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Neonatal brainstem dysfunction risks infant social engagement

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The role of the brainstem in mediating social signaling in phylogenetic ancestral organisms has been demonstrated. Evidence for its involvement in social engagement in human infants may deepen the understanding of the evolutionary pathway of humans as social beings. In this longitudinal study, neonatal brainstem functioning was measured by auditory brainstem-evoked responses (ABRs) in 125 healthy neonates born prematurely before 35 weeks' gestational age. At 4 months, infants were tested in a set of structured vignettes that required varying levels of social engagement and cardiac vagal tone was assessed. Data show that neonates with a disrupted I–V waveform, evident mostly by delayed wave V, exhibit shorter latencies to gaze averts in episodes involving direct face-to-face interactions but engage gaze as controls when interacting with masked agents or with agents whose faces are partly veiled by toys. Analysis of variance of infants' social engagement with ABR, neonatal risk, maternal stress and cardiac vagal tone showed a main effect for ABR and an ABR by gestational age interaction. The integrity of brainstem transmission of sensory information during the final weeks of gestation may scaffold the development of social disengagement, thereby attesting to the brainstem's preserved evolutionary role in developing humans as social organisms prior to engaging in social encounters.

Keywords: brainstem; gaze

INTRODUCTION

From the very beginning, human infants are acutely sensitive to social stimuli, especially faces (Maurer and Salapatek, 1976; Morton and Johnson, 1991; Striano and Rochat, 1999), and from 3 to 5 months their gaze and affective behavior reflect increased sensitivity to their partner's slight deviations in gaze and facial expressions (Symons *et al.*, 1998; Striano and Stahl, 2005). The majority of the research concerning the development of social and affective behavior has concentrated on cortical-related activity, mostly the amygdala–limbic system and the medial prefrontal and fronto-parietal systems (Amodio and Frith, 2006). Along with these essential cortical systems, the underpinning distributed network that subserves social engagement has been thought to involve ancestral brainstem streams, as well as the later emerging central thalamus–dorsal striatum and medial–dorsal thalamus (Bolhuis *et al.*, 2010).

Despite this compelling framework, no direct evidence has yet been presented for the involvement of brainstem projections in the social engagement of humans, particularly of human infants. Given the brainstem's phylogenetic evolutionary tenure and its role in generating behaviors that mediate social signaling in early organisms (Bass *et al.*, 2008), evidence for brainstem involvement in social engagement may deepen the understanding of the evolutionary pathway of humans as social beings. MacLean's (1990) conceptualization of the triune brain, comprising three major systems; the first, corresponding to the basic reptilian brain (hind- and midbrain systems); the second, to the mammalian brain (palaeocortex, subcortical systems) and the third to the primate brain (broadly, the neocortex); has not yet been tested developmentally in the human model. We proposed a comparable vertically integrative model for the development of self-regulation in the human infant. This model highlights longitudinal links between brainstem functions and the development of regulatory capacities across early childhood in several areas of development, including physiological regulation of vagal tone, arousal, attention regulation, parent–infant synchrony and socio-emotional regulation (Geva and Feldman, 2008). The model implicates direct relations between brainstem-mediated functions, such as the ABR, social self-regulatory behaviors and social engagement.

Prenatal structural and functional susceptibility of the brainstem

Animal de-cortication models and other basic scientific research highlight the effect that brainstem structures have on emotional and attentional behaviors. These studies show that

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the brainstem plays a role in behavior and conscious awareness through the integration of external sensations and personal conscious thoughts and feelings (Merker, 2007). This type of research has also found that higher level cognitive functioning that involves cortical activity also involves brainstem and limbic level functioning, indicating that brainstem systems play an integral role in these higher level capacities such as self-regulation. Because brainstem structures mature earlier than those of the limbic and cortical systems, impairment in the development of the brainstem structure could signify neurofunctional deficits, as well as deficits in self-regulation throughout life.

