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Sahrudh Dharanendra April 4, 2018

The development of mother-infant social synchrony, sensory-motor reflexes, and temperament in infant rhesus macaques (*Macaca mulatta)*

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Abstract

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Investigations of the biological and environmental factors that guide neurodevelopmental changes occurring during the first weeks/months after birth are clearly needed, as many neurodevelopmental disorders emerge from brain abnormalities in early infancy. Previous research in infant monkeys has indicated that typical development of infant social skills occurs during infant-caregiver interactions from birth to six months. This period represents a pivotal transition period (up to twelve months in monkeys), which may lay the foundation for further neural and behavioral maturation. The aim of this project was to use a rhesus macaque model to characterize transitions in early mother-infant social synchrony (i.e. mutual gaze and other bonding behaviors) and how did they relate to transitions in sensory-motor skills. To this end, four infant rhesus monkeys and their mothers were observed in their large social compounds to assess social contingency during mother-infant interactions (including mutual gaze) for the first four weeks of life. During the same period, sensory-motor measures were taken to determine transitions from reflexive to more voluntary controlled behaviors in infant monkeys. Infant-mother mutual gaze was very low during this first postnatal month, with the mother mostly initiating looking behavior towards their infants. All sensory-motor reflexes were present with only the Rooting reflex declining at the end of the first postnatal month. Changes in infants' temperament were also observed with a slight increase in fearfulness and Vocal Response Intensity and reduced Consolability, indicating greater distress while infants were separated from their mothers. Although only

few behavioral changes were observable during the first month of life, the trend of our current results indicate the need to expand our study past the first month as the infants will further mature and to increase our sample size to provide significant power to the changes observed.

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Introduction

Neurodevelopmental disorders, including Autism Spectrum Disorder (ASD), social communication disorders, intellectual disability, and attention deficit hyperactivity disorder are examples of clinically heterogeneous psychiatric illnesses shaped by aberrant brain development (American Psychiatric et al., 2013; Hansen et al., 2013; Homberg et al., 2015). Neurodevelopmental disorders can create high levels of distress in life and consistent behavioral and cognitive impairments and difficulties in social communication (American Psychiatric et al., 2013; Hansen et al., 2013). These disorders tend to present in childhood with abnormal neural development often occurring in embryogenesis leading to long-lasting behavioral and physiological deficits in both childhood and adulthood (Bergner et al., 2010; Buckley et al., 2009; Krishnan, 2005). For example, ASD is a developmental disorder characterized by altered engagement with the social world that is already apparent very early in infancy (Jones and Klin, 2013). Thus, increased knowledge on the critical periods of typical development during which early social skills emerge and mature and on the underlying neurobiological systems that support these skills will give unprecedented opportunity to further understand the neurobiological source of early social derailment in ASD and develop new treatments. Although research examining the precursors of human social abilities during early infancy has significantly increased in the last few years, critical information on the causes and neural bases of these early developing social skills is still lacking; the main limitations being neuroimaging of the human brain in infancy and acquisition of densely-sampled longitudinal brain-behavior relationship across development. Thus, knowledge in this domain must emerge from translational research examining both human populations and animal models. Rodent models offer suitable and robust models for ASD and many other neurodevelopmental disorders, since rats and mice prefer group-living and are considered social species that display a large variety of social behaviors (Homberg et al. 2016) and their genes can be manipulated to examine the genetic bases of social behavior. However, rodent models have inherent limitations that decrease the validity of their use in researching neurodevelopmental phenomena. For example, infant rats often have insufficient development in their sensory and motor systems to properly serve as a model (Homberg et al. 2016) and their social behaviors are limited as compared to those of primates. In addition, rodents have brain much less developed at birth and their postnatal brain maturation is much more compressed over time (4 weeks) than humans (20 years). In contrast, non-human primates (NHP), such as Rhesus macaques, have a great degree of similarity to humans (1) in genetic composition and physiology, (2) they live in rich and complex social structure in which they develop and navigate, (3) they show a progressive development of the basic social skills required to develop normal social relationships, (4) they mostly use vision for detecting social signals, and (5) share similarity with humans in brain and cognitive functions development (Dettmer et al. 2014). Thus, the characterization of early social skills in monkeys and their neural signatures may yield a critical NHP model of early social development for ASD that will be used in future studies to (a) assess how genetic variations and molecular and/or experimental manipulations of social neural networks alter infant social development, and (b) validate the efficacy of therapeutic treatments for attenuating social deficits in ASD. We also foresee this NHP model's relevance to studies of pathogenesis and neural bases of other human neurodevelopmental disorders associated with atypical social skills in infancy, such as Williams Syndrome. For these reasons, our laboratory has begun a series of studies to characterize the development of early social skills in infant rhesus monkeys from birth to 6 months of age, which corresponds to 2 months to 2 years in human infants. Prior research in the lab showed that social visual engagement (the ability to prefer gazing at social stimuli, such as faces) follows an identical trajectory in rhesus macaques from 2-22 weeks (Wang et al., 2017) and in humans from 2-24 months (Jones and Klin, 2013). More specifically, in both species, fixation to the eyes in the monkeys increases sharply to reach a peak around 5-6 weeks (9 months in human infants), followed by a decline that reaches a trough around 16 weeks (16 months in human infants) before a continuous rise thereafter until the last age point assessed (i.e. 24 weeks; 24 months in human infants). These provocative data suggest that shifting patterns in monitoring and responding to social cues during the first few weeks (months in humans) are phylogenetically conserved and indicate that the monkeys could be used as translational model to study early social development in human. The current project will build on this earlier study and will continue to characterize early developing social skills in monkeys by measuring infant-mother interactions during the first four weeks of life. In addition, motor abilities play a determinant role in aspects of perceptual as well as of cognitive skills in early infancy (St John et al, 2016; Nebel et al., 2016), while individual differences in infant temperament in Rhesus monkeys have shown to affect social relationships and attachment as well (Weinstein and Capitanio 2008). We will perform parallel assessments of sensorimotor development in infant monkeys to measure sensory and motor reflexes and voluntary control motor behaviors during the same age period as well as characterize infants' temperament during the behavioral testing.

