the program were to help mothers teach infants to self-settle at bedtime and nighttime wakeings to sleep and to resettle themselves at nighttime wakeings. Other issues involved in feeding and infant care were addressed as part of the program’s focus on improving mother–infant interactions around care and sleep.

Based on the program protocol, nurses instituted an unmodified extinction sleep training program [23] and provided all nighttime care and naptime care for infants, including responsibility for the transitioning of the infant to sleep. At all transitions to sleep, nurses and mothers would attend to preparing infants for transition to sleep by changing, feeding, and other naptime or bedtime activities. Following these activities, infants were placed to sleep in their own crib in a room separate from their mothers. Once placed in the crib for sleeping, infants were required to self-soothe and self-settle. Although mothers were present on the Unit and were aware of their infants’ transition to sleep, inclusive of any signaling of distress during self-settling, mothers did not attend to infants’ nighttime care while infants were learning to self-settle. Mothers were responsible for infants’ awake-time care, although nurses remained responsible for transition to sleep during the first nights in the program. During infants’ awake times, mothers and infants could spend time in the shared lounge with other program participants, in the mothers’ room, or could run errands or take walks with their infants.

4.3. Recruitment and procedures

Based on program protocol, all mothers referred to the sleep training program were contacted by the Unit Director to set up the time of their attendance and to outline the sleep training protocol. Following this initial contact, the Unit Director sent mothers program information and other materials through the post. During the time of this study, all mothers were told about the project during the Director’s initial contact and received a written invitation and informed consent in their admission packet. Mothers who agreed to participate returned their informed consent during their admission to the Unit and were provided with questionnaire packets to complete during their Unit stay. Mothers were assured that they may discontinue participation at any time without penalty. One of the authors conducted training sessions on research practices for all nurses and the Unit director. Training resulted in an on-line certification in research protocols through the National Institutes of Health Web-Based training course, “Protecting Human Research Participants.”

During the initial in-take meeting with the Unit Director and Unit Nurse, all participating mothers were invited to ask questions about the study. At this time, mothers received instructions regarding how to complete their own salivary sampling. In addition, mothers were informed that nurses would collect infants’ salivary samples. Nurses outlined the sampling protocol, in which mothers’ and infants’ samples would be collected on the first and third day of the sleep training program both at initiation of the night sleep routine the first day of the program and 20 min after infants’ onset of sleep. Following Granger and colleagues’ protocol [25], mothers donated whole saliva by passive drool. Mothers completed their sampling at the nurses’ station, which assured compliance with the timing of sampling and the sampling procedures. Infants’ saliva was collected by mothers using microsponges. All samples were transported on ice to Gribbles Laboratory, Te Rapa, New Zealand, and stored frozen at $−80^\circ\text{C}$ until assayed for cortisol.

4.4. Measures

4.4.1. Salivary analytes

Nurses and mothers completed salivary sampling at initiation of the infants’ sleep routine and 20 min post infants’ sleep onset on the first and third day of the sleep training program. Salivary cortisol samples were assayed using a highly-sensitive enzyme immunoassay (Salimetrics, State College, PA). The test used 25 μl of saliva, had a lower limit of sensitivity of .007 μg/dl, range of sensitivity from .007 to 3.0 μg/dl [average intra- and inter-assay coefficients of variation of less than 10% and 15%, respectively]. Outliers were identified as individual scores that exceeded their respective means by at least 3 standard deviations. Analyses were run with and without outliers removed to verify that they were not driving the relationships of interest.
To correct positively skewed distributions, following Gordis and colleagues [26], cortisol scores were subjected to ln transformation.

4.4.2. Infants’ signaling and distress behaviors
Nurses’ records documented duration of infants’ signaling across the sleep training program. These levels of behavioral distress, based on length of infants’ crying after being placed down to sleep for their nighttime sleep, were provided to the researcher by the nurses following mothers’ program participation.

4.4.3. Nature of sleep routine
Mothers participating in the research project were asked to complete a packet of questionnaires including the Sleep Practices Questionnaire [27], the Attachment Q-Sort [28], and the Maternal Separation Anxiety Questionnaire [29]. This information was not included in this set of analyses.