Structural brainstem aberrations in human infants seem to be rather rare due to their fatal implications, thus this area is still under-studied using imaging techniques to document neonatal susceptibility of brainstem-related systems. Nevertheless, there are indications of structural white matter volume reductions with peaks in brainstem areas in adolescents who were very preterm at birth (Nosarti *et al.*, 2008). These may be related to diagnosable conductance changes early on in development.

Conductance efficacy is dependent upon the spatiotemporal coefficients of myelin (Moore *et al.*, 1995). The progression of myelin development proceeds from deep white matter (brainstem, cerebellum and internal capsule) (Tanaka *et al.*, 1995) to superficial regions (optic radiations, corpus callosum and frontal white matter) (Kinney *et al.*, 1988). Disruptions in myelination may disrupt white matter maturation and the integrity of neural connectivity and synchronization of neural oscillations. These in turn may bear implications for the establishment of emotional and attentional functions (Doesburg *et al.*, 2011).

Indeed, *functional* brainstem changes are sometimes expected in infants born prematurely and in infants who are affected by neonatal complications. Early recordable maturational changes using auditory brainstem-evoked responses (ABRs) offer a window to evaluate 'functional efficacy' of emerging brainstem projections *in vivo* in neonates born prematurely using surface electrodes (Jiang *et al.*, 2009).

Certain brainstem functions, essentially the ABR function, first emerge around 30–33 weeks' gestation (Jiang *et al.*, 2009), a period at which many premature births occur. This period is a critical one for major developmental changes in the equilibrium and the auditory pathways in the brainstem, including myelination, axonal sprouting, formation of central synaptic connections, improvement of synaptic efficiency, increase in axonal diameter and development of central dendrite properties during this period (Krumholz *et al.*, 1985; Moore *et al.*, 1995; Jiang *et al.*, 2009).

ABRs are testable in infants who are born preterm (Jiang *et al.*, 2009; Geva *et al.*, 2010;) and are susceptible to neonatal risk factors that accompany prematurity, such as hypoxic-ischemic events (Jiang *et al.*, 2009), bronchopulmonary dysplasia (Wilkinson *et al.*, 2007), brain insult or hydrocephalus (Karmel *et al.*, 1988). It is expected that the preliminary brainstem function, even when abnormal at first, would be resolved in the great majority of cases rapidly, due to the importance of these structures and more so, their surrounding substrates, for survival. Nevertheless, remnants of this highly vital abnormality, which would scaffold later phases of development, should be expressed as the developmental process progresses.

Neonatal brainstem dysfunction and disrupted development of regulatory capacities

Brainstem injury has been found to disrupt physiological regulation and homeostasis. These disruptions impact the autonomic nervous system, such as the cardiac vagal tone (Porges, 1992). They also affect circadian arousal regulation (Karlsson *et al.*, 2005), as well as visceral homeostasis modulation of internal states, such as hunger and thirst (Batterham *et al.*, 2007). All of these systems are interrelated and moderate emotional and attentional regulation in infants during the neonatal phase (Geva *et al.*, 1999). Behavioral studies from the neonatal period show a relationship between neonatal ABR and attention regulation deficits in 1-month-old infants, such that the infants who exhibited neonatal ABR dysfunctions show difficulties in regulating attention to stimuli as a function of arousal states (Gardner *et al.*, 2003). Similarly, a prospective follow-up showed poorer attentional responses in these infants that were hyper-responsive to increased endogenous arousal at 4 months (Karmel *et al.*, 1996).

Later maturational changes in collicular–basal ganglia functions and the development of the posterior attention systems (Posner *et al.*, 1988), as well as connectivity to the thalamus and the entire limbic system (Tucker *et al.*, 2005), all through prefrontal connectivity (Diamond, 1990), and may depend on the prenatal integrity of lower brainstem structures. Indeed, we have shown that infants with compromised neonatal ABR function exhibited less regulated inhibitory control on rapid automatized naming tasks at 3 years of age (Geva, 1995; Geva *et al.*, 2010).