Social development and interactions with caregivers early in life is heavily implicated in predicting future interactions and social stability (Wan et al. 2013). Additionally, familial history of ASD can lead to changes in parental interactions with younger children that exacerbate symptoms of ASD (Wan et al. 2013). One particular social interaction that has been studied as a measure of social information transfer is *social synchrony*, defined as the coordination of nonverbal behaviors between social partners during interpersonal behaviors (Atzil et al. 2014, Feldman 2007). This coordination is dependent on a response-based interaction and is thus different from mirroring or imitative behaviors (Leclere et al. 2014). Synchrony is also dependent on the emotional capacity of the pair to respond to one another, involving a matching of behavior and biological rhythms (Leclere et al. 2014). Social synchrony functions as the crux of the development of bonds and affiliation; therefore, its presence in social contexts is vital for bond formation and for requisite social functioning (Atzil et al. 2014). Within the framework of social synchrony, studies in humans have indicated that maternal bonding may provide the foundation for the infant's development of social understanding and empathy exhibited across childhood and adolescence (Atzil et al. 2014, Feldman 2007). Research specifically shows that maternal bonding behavior creates a brain network of social signaling in infants that helps in the differentiation of maladaptive and adaptive social behavior (Atzil et al. 2014, Nelson and Panksepp, 1998). Similarly in monkeys, the matrilineal hierarchy system present in the social groups can increase the effect and depth of this bonding by shaping how infants and mothers interact with other monkeys in the social group. This effect is seen in research that shows detection of deviant social interaction by mothers when scanning other mother-infant pairings (Atzil et al. 2014). Bonding behavior includes cradling and ventral contact, when the infant monkey spends extended periods of time clinging to the mother's breast (Hansen 1966). Eye-gazing is another specific form of maternal bonding and is highly beneficial for creating an interactive environment that contains prototypical eye-contact cues utilized by young infants (De Pascalis et al. 2017). This type of communication is especially important in early infancy, as eye-gazing precedes and guides non-vocal communications during the transition to active communication (De Pascalis et al. 2017). Specifically, mutual eye-gazing has been implicated as a highly necessary component of the mother-infant bond in rhesus macaques and the disruption of which negatively impacts infants' social and physiological development (Dettmer et al. 2016). The Dettmer study found sharp increases in mutual gaze following the first post-natal month, whereas instances of mutual eye-gaze remained low, with a slight nonsignificant decrease during the first post-natal month. The study found that mutual gazing was more commonly displayed amongst first time mothers as compared to multiparous mothers, suggesting mothers may become better at communicating with their infants or that a novelty effect may result in decreased mutual gazing after the first infant (Dettmer et al. 2016). Mutual eye-gazing is associated with neonatal imitation and information transfer about emotional communication as well (Dettmer et al. 2016). Thus, mutual-eye gazing acts as a foundation for later early social development and competency. As this was the first major study in monkeys that focused on mother-infant mutual gaze, improvements to the methodology can be made. For example, the Dettmer study relied on live coding, which may result in missing some instances of behaviors; as such, the current study uses video recordings to allow for more thorough examination of the actual occurring behaviors.

Motor abilities and temperament also play a determining role in aspects of perceptual and cognitive skills in early infancy (St John et al. 2016; Nebel et al. 2016; Capitanio 1999) and visuo-motor functional connectivity is known to be disrupted in ASD. For example, in typically developing infants, the experience of self-locomotion, such as walking, as well as various motor functions, such as reaching and standing, and gross and fine motor skills have been associated with the development of executive functions (Smith et al., 1999; Wassenberg et al., 2005; Livesey et al. 2006; Piek et al. 2008). Interestingly, interventions that improve motor skills in children with ASD may improve certain aspects of their executive functions (Hilton et al., 2014). Common reflexive behaviors of infant rhesus macaque include the Moro reflex, rooting reflex, and Galant's response (Schneider 1992). Typical social actions are linked to these motor skills, and other reflex-like behaviors transitioning through added context (i.e. the rooting reflex transitioning to head turning motions at 2-3 weeks in rhesus macaques) (personal communication from Dr. S. Schultz). When these transitions do not properly occur, lack of social skills may be indicated by disturbance in behaviors, such as convulsive jerking and vocalizations (Hansen 1966).

Another factor that may affect the development of early social skills is infant temperament. Previous research conducted in rhesus macaques indicates that individual temperament did predict the number and quality of social affiliative relationships formed by rhesus macaque monkeys (Weinstein and Capitanio, 2008). The study used focal observations to study the number of proximity, play, contact, and grooming behaviors amongst 57 rhesus macaque monkeys. Specifically, the results indicate adaptability and equability to be good predictors of large and stable social network sizes (Weinstain and Capitanio, 2008). Temperament did remain a significant predictor of affiliative preference even when other variables such as kinship, rank and sex were controlled for (Weinstein and Capitanio, 2008). Studies in aggression and impulsivity specifically have indicated that these aspects of temperament reflect personality traits that affect later social attachment (Weinstein and Capitanio, 2008). Thus, we also measured temperament of the infant monkeys of this study to investigate whether any aspects of temperament could impact mutual eye-gaze measure.

Based on the existing literature reviewed above, the goal of the current study was two-fold: (1) to examine the development of mutual-eye gazing and maternal bonding in infant rhesus macaques from birth to 4 weeks of age, using video recording and fine grain analyses of the frequency and duration of this behaviors especially in the first month of age, and (2) to measure sensory-motor reflexes and visuo-motor skills during the same age period as well as infants' temperament while being removed from their mother and tested. We hypothesized that frequency and duration of mother-infant or infant-others mutual face to face interactions will slightly decrease during this period of age and will follow the decline of reflexive behaviors measured in (2). We hypothesized that pivotal developmental transitions from reflexive to voluntary control of motor behaviors will occur during the first 4 weeks of age and these transitions in motor skills will correlate with transitions in mutual-eye gazing measured in (1).