5. Results
5.1. Preliminary descriptive analyses
On average, on the first day of the sleep training program there was no significant increase in cortisol levels from before to after the sleep routine for infants (before: M = .453, SD = .769, n = 24; and after: M = .580, SD = .904, n = 18; n.s.) or for mothers (before: M = .278, SD = .730, n = 16; and after: M = .329; SD = .777, n = 16; n.s.). For infants, there was no significant change in cortisol levels from before to after the sleep routine on the third day of the program (before: M = .512, SD = .900, n = 19; and after: M = .412; SD = .675, n = 18; n.s.). By contrast, for mothers there was a significant decrease in cortisol levels from before (M = .270, SD = .705, n = 17) to after the sleep routine (M = .093; SD = .089, n = 12), t (9) = 2.84, p < .02. Across sampling times, the number of mothers’ or infants’ assays available for analyses varied somewhat based on the sufficiency of saliva in each sample.

Notes in program records were the source of information about changes in infants’ behavioral signaling of distress between the first day and the third day of the sleep training program. Based on a review of these program records, all infants exhibited behavioral distress on the first day. Distress was noted by infants’ crying during the first day of the sleep training program. Given the nature of the program, it was possible to explore the change in mother–infant synchrony across a context in which infants experienced the challenge of separation from the mother at transition to sleep and lack of maternal responsiveness to their behavioral distress signaling. Within this context, we found that the extinction of infants’ behavioral signaling of distress was associated with asynchrony in mothers’ and infants’ physiological stress responses.

Findings highlighted the importance of infants’ behavioral cues as a foundation for synchrony in infants’ and mothers’ physiological attunement. On the first day of a sleep training program, mothers’ and infants’ physiological responses were synchronized at the beginning of infants’ nighttime sleep routine, supporting previous research in which shared engagement in activities, as occurred between mothers and infants during the daytime activities of the sleep training program, was associated with synchrony in physiological response. Mothers’ and infants’ physiological responses were also attuned after infants’ transition to nighttime sleep on Day 1 of the sleep training program. On Day 1, infants signaled their distress vocally by crying, which enabled the mothers to perceive and react physiologically to their distress levels. Infants’ distress, marked by their salivary cortisol levels, would have been associated with the lack of response to their behavioral signaling of distress: mothers’ distress would be in response to the infants’ behavioral signaling, as well as being prohibited by the nature of the extinction program to attend to the behavioral cues.

These correlations demonstrate the physiological attunement that occurred between mother and infant in the presence of synchronous interaction, as well as the role that maternal sensitivity plays in this attunement [6,19]. As mothers were able to sensitively perceive their infants’ distress signals during synchronous nighttime interactions and when the infants cried after the initiation of the sleep routine, mothers’ physiological stress levels increased when infants’ physiological stress levels increased. These results extend upon previous work [11] that showed a significant correlation between maternal sensitivity and physiological attunement during a stressful daytime interaction. This study is unique in that it supports a role for sensitivity in physiological synchrony during nighttime interactions, which has not been previously explored.

On the third day of the sleep training program, nurses reported that infants no longer exhibited behavioral cues indicating presence of distress. Rather, as anticipated based on previous research and program expectations for infants’ behavior, infants’ vocalization of distress at transition to sleep without caregiver (i.e., Unit nurse) response was absent. However, an examination of infants’ physiological state identified a disconnect in infants’ behavior and physiological expressions of distress. Although infants exhibited no behavioral cue that they were experiencing distress at the transition to sleep, the infants continued to experience high levels of physiological distress, as reflected in their cortisol scores. Based on analyses in this study, infants’ cortisol levels did not differ significantly on the first and the third day of the sleep training program. Thus, infants’ internal physiological distress levels did not change but remained high despite the absence of infants’ behavioral cues of distress through vocally signaling distress to the mother.

5.2. Main analyses
5.2.1. Were mothers and infants cortisol levels associated prior to, and following, the transition to sleep at the initiation of the Sleep Training Program?
To test the hypothesis that mothers’ and infants’ levels of salivary cortisol were associated at initiation of the bedtime sleep routine, Pearson correlations were conducted. As expected, a significant, positive association, r (15) = .776, p < .001 (two-tailed), between mothers’ and infants’ cortisol levels was found. Following the infants’ transition to sleep on the first day of the sleep training program, after a transition marked by infants’ vocal expression of distress, mothers’ and infants’ cortisol levels were also positively correlated, r (11) = .748; p < .01, (two-tailed).
Overall, outward displays of internal stress were extinguished by sleep training. However, given the continued presence of distress as evidenced by their physiological response, infants were not learning how to internally manage their experiences of stress and discomfort. The sleep training program, therefore, was successful after just three trials in its primary goal of teaching infants how to self-soothe in order to settle to sleep at night. However, after only three trials of the program the infants’ physiological response to the self-settling experience had yet to habituate. It is particularly interesting that the behavioral component of the stress response habituated more quickly than the HPA component of the stress response. This observation raises the possibility that given more experience with the self-settling program that the HPA response would habituate and that mother–infant physiological synchrony would be re-established.