From the third trimester, brainstem connectivity to the limbic circuit emerges (Tucker *et al.*, 2000). This transition, evident in sleep–wake measures and in vagal regulation measures during 31–34 weeks' conception age, were reported to support emotional signaling and affect sharing at the 3- to 6-month stage (Prechtle, 1992; Tucker *et al.*, 2000; Levitt, 2003; Porges, 2003; Feldman, 2006). It is important to note that sleep–wake regulation and vagal reactivity are thought to be mediated by brainstem distributed systems, yet, to date no direct effects of brainstem integrity on social or affective responses were shown. In view of the above, it is hypothesized that early brainstem dysfunction detected during its major maturational spurt in the late prenatal period will directly affect the modulation of gaze as a function of arousal to social stimuli, thereby compromising social engagement.

Prematurity and social engagement

In comparison with typically developing infants, some preterm infants have difficulty orientating to social stimuli and maintaining social interactions. These infants are less responsive to faces, and therefore, take more time to engage with them (Field, 1977, 1979; Masi and Scott, 1983; Barratt *et al.*, 1992; Eckerman *et al.*, 1999;). Others report increased difficulty in bringing preterm infants to an attentive state for en-face exchanges. Once brought to an attentive state, it is more difficult for them to maintain the interaction with positive affect and their actions include increased crying, sad expressions and gaze aversion (Field, 1981; Harel *et al.*, 2010).

Data collected so far, do not enable targeting the specific subgroup of premature infants who may be more prone to experience social engagement difficulties. Diagnosing brainstem functional compromise when it emerges in preterm infants may enable, for the first time, to study the contribution of fetal brainstem integrity to social engagement and target those preterm infants that may be at risk of experiencing social engagement difficulties. It is thus of central theoretical and clinical importance to examine how subtle disturbances at the brainstem level during the neonatal period affect social engagement functions, which were recently reported to be related to activity in the limbic and cortical levels of the central nervous system (Swain, 2011) and examine the neonatal period, before the mother–infant effortful interactive patterns become a full-blown learning and social communication disorder.

METHODS

Participants

This study is part of a longitudinal study on infant development from 0–7 years of age. The study consists of 125 low-risk premature infants with a mean gestation age (GA) of 32.9 weeks (s.d. = 1.4; range: 29–36.1 weeks) and mean birthweight of 1745 g (s.d. = 344.3; range: 830–2644 g). The infants were recruited from a Level III Neonatal Intensive Care Unit (NICU) at Sheba Medical Center, Ramat Gan, Israel. To minimize external sources of socio-emotional stress, inclusion criteria were set so that all of the mothers were at least 21 years old, all lived with the infants' fathers, none reported use of psychoactive drugs or psychiatric medication during pregnancy and after birth and according to Israeli standards (Harlap *et al.*, 1977), were all rated as middle-class. None of the participants were diagnosed with intraventricular hemorrhage or periventricular leukomalacia on cranial ultrasound. In total, 30% of the mothers approached declined to participate, citing time constraints, partner's refusal or not feeling ready to deal with developmental issues as main reasons.

Totally, 86.4% of the original sample took part in the experimental procedure at 4 months ($N = 108$). These mothers and infants did not differ from the nonparticipating families on any of the demographic or medical variables.

Table 1 Demographic characteristics (mean and standard error) of the participants in each group