Methods and Materials

-*Subjects*: Subjects consisted of 4 newborn male monkeys (*Macaca mulatta)* living with their mothers in large and socially diverse groups at the Yerkes National Primate Research Center Field Station (Lawrenceville, GA). The infants were integrated into the matrilineal social hierarchy of the species, and could be influenced by social variables. Infant monkeys were selected from multiparous mothers from low- to high-social ranking. The infant-mother dyads remained in the social groups for the entire period, except for behavioral measures when they were separated from the social groups for one to one and half hour.

Behavior recordings: Video recordings were collected for social behavior data, utilizing real time focal observations from towers located throughout social compounds for four mother-infant pairs. Videotapes of infant social interactions were collected once a day for 5 days per week for the first 4 weeks based on the need to capture fast changing social changes in the first few weeks of life, particularly in mother-infant interactions and face-to-face contacts, which heavily decline by the second month of life. All data were collected between eight and eleven in the morning, when the observed animals are the most active. Thirty minutes of recording per day were coded for data analyses. Descriptions of the recorded behaviors are listed and defined in Table 1.

Reflex Analysis: Sensorimotor development of infant monkeys was measured through parallel assessments that identify pivotal developmental transitions from reflexive to voluntary control of sensory processes and motor actions. Infant monkeys were given the Schneider Neonatal Assessment for Primates (SNAP) to determine parallel transitions in orienting and neuromotor behaviors at about four weeks of age. This scale originated from the human Brazelton Neonatal Behavioral Assessment Scale, which measures auditory and visual attention and orienting reflexes, neuromotor functioning/reflexes, muscle tone, coordination and temperament and was administered for twenty minutes at seven, fourteen, twenty-one, and twenty-eight days of age. Table 2 provided the list of behaviors recorded, their definition and the scoring scale for each.

Data analyses: Rhesus-specific behaviors were scored using a frame-by-frame coding scheme using early mother-infant (as well as infant-others) social contingent behaviors. The project focused mainly on mutual gaze (Face/Face interactions or mutual eye gaze). Given that frequency and duration of behaviors were not normally distributed, we conducted nonparametric tests, including the Kruskal Wallis test with weeks as the grouping variable followed by Mann Whitney U test to compared data between weeks. The data for sensory-motor reflexes and temperament were analyzed for all subjects across the four weeks of the study, using ANOVAs with repeated measures. The within-subjects variable was Time, with four times representing the four weeks of data collection.

Results

As shown in Table 3, although all frequency and duration of mutual social interactive behaviors between the Mothers and Infants declined from Week 1 to Week 4, this decline did not reach significance (all p values > .05), except for the duration of Mother Looking at Infant's Head that showed a trend towards significance (H = 7.32, df = 3, p = .06; see Figure 1). None of the social interactions with partners reached significance (all p > .05).

Table 4 showed that all sensory-motor reflexes were present during the first postnatal month and showed no decline over time, except for the Rooting reflex on the left that significantly decline ($F_{3, 9} = 4.47$, $p < .04$) especially from Week three to Week four (p=.01). Measures of motor abilities did not vary during the first postnatal month, except for a slight increase in motor activity and motor coordination, which did not reach significance. The temperament measures also indicated a slight, but not significant, increase in fearfulness, but a significant increase in vocal response intensity (F3, 9 = 5.15, p = .02; see Figure 2) with a trend towards significance from Week 1 to Week 2 (p=.08). Furthermore, Consolability of animals during testing significantly decreased ($F_{3, 9} = 14.85$, $p = .001$; see Figure 2) during the first postnatal month, with a trend towards significance from Week 3 to Week 4 (p= .08).

Discussion

The study traced the development of mother-infant and partner interactions and sensory-motor reflexes during the first month of life in rhesus monkeys. The results indicate that, although frequency and duration of mutual gaze as well as Infant Looking at Mother and Mother Looking at Infant did not change significantly across the 4 weeks, these social behaviors showed a slight decline from Weeks 1-2 to Weeks 3-4. Furthermore, sensory-motor reflexes were present during the first postnatal month and only decline for the Rooting Reflex while motor activity and motor coordination slightly increased. Measures of temperament during the behavioral testing indicated a slight rise in fearfulness, significant increase in Vocal Response Intensity but significant decrease in Consolability. Although we intended on analyzing correlations between reflexes/motor activities/temperament and social behaviors, the small sample size, the large proportion of missing values, and lack of data points at some ages for some animals made those correlations difficult and not useful to run.

Instances of mutual gazing across the first postnatal month were low but still fairly common and consistent between animals. Low social scores were mostly due to the infants being asleep while sucking on the mother's nipples for most of the video recording sessions. This low level of mother-infant synchrony during the first 4 weeks parallels data previously reported for frequencies of mutual gaze by Dettmer and colleagues (2016). Thus, frequency for the social synchrony declined only slightly from 2.25 to 1.33 instances from Week 1 to Week 4 for 30-minutes long videos in the present study and from approximately 0.6 to 0.4 instances for 15-minutes videos in Dettmer's study for the same first month of life.

The frequency of social behaviors displayed was highest for the Mother Looking at Infant's Head, with over 15 instances of the behavior per week in some animals. However, mutual gaze between the infants and other partners in the groups occurred very infrequently across the four weeks- even when partners were visible in the video- with no instances for the Infant Looking at Partner's Eyes or Looking at Partner's Head for each week.