In the current group of mothers and infants, it is possible that infants’ transition to sleep represents a protracted period of asynchrony in mother–infant behavioral interactions. Mothers who attend the sleep training program present after a long period of difficulty in establishing a sleep routine with their infant. Approaches to establishing a routine that mothers might have tried before entering the program would have been marked by both maternal non-responsiveness to signaling, responsiveness to infants prolonged signaling of distress, as well as maternal presence during infants’ transition to sleep following lack of success in teaching infants to self-settle. Thus, infants would have experienced the transition to sleep as mixed in terms of maternal responsiveness – sometimes marked by maternal presence, sometimes by lack of maternal presence, sometimes by presence but no contact – but generally associated with maternal distress.

Given the extent of felt distress among mothers who would participate in a sleep training program, it is plausible that just being in the program and learning more about expected infant behaviors would relieve some distress. This relief, as well as the potential for an increase in mothers’ confidence in their nighttime care, may contribute to changes in mothers’ stress levels during their attendance at the sleep training program. With the support of nurses helping to clarify infants’ behavior around sleep and feeding, mothers may feel more comfortable with addressing infants’ care needs. Conversely, some mothers when attending the sleep training program may experience greater distress during infants’ transition to sleep given the new setting and focus on infants’ nighttime behavior. In this instance, it is plausible that mothers’ exhibit an increased stress response around the sleep routine, resulting in a positive correlation in mothers’ and infants’ physiological response. Given these possible interpretations of the present findings, it may be helpful to examine mothers’ and infants’ physiological responses during attendance in a residential based program that did not include extinction of infants’ crying.

Research continues to identify an association between early maternal care and infants’ developing physiological responses—particularly as they affect epigenetic modification of physiological systems that impact later social behavior and mental and physical health [30–32]. One possible contributing factor to the challenges faced by mothers and infants whose sleep routines are associated with distress and disruption of synchrony may arise from factors associated with predisposition to difficulty in regulating stress response. It is plausible that the infants in these mother–infant dyads have a more sensitive, intense physiological stress responses system based on genetic predisposition that contributes to a greater difficulty in self-regulation and self-settling [14,33,34]. Conversely, it may be that mothers who find the negotiation of maternal care during this time of separation as a challenge have experienced asynchronous maternal care that contributed through epigenetic modification of their responses to their infants’ signaling of distress [30]. The continued presence of distress without caregivers’ responsiveness in regulating the stress response may be associated with similar activation of the HPA component without habituation, as seen in infants with the dysregulated stress responses associated with insecure attachment status [6,35].

Considered more broadly, this asynchrony in habituation of behavioral and physiological stress response underscores the possibility that maternal–infant physiological synchrony is not static or trait-like. That is, as novel and unfamiliar experiences are introduced into children’s lives there may be periods or episodes of asynchrony punctuated by longer periods of synchrony. Perhaps the developmentally significant aspect of physiological synchrony will be revealed in the patterns of its continuity and change. Clearly, research focused on the developmental trajectory of physiological synchrony across early childhood would be a worthwhile next step.

Research is needed to further delineate the intrinsic individual differences and social forces that establish and maintain maternal–infant synchrony, as well as enable synchrony to be re-established after disruption.

7. Conclusions

This study provides an important first look at change in the synchrony between mothers’ and infants’ physiology during extinction protocol of infants’ behavioral signaling during the sleep transition. During the sleep training, mothers’ cortisol levels decreased resulting in asynchrony in mothers’ and infants’ cortisol levels. Given the importance of the social environment in helping infants’ learn to regulate their responses to threat and challenge further exploration of the implications of the disruption of maternal–infant physiological synchrony for early childhood developmental milestones is warranted.

Conflict of interest statement

In the interest of full disclosure, we note that Douglas A. Granger is the founder and Chief Scientific and Strategy Advisor of Salimetrics LLC (State College, PA), and this relationship is managed using the policies of the Conflict of Interest Committee at the Johns Hopkins University School of Medicine.

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References