Demographic characteristics	NBSF ($N = 68$)	CBSF ($N = 40$)	*P*
Infant			
GA (weeks)	33.21 ± 0.15	32.66 ± 0.21	0.04
PCA at ABR test	34.87 ± 0.17	34.50 ± 0.27	NS
Birthweight (g)	1776.98 ± 37.35	1743.64 ± 56.37	NS
CRIB score	0.22 ± 0.04	0.32 ± 0.07	NS
NBRS score	1.98 ± 0.21	2.29 ± 0.33	NS
Days at NICU	29.0 ± 1.49	29.0 ± 1.98	NS
Gender, female (%)	40	60	NS
Fetal position, vertex (%)	62.6	57.9	NS
Birth, CS (%)	59.4	58.5	NS
Fetal distress (%)	14.9	24.3	NS
ELBW <1250 g (%)	5.2	2.5	NS
Familial			
Mat Age	33.49 ± 0.79	32.29 ± 0.75	NS
Pat Age	35.78 ± 0.80	34.30 ± 0.72	NS
Mat educ level	4.00 ± 0.14	3.88 ± 0.17	NS
Pat educ level	3.77 ± 0.13	4.08 ± 0.16	NS
Pat work profic	1.77 ± 0.76	1.81 ± 0.10	NS
Mat STAI-T	31.9 ± 0.86	33.25 ± 1.52	NS
Mat BDI	5.90 ± 0.81	7.47 ± 1.38	NS
Birth order, 1st (%)	58.2	72.5	NS

CBSF, Compromised brainstem functions; NBSF, Normal brainstem functions; GA, gestational age; PCA, post conceptional age; CRIB, Clinical Risk Index for Babies (CRIB and International Neonatal Network, 1993); NBRS, Neurobiologic Risk Score (NBRS) (Brazy *et al.*, 1991); CS, cesarean section; ELBW, extreme low birth weight <1250 g; Mat, Maternal; educ, education; Pat, Paternal; profic, proficiency; STAI-T, State and Trait Anxiety index-Trait; BDI, Beck depression questionnaire (Beck *et al.*, 1988); NS, non-significant.

The cohort was divided into two groups according to normality of brainstem functions for the infant's gestational age. Descriptive characteristics of the groups are presented in Table 1. The table shows that the groups were comparable on prenatal, neonatal and familial variables, except for a difference in gestation age, such that participants in the compromised group were born on average 3 days earlier than participants in the control group.

Procedure and design

The study was approved by Sheba Medical Center Institutional Review Board, and the design was a longitudinal cross-sectional one. Parents were recruited at the NICU during the first 24 h postbirth. Infants of consenting families went through a bedside ABR study at the NICU when the infant's status permitted the evaluation, typically within the first 2 weeks postbirth (mean age at test = 2.1 ± 1.2 weeks). ABR evaluations were conducted by an audiologist who specializes in neonatal evaluations.

The infants were then enrolled to the follow-up program in which a complete double-blind protocol was observed (e.g. neither parents nor testers in the follow-up phase were aware of the ABR status).

At 4 months, the corrected age infants visited a university laboratory and were tested using the Behavioral

Responsiveness Paradigm (BRP) (Garcia-Coll *et al.*, 1988). In addition, Cardiac vagal tone was collected during a free-play interaction with the mother. In the BRP procedure, the infant is presented with a series of stimuli, each lasting for 20 s followed by a 10-s break. The BRP entailed a series of 17 structured vignettes in which an experimenter interacted with the neonate. In seven of these vignettes, the experimenter–infant dyads are positioned in a face-to-face setting and the infant was able to spontaneously engage in eye contact. These vignettes differed in their level of social loading and were therefore, analyzed for purposes of the current study.

In Level 1, social interaction was minimal. These vignettes revolved around a toy, which was presented by the social agent. The agent's face was in the background, away from the center of the infant's eye-field and was somewhat veiled by the moving object in front of it. These scenes included: Scene 1, in which a set of colorful keys were joggled by the experimenter in front of the infant; Scene 9, in which the experimenter rang a bell for 5 s, took a 5-s break and then rang it again for 5 s; Scene 10, in which the experimenter shined a flashlight into the infant's eye for 5 s, removed it for 5 s and then shined it again for 5 s; and Scene 15, in which the infant was shown a toy car that had flashing red lights and made noise.