The duration of behaviors further supports the data on frequencies of displays. Again, the highest durations were found in the Mother Looking at Infant's Head as well as in Mutual Eye Gaze, followed by the Infant Looking at Mother's Head. They ranged from 0 to over 500 seconds, 0 to over 50 seconds and 0 to over 25 seconds across weeks, respectively. Again, the lowest durations were for duration of looking at partners, with no time spent interacting with partners for most of the weeks, even when partners were frequently near the mother-infant pair. Thus, the data indicate that most of the visual social contingency between infants and their mothers during the first postnatal month was initiated by the mothers. Although the limited amount of eye-eye contacts could have resulted from the presence of other animals or other stimuli in the social compounds where the videos were recorded from that could have distracted both the infant and the mother from one another, it is more likely that the lack of social synchrony (eye-eye or eye-head) from the infant towards the mother may have come from the tight physical contacts between infant and mother. Indeed, for most of the recordings, the infants tended to spend most of their time on the mother's ventrum and some time being asleep while sucking on the mother's nipple.

The infants displayed moderate to strong sensory-motor reflexes, except response speed that could not be collected for the majority of the tests. However, there were no changes in the intensity of the majority of these reflexes during the first postnatal month, except from the decline in Rooting reflex. These findings contrast with those of a previous report (Schneider and Suomi, 1992) indicating that many of the reflexes studied in the current experiment changed in intensity within the first few weeks of life. The only similarity between the two studies was in the decline of the Rooting reflex over the course of the four weeks. As discussed below, procedural differences in the rearing conditions of the infants may explain the differential results observed.

The infants also displayed moderate to strong measures of temperament for all measures, except for aggression and fearfulness, for which they had the lowest scores. Interestingly, the data indicate a slight, but not significant, increase in fearfulness, which was associated with a rise in Vocal Response Intensity, indicating a greater magnitude of distress during the behavioral testing of the infants. The decreased Consolability and increased vocal response intensity may represent an increased level of attachment between mothers and infants (Weinstein and

Capitanio, 2008). These findings are consistent with the emergence and maturation of fear to social strangers documented in the first few months of life as the infants become to explore their environment and leave the mother for short periods of time (Rosenblum and Alpert, 1974). At the same time, the infants became more difficult to soothe as revealed by the decrease in measures of Consolability. The present results of Consolability differ from the slight increase in this measure over four weeks in the earlier report by Schneider and Suomi (1992). The differences noted between the two studies in some measures of reflexes and temperament may be attributed to the differential infant rearing conditions between the two studies. The current study used subjects that were mother reared in large social compounds, whereas those in the Schneider's study were nursery raised. This rearing difference may specifically have affected Consolability scores in the mother-reared infants, since the separation from the mothers may have increased infants' fearfulness and vocal distress and reduced their ability and willingness to be consoled. Additionally, the use of four time points to test the reflex development in the current study as compared to the 8 time points from day 1 to 29 used in the Schneider's study may have obscured slight changes in reflexes intensity, especially during the last week of testing. Indeed, for the Rooting reflex, a slight but significant decline was seen only between the third and fourth week of testing.

The main limitation of the current study comes from its small sample size. With a subject size of 4, the study is underpowered and vulnerable to individual variations in the behavioral measures. For example, one of the animal (LC19) had missing data for many of the tactile response reflex tests, as well as for the social video behavioral data. However, when we re-analyzed the data with this case excluded, the statistical results remained unchanged, indicating that these missing data points for this animal did not affect the significance of the results. Also, for the social videos, the data showed large individual differences with some animals having an overall greater number of behavioral responses than others. However, the developmental trend of their data points followed the same pattern as the other animals. While there was no significance reported for the behaviors in the video coding, this was perhaps due to the overall low number of responses by many of the animals. However, this low frequency of social behavior in the first postnatal month was expected since at this early age infant monkeys remain mostly on the ventrum of their mothers with frequent episodes of sleep during the day. While the use of real time focal video recordings reduces the limitations of the study, the collection of more complete videos may be improved by having cameras at opposing angles. For example, there were multiple instances where the mother would turn her back on the camera, making the coding of behavior impossible. Using longer lengths of video would also aid in providing a more robust amount of data. Another possible developmental limitation of the study could be that the infant monkeys simply have not had enough development of their visual abilities to adequately display mutual gaze behavior. Research in rhesus macaque monkeys has shown that the visual system undergoes remodeling during the first few weeks, specifically with the higher order pathways developing later than the primary visual areas (Kovacs-Balint et al. 2018). Although functional connectivity in the visual stream pathways does seem to exist at week 2, this connectivity seems to further strengthen between week 8 and 12 (Kovacs-Balint et al. 2018). However, research in eye fixation of human and Rhesus macaque monkey infants indicates that infant monkeys do possess sufficient visual abilities to fixate at a young age (Wang et al. 2017; Jones and Klin, 2013). Previous research conducted by the lab also indicates that social contingency may become more apparent in rhesus macaques after four weeks, when infant monkeys are becoming more alert and start to visually explore their environment while remaining in close contact with their mother (Wang et al. 2017). Indeed, Dettmer and colleagues (2016) reported a significant increase in the frequency of mutual gaze between infants and their mothers (from 0.5/15minutes to 1.0/15 minutes) during Week 5 to Week 7. In fact, our measures of temperament indicate greater attachment to the mother by the end of the first months as revealed by greater levels of distress by the infants when removed from their mother, suggesting that greater attachment to the mother may lead to an increase mutual synchrony between infants and their mothers beginning at the end of the first postnatal month.

The rhesus macaque observational model has many advantages and limitations as a model of early infant development. This model can take research further if strengthened through larger sample sizes and more complete representation of activity (i.e. recordings from all times of day). Furthermore, a longitudinal model would help in charting both the development of early behaviors as well as their predictive value on later social behaviors. As rhesus macaques have similar eye fixation development to human infants, they present a particularly strong model for examining mutual eye gaze (Jones and Klin, 2013). However, NHP models will face the common limitation of not being able to completely represent human models. Additionally, the matrilineal hierarchy of rhesus macaques differs from the system seen in humans, presenting another limitation. Despite these limitations, further testing of the infants beyond 4 weeks of age and the inclusion of additional subjects to obtain a larger sample size will aid in better defining the developmental trajectories of early social skills as well as those of the sensory-motor reflexes in the first few months of life in monkeys.