In Level 2, social interaction was somewhat veiled; the social agent wore a 'screen', such as a mask, while interacting with the infant, or talked directly to the infant while jiggling a toy in front of his or her face. These scenes included: Scene 2, in which the same stimulus used in Scene 1 was presented while the experimenter spoke to the infant; Scene 11, in which the experimenter wore a scary mask and spoke to the infant and Scene 12, in which the experimenter wore a human mask and spoke to the infant.

In Level 3, social interaction was direct and uninterrupted: The experimenter initiated a direct face-to-face interaction, such as in Scene 3, in which the experimenter leaned closely toward the infant and spoke with the infant, as caretakers would naturally do. Scenes that did not include a face-to-face opportunity (Scenes 4–8, 13–14) were not analyzed for purposes of the current report as they entailed very limited opportunity for eye contact (i.e. holding the infant; brushing his/her hair, passing a cotton wool over the infant's face, hand wiping, etc.).

The experiment was video-recorded digitally and was later micro-coded for gaze eye-contact lengths using a computerized system that was set to 0.1-s accuracy.

Measures

Three main measures were obtained: (i) Time to Engagement, the time between the presentation of the stimulus and the infants' first engagement with the stimulus; (ii) Time to Disengagement, the time between the first engagement and the first gaze avert and (iii) Gaze Shift Length, the time between the first engagement with the stimulus and the first gaze at the experimenter, in the event that this type of gaze occurred. Inter-rater agreement correlations on 12 video clips between two raters on the three measures were 0.96, 0.94 and 0.94, respectively.

To obtain an estimated neonatal risk that is not necessarily directly related to brainstem compromise, infants' neonatal medical risk was assessed using the Clinical Risk Index for Babies (CRIB) (CRIB and International Neonatal Network, 1993). This index predicts risk by taking into account birth weight, GA, congenital malformations, minimum and maximum fraction of inspired oxygen at the first 12 h of life, and minimum base excess at the first 12 h of life. Higher risk is indicated by a higher CRIB score.

Apparatus

Neonatal ABR

ABR were collected by a trained audiologist as soon as the neonatal medical status was stabilized. The recording was carried out, on average, during the second week of postnatal life (mean 2.04 ± 1.22 weeks) to increase the likelihood of documenting ABR compromise prior to its recovery. Neonatal age at the ABR test was, on average, at 35.18 ± 1.48 weeks postconception age. Testing was conducted with a Biologic Navigator Pro (model 907, FDA approved).

Three to four consecutive runs of 1024 100-μs square wave monaural rarefaction clicks, 75 dB hearing level, at a 10.1 Hz rate, were presented to the left auditory canal using micro insert earphones to minimize the risk of a collapsed ear canal (Jiang and Wilkinson, 2006; Jiang *et al.*, 2006), and the ear canal was examined for any vernix by a neonatologist. Recording was initiated after the infant was calm, postmid-morning feed, without sedation. Surface gold-plated electrodes were used and placed at the vertex behind the frontal fontanel (active), on the ipsilateral mastoid (referent) and middle forehead (ground). Impedance levels were maintained at $<5\,k\Omega$. Data were digitized at 50-μs intervals for 12-ms sweeps and averaged to produce the ABR wave form. The peak-to-peak voltage level was used to establish an artifact rejection algorithm. Unusual excessive static noise and or excessive muscle artifacts in records resulted in manual cessation of data collection and resampling. Recordings from the left ear were reported (Jiang and Wilkinson, 2006; Jiang *et al.*, 2006). A compromised function was defined according to wave component latencies I, III and V, as compared with latency norms for gestation age (Karmel *et al.*, 1988). Delays >1.5 s.d. for gestation age were classified as compromised auditory brainstem function (CBSF). Scores <1.5 s.d. were marked as normal brainstem functions (NBSF). All infants were retested using a clinical ABR screen before discharge as part of the routine discharge protocol. Only one infant did not pass the discharge screening, but his hearing, as with all others, was within expected range upon audiologic follow-up. Inter-rater agreement correlation rate on scoring the empirical ABR on 12% of the cases was 0.94.

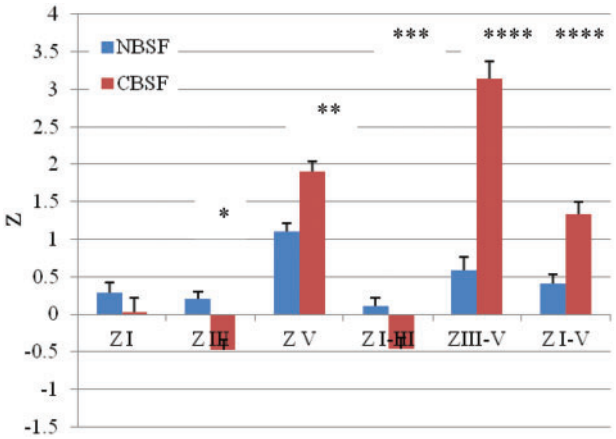

Fig. 1 Standardized ABR major wave latencies (Mean and SEM) as a function of group, NBSF, Normal brainstem functions; CBSF, Compromised brainstem functions; SEM, Standard error of measurement. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0005$.

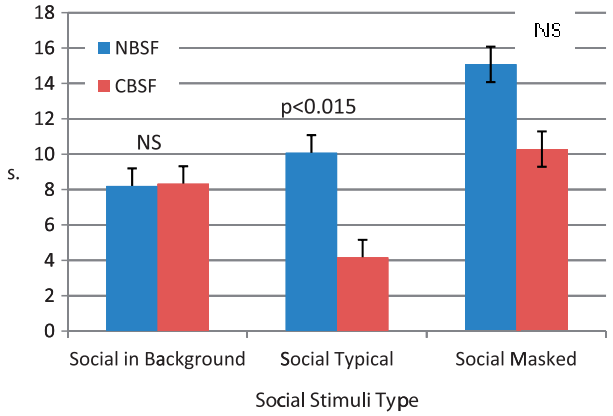

Fig. 2 Time to disengagement (means and SEMs) as a function of social load and brainstem integrity. NBSF, Normal brainstem functions; CBSF, Compromised brainstem functions; SEM, Standard error of measurement.

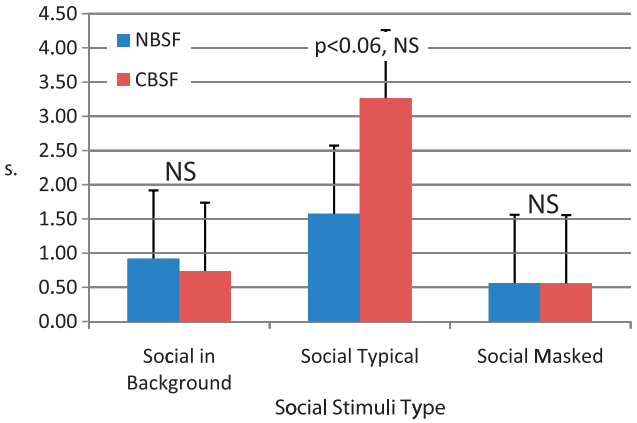

Fig. 3 Time to engagement (means and SEMs) as a function of social load and brainstem integrity. NBSF, Normal brainstem functions; CBSF, Compromised brainstem functions; SEM, Standard error of measurement.

ABR

Differences were noted between the groups in all major indexes of the ABR, except for Wave I latency, indicating that the differences were not due to a conductive middle ear source, but rather were related to differences in neural transition rate past the cochlear ganglion (Figure 1). Differences between the groups seem to increase, the further the loci along the auditory pathway, such that absolute latencies diverted from the mean mostly in Wave V and the difference between the groups were the greatest in the III–V transmission interval (Figure 1).