Table 1: Description of Social Behaviors

Behavior	Description
Mutual Gaze- Frequency	Number of instances within the time period that the infant and mother looked at one another in the eyes
Infant looking at Mother's Head- Frequency	Number of instances within the time period that the infant looked at the mother's head without looking at the mother's eyes
Mother looking at Infant's Head- Frequency	Number of instances within the time period that the mother looked at the infant's head without looking at the infant's eyes
Infant looking at Partner's Eyes- Frequency	Number of instances within the time period that the infant looked at another monkey's eyes while the partner also looked at the infant's eyes
Infant looking at Partner's Head- Frequency	Number of instances within the time period that the infant looked at another monkey's head
Mutual Gaze- Duration	Length of time (in seconds) of instances within the time period that the infant and mother looked at one another in the eyes
Infant looking at Mother's Head- Duration	Length of time (in seconds) of instances within the time period that the infant looked at the mother's head without looking at the mother's eyes
Mother looking at Infant's Head- Duration	Length of time (in seconds) of instances within the time period that the infant's head without looking at the infant's eyes
Infant looking at Partner's Eyes- Duration	Length of time (in seconds) of instances within the time period that the infant looked at another monkey's eyes while the partner also looked at the infant's eyes
Infant looking at Partner's Head- Duration	Length of time (in seconds) of instances within the time period that the infant looked at another monkey's head

Table 2: Description and Scoring of Reflexes, Motor Activities, and Temperament

Behaviors	Behavior Description	Scale Description
Visual Orient- R	Eyes orienting towards stimulus on right	0-No orient 1-direct brief visual contact 2-direct prolonged contact
Visual Orient- L	Eyes orienting towards stimulus on left	0-No orient 1-direct brief visual contact 2-direct prolonged contact
Visual Orient- U	Eyes orienting towards stimulus upwards	0-No orient 1-direct brief visual contact 2-direct prolonged contact
Visual Orient-D	Eyes orienting towards stimulus downwards	0-No orient 1-direct brief visual contact 2-direct prolonged contact
Visual Follow- H	Eyes following moving object in horizontal direction	0-contact but no following 1-starts to follow but stops before the stimulus 2-complete following
Visual Follow-V	Eyes following moving object in vertical direction	0-contact but no following 1-starts to follow but stops before the stimulus 2-complete following
Attention Span	Examiner rating of attention paid for previous items	0-lack of attention on all items 1-attentive 25% of time 2- attentive 75% or more of the time
Orient to Auditory-R	Eyes orienting toward lipsmacking noise towards the right	0-no orient 1-partial orient 2-full orient with visual inspection
Orient to Auditory-L	Eyes orienting toward lipsmacking noise towards the left	0- no orient 1- partial orient 2- full orient with visual inspection
Palmar Grasp-R	Infant's reflex to close hand when palm is stroked on right hand	0-no grasp 1-weak, digits closed loosely 2-strong
Palmar Grasp-L	Infant's reflex to close hand when palm is stroked on left hand	0- no grasp 1- weak, digits closed loosely 2- strong
Plantar Grasp-R	Infant's reflex to close hand when palm is stroked on right foot	0- no grasp 1- weak, digits closed loosely 2- strong
Plantar Grasp-L	Infant's reflex to close hand when palm is stroked on left foot	0- no grasp 1- weak, digits closed loosely 2- strong
Tactile Response-RA	Response to touch on right arm	0-no response 1-slight response 2-definite or exaggerated response
Tactile Response-LA	Response to touch on left arm	0-no response 1-slight response

		2- definite or exaggerated response
Tactile Response-RL	Response to touch on right leg	0-no response 1-slight response 2- definite or exaggerated response
Tactile Response-LL	Response to touch on left leg	0-no response 1-slight response 2- definite or exaggerated response
Galants-R	Response to tactile stimulus lateral and parallel to vertebral column on the right side	0-no response 1-slight response 2- definite or exaggerated response
Galants-L	Response to tactile stimulus lateral and parallel to vertebral column on the left side	0-no response 1-slight response 2- definite or exaggerated response
Rooting-R	The infant turning its head when the cheek or lip is stimulated- right side	0-absent 1-weak turn 2-full turn
Rooting-L	The infant turning its head when the cheek or lip is stimulated- left side	0-absent 1-weak turn 2-full turn
Labyrinthian Righting-R	Realignment of head when body is tilted 45 degrees sideways- right side	0-head in same plane as body 1-head partially rights 2-head rights in 5 seconds
Labyrinthian Righting-L	Realignment of head when body is tilted 45 degrees sideways- left side	0- head in same plane as body 1 head partially rights 2 head rights in 5 seconds
Body Righting	Time noted for infant to turn from supine to prone	0-no righting in 15 seconds 1-rights in 5-15 seconds 2-rights in less than 5 seconds
Aversion on Back	Vocalizations while on back	0-none 1-slight 2-definite
Active Power	Strength of muscles when actively contracting	0-unable to withstand slight resist 1-able to withstand moderate resistance 2-difficult to restrain
Response Speed	Time taken by infant to respond during testing	0-Slow- 25% of time, quick 1-Moderate- 75% of time, quick 2-High- All responses, quick
Head Posture Prone	Ability to hold head up when held prone	0-flaccid tone with head hanging done 1-head lifted but not maintained for 3 seconds 2- head lifted but maintained for at least 3 seconds
Head Posture Supine	Ability to hold head up when head supine	0- flaccid tone with head hanging done 1- head lifted but not maintained for 3 seconds 2- head lifted but maintained for at least 3 seconds