ABR effect on engagement

ANOVA (GLM multivariate) tests were conducted to examine ABR grouping effect on the time to engage and engagement length measures at 4 months. An overall significant effect for ABR was found specifically for engagement length, $F = 4.916$, $P = 0.029$. The effect was such that infants with abnormal ABR were found to have significantly lower overall engagement length durations than infants with typical ABR. This reflects difficulty in sustained attention. Further analysis with gestational age, weight and gender, tested as confounders showed that there were no associations with between factors and engagement lengths.

ABR*Degree of sociability

The main effect of ABR grouping was maximized in the context of the sociability load [$F(1, 93) = 6.495$, $P = 0.012$]. Engagement length duration changed as a function of sociability load levels [$F(2,92) = 3.2$, $P < 0.045$]. Posthoc tests showed that the high sociability condition was most sensitive to the ABR susceptibility [$F(1, 106) = 6.166$, $P = 0.015$]. Infants in the compromised ABR group experienced more difficulty sustaining attention in the direct interaction condition (Social typical) than infants with normal ABR functions (Figure 2).

Figure 3 presents the results of time to engage as a function of degree of sociability and brainstem integrity. Although the graph seems to indicate a difference between the groups in the Social × Typical interaction condition, the variance in both groups in this measure precluded a significant effect given the current sample size ($P < 0.06$). There were no differences between the groups in the gaze shift length, as this behavior was scarce at this age in both groups.

Finally, analysis of variance was conducted to examine whether the main effect of ABR on time to disengagement continues to hold in more elaborate models. This analysis showed that the interaction effect of ABR and very low birth weight for the mean gestational age of the current cohort, was significant as well ($F = 4.554$, $P < 0.037$), and the factors of gender, maternal stress trait, neonatal CRIB and infant's heart rate variability, were all nonsignificant in this context (Table 2).

Table 2 Tests of between-subjects effects on time to disengagement

Source	*F*	*P*	Partial Eta squared	Observed power[a]
ABR	8.556	**0.005**	0.135	0.820
Infant's VT during free play at 4 months	0.005	0.946	0.000	0.051
CRIB	2.155	0.148	0.038	0.303
Maternal neonatal STAI Trait scores	0.617	0.436	0.011	0.121
VLBW* for mean gestational age	0.816	0.370	0.015	0.144
Gender	1.206	0.277	0.021	0.190
ABR * VLBW	4.554	**0.037**	0.076	0.554
ABR * Gender	0.975	0.328	0.017	0.163
VLBW * Gender	0.952	0.333	0.017	0.160
ABR * VLBW * Gender	2.607	0.112	0.045	0.355

[a]Computed using alpha = 0.05. *VLBW, very low birth weight (<1400 g, expected 5th percentile weight for 33 weeks gestation); VT, Vagal tone; STAI-T, State and Trait Anxiety index-T index, values in bold = effects accounted by neonatal brainstem dysfunction.

DISCUSSION

The vertical integrative model (Geva and Feldman, 2008) proposed a specific set of hypotheses regarding brainstem input to social engagement. Evaluation of ABR at the time of its emergence was shown to be fruitful in targeting infants' social engagement skills at 4 months of age. This finding shows for the first time that neonates who are born preterm and show perinatal CBSF are at a greater risk to exhibit difficulties in regulating gaze during a face-to-face interaction at 4 months of age. This is highly intriguing in demonstrating a direct role of brainstem input to social behavior.

Another important notion that may be contemplated based on this finding emerges from the finding that the integrity of brainstem pathways at 33–35 weeks of gestation is related to social engagement later on in life, thereby presenting support to the notion that humans are programmed for social behavior at a period *preceding* social encounters.

It is important to note that ABR evaluation in the current study was conducted at a sensitive period, earlier than routine ABR screens, which are typically conducted just before discharge from the NICU. This may point to a sensitive period for brainstem scaffolding of the social engagement network. The finding of a significant interaction effect between ABR and very low birth weight (VLBW), points also to the increased power of brainstem maturation aberrations in infants who are born VLBW for their gestation age. This finding is compatible with reports of increased susceptibility for social difficulties in infants born ELBW (Hille