Pull to Sit	Infant is pulled from supping to sitting	0-limbs extend and head lags 1-arms moderately flexed with no head lag 2-resistance to supine position with attempts to turn over
Locomotion	Quality of locomotion activity	0-none 1-weak 2-coordinated locomotion
Coordination	Quality of movement rated	0-clumsy 1-adequate 2- agile movements
Activity	General state of motor activity	0-motion up to 25% 1-motion from 50-75% 2-motion from 76-100%
Vocal Response Intensity	Strength of vocalizations during testing	0-mild intensity 1-moderate intensity 2- extremely loud intensity
Vocal Number	Number of vocalizations in the testing period	0-none 1-25% of the time 2-almost continuously
Temperament: Predominant State	State of infant during examination	0-alert, awake, and aware 1-alert but somewhat agitated 2-extremely agitated
Temperament: Fearfulness	Fear grimaces or trembling	0-none 1-grimaces early in session 2-fear noted frequently
Temperament: Struggle During Test	Amount of squirming during testing	0-25% of the time 1-50% of the time 2-constant struggle
Temperament: Irritability	Amount of distress noted during the examination	0-continuous distress 1-distress apparent 50% of the time 2- distress not apparent
Temperament: Consolability	Ease of calming the infant down	0-impossible to soothe 1-consoled with difficulty 2-infant is easy to console
Temperament: Cuddliness	Ease of cuddling the animal	0-None 1-slight molds after cuddle 2-definite molds and cuddles initially
Temperament: Aggression	Measured by attempts to bite during testing	0-absent 1-two attempts 2-continuous biting

Table 3: Reflexes, Motor Activities and Temperament data and statistical results

Behaviors	Week 1	Week 2	Week 3	Week 4	F (df)	p values
Visual Orient-R	2 ± 0	1.75 ± .25	2 ± 0	2 ± 0	(3,6) =1.00	.46, ns.
Visual Orient-L	1.75 ± .25	1.75 ± .25	2 ± 0	2 ± 0	(3,6) =1.00	.46, ns.
Visual Orient-U	2 ± 0	1.75 ± .25	2 ± 0	2 ± 0	(3,6) =1.00	.46, ns.
Visual Orient-D	1.75 ± .25	1.75 ± .25	2 ± 0	2 ± 0	(3,6) =1.00	.46, ns.
Visual Follow-H	1.75 ± .25	1.38 ± .47	1.75 ± .25	1.5 ± .5	(3,3) =.86	.55, ns.
Visual Follow-V	1.38 ± .24	1 ± .41	1.63 ± .24	.75 ± .25	(3,3) =.58	.5, ns.
Attention Span	1.67 ± .33	1.33 ± .33	1.75 ± .25	.5 ± .29	--	--
Orient to Auditory-R	2 ± 0	2 ± 0	2 ± 0	2 ± 0	--	--
Orient to Auditory-L	1.75 ± .25	2 ± 0	2 ± 0	2 ± 0	--	--
Palmar Grasp-R	1.25 ± .25	1.5 ± .29	1.5 ± .29	.67 ± .33	(3,6) =1.46	.32, ns.
Palmar Grasp-L	1.5 ± .29	1.5 ± .29	1.38 ± .24	1.38 ± .24	(3,9) =.08	.97, ns.
Plantar Grasp-R	.88 ± .31	1.67 ± .29	1.25 ± .33	1.13 ± .13	(3,6) =1.44	.32, ns.
Plantar Grasp-L	1 ± 0	1.25 ± .25	1.38 ± .24	1.38 ± .24	(3,9) =.69	.58, ns.
Tactile Response-RA	1.67 ± .33	1 ± .58	.67 ± .33	1 ± .58	(3,3) =1.00	.5, ns.
Tactile Response-LA	.83 ± .6	1 ± .58	.67 ± .67	1 ± .58	(3,3) =1.00	.5, ns.
Tactile Response-RL	1.63 ± .24	1 ± .58	1 ± .58	1 ± .58	(3,3) =1.00	.5, ns.
Tactile Response-LL	.75 ± .5	1.33 ± .33	.67 ± .33	1.33 ± .67	(3,3) =1.00	.5, ns.
Galants-R	1 ± .58	1.13 ± .43	.38 ± .38	.67 ± .33	(3,6) =2.33	.17, ns.
Galants-L	1.33 ± .33	.75 ± .25	.75 ± .41	.83 ± .44	(3,6) =1.29	.36, ns.
Rooting-R	1 ± .58	.75 ± .48	1.63 ± .24	.25 ± .25	(3,6) =1.10	.42, ns.
Rooting-L	1.25 ± .48	1.25 ± .48	1.63 ± .24	0 ± 0	(3,9) =4.47 3 vs 4 (33)	.04 .01
Labyrinthian Righting-R	.75 ± .48	.5 ± .29	1.13 ± .31	0 ± 0	(3,6) =1.26	.37, ns.
Labyrinthian Righting-L	.5 ± .5	.25 ± .25	1 ± .58	33 ± .33	(3,6) =.73	.57, ns.
Body Righting	1.88 ± .13	2 ± 0	2 ± 0	2 ± 0	(3,9) =1.00	.44, ns.
Aversion on Back	2 ± 0	2 ± 0	2 ± 0	2 ± 0	--	--
Active Power	1 ± 0	1 ± 0	1 ± 0	1.33 ± .33	--	--

Response Speed	2	--	--	0	--	--
Head Posture Prone	1 ± .58	2 ± 0	2 ± 0	2 ± 0	(3,3) =1.00	.50, ns.
Head Posture Supine	1.67 ± .33	1.75 ± .25	1.75 ± .25	2 ± 0	(3,6) =.33	.80, ns.
Pull to Sit	1.75 ± .25	1.67 ± .33	2 ± 0	2 ± 0	(3,6) =1.00	.46, ns.
Locomotion	1.5 ± .29	.75 ± .75	1.75 ± .25	1.67 ± .33	--	--
Coordination	.75 ± .25	.75 ± .25	1.25 ± .48	1.5 ± .29	(3,9) =1.65	.25, ns.
Activity	0 ± 0	.33 ± .33	.5 ± .5	1.25 ± .48		
Vocal Response Intensity	.5 ± .35	1.13 ± .13	1.25 ± .43	1.5 ± .2	(3,9) =5.15 1 vs 2 (6.82)	.02 .08
Vocal Number	1.38 ± .24	1.5 ± .29	1.75 ± .14	1.88 ± .13	(3,9) =1.50	.28, ns.
Temperament: Predominant State	.83 ± .38	1 ± .25	1.25 ± .36	1.75 ± .25	(3,6) =2.59	.15, ns.
Temperament: Fearfulness	0 ± 0	0 ± 0	.13 ± .13	.25 ± .25	(3,9) =.67	.59, ns.
Temperament: Struggle During Test	.5 ± .5	.75 ± .48	.25 ± .25	.4 ± .48	(3,9) =1.44	.30, ns.
Temperament: Irritability	1 ± .41	.88 ± .31	1 ± .35	.13 ± .13	(3,9) =3.4	.07, ns.
Temperament: Consolability	1.63 ± .38	1.75 ± .25	1.13 ± .43	.4 ± .24	(3,9) =14.85 2 vs 3 (6.82)	.001 .08
Temperament: Cuddliness	1.75 ± .25	1.75 ± .25	1.5 ± .29	1.38 ± .38	(3,9) =1.65	.25, ns.
Temperament: Aggression	0 ± 0	.25 ± .25	.25 ± .25	.25 ± .25	(3,9) =.36	.78, ns.

Table 4: Frequency and Duration of Social Behaviors and Statistical Results

Behaviors	Week 1	Week 2	Week 3	Week 4	H	p values
Frequency-Mutual Eye Gaze	2.25 ± .75	1.75 ± 1.03	0 ± 0	1.33 ± .82	5.489 (3)	.139, ns.
Frequency-Infant Looking at Mother's Head	2.25 ± 1.11	.75 ± .48	0 ± 0	.42 ± .42	5.348 (3)	.148, ns.
Frequency-Mother Looking at Infant's Head	25.75 ± 14.57	10.00 ± 6.49	3.25 ± 2.36	4.42 ± 4.09	5.272 (3)	.153, ns.
Frequency-Looking at Partner's Eyes	.75 ± .48	.75 ± .75	2.50 ± 2.50	.67 ± .41	.248 (3)	.969, ns.
Frequency-Looking at Partner's Head	.50 ± .50	.50 ± .50	1.25 ± 1.25	.42 ± .42	.086 (3)	.969, ns.
Duration-Mutual Eye Gaze	6.25 ± 2.30	15.20 ± 12.75	0 ± 0	2.64 ± 1.79	5.940 (3)	.115, ns.
Duration-Infant Looking at Mother's Head	9.66 ± 6.07	2.39 ± 1.42	0 ± 0	2.78 ± 2.78	4.522 (3)	.210, ns.
Duration-Mother Looking at Infant's Head	280.76 ± 97.06	80.72 ± 49.24	13.77 ± 8.19	29.72 ± 24.6	7.318 (3)	.062, ns.
Duration-Looking at Partner's Eyes	8.03 ± 4.64	19.55 ± 19.55	1.33 ± 1.33	4.15 ± 3.45	1.012 (3)	.798, ns.
Duration-Infant Looking at Partner's Head	1.02 ± 1.02	2.07 ± 2.07	9.75 ± 9.75	.31 ± .31	.095 (3)	.992, ns.

Figure 1: Duration (seconds) of Mother looking at infant's head per 2.5 hours

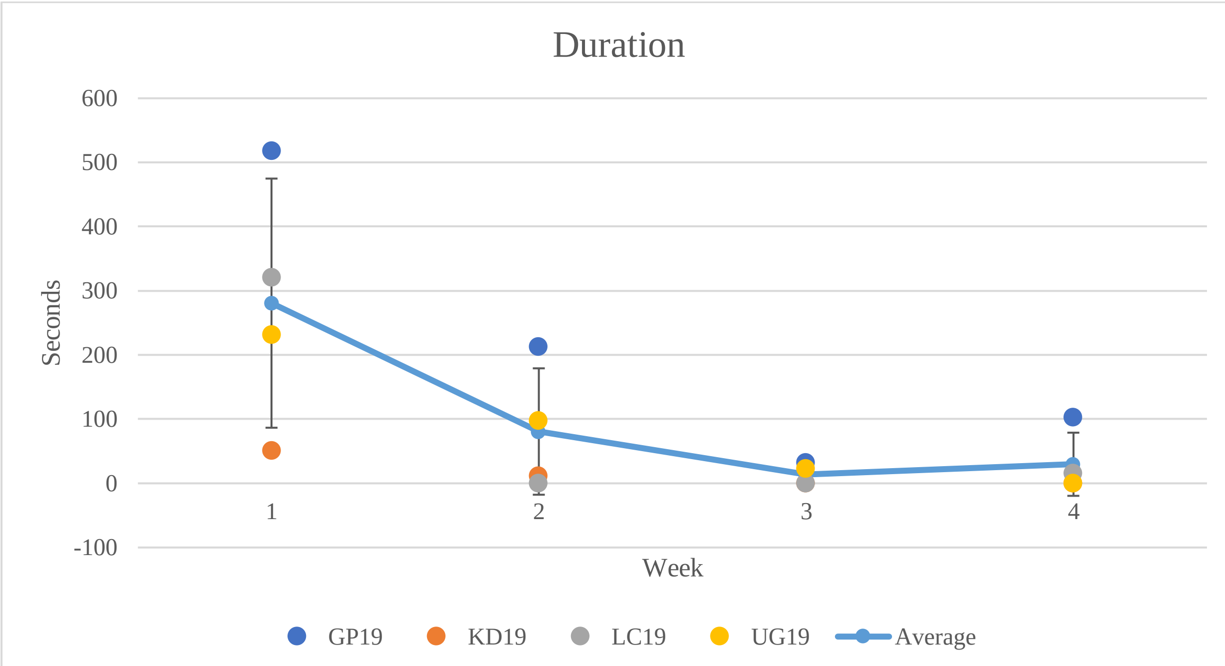
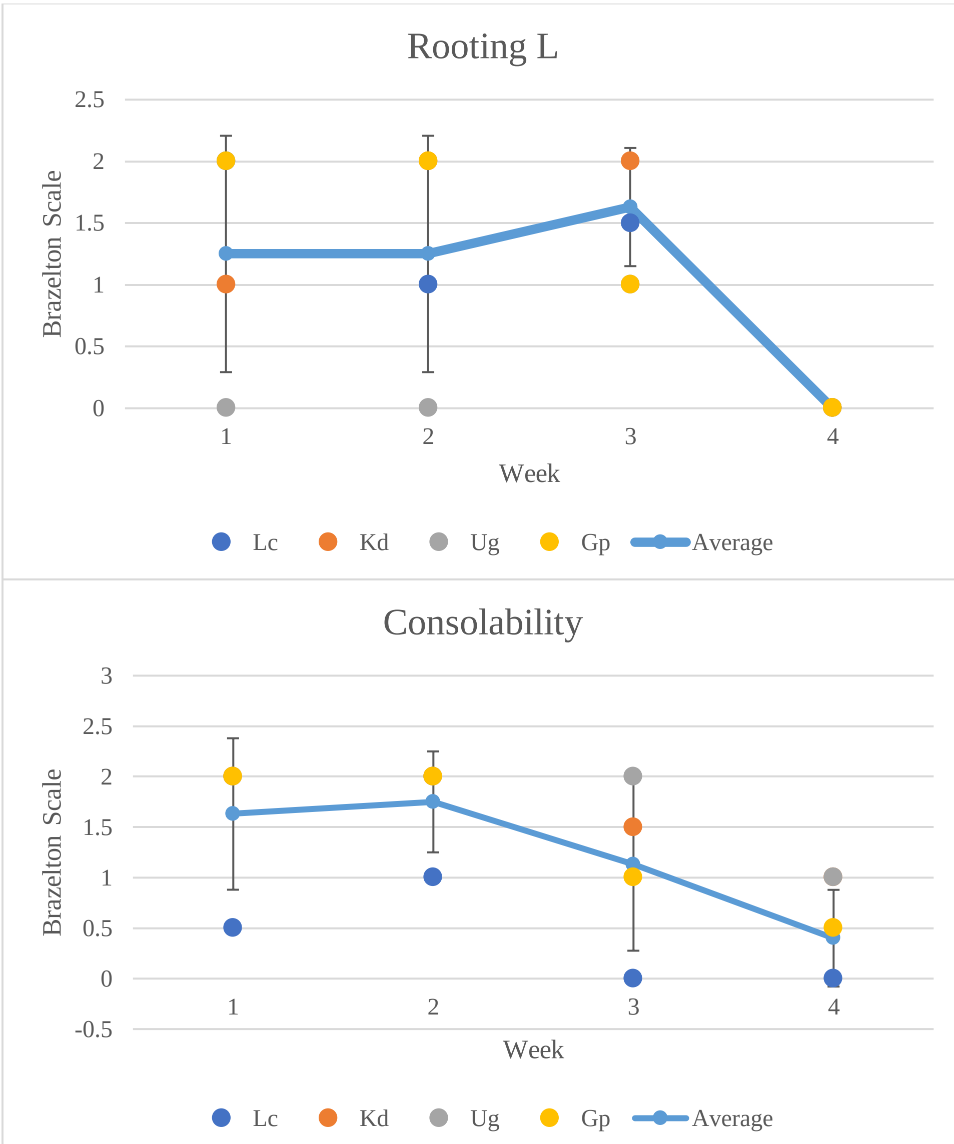
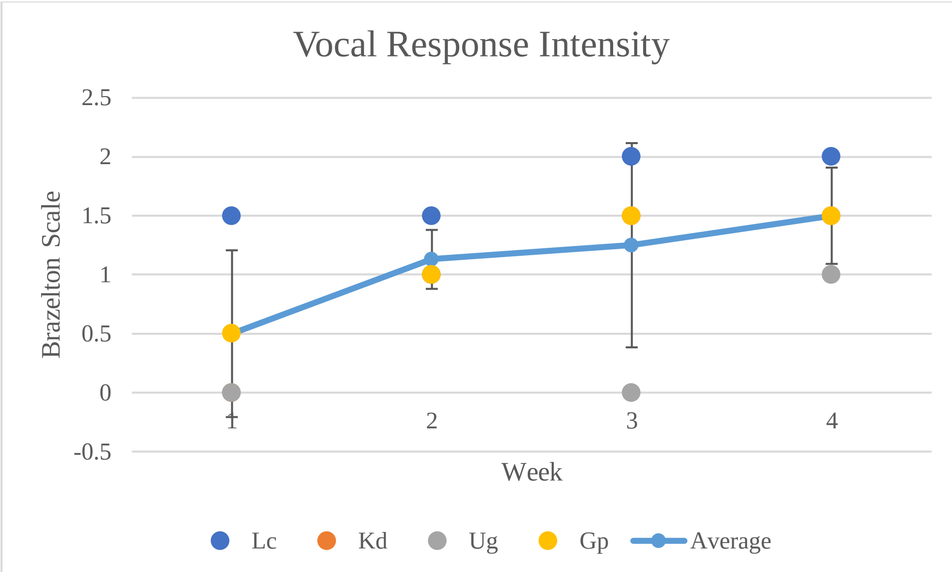


Figure 2: Scores of Left Rooting Reflex, Consolability, and Vocal Response Intensity




Vocal Response Intensity
Brazelton Scale
2.5
2
1.5
1
0.5
0
-0.5
1
2
3
4
Week
Lc
Kd
Ug
Gp
Average

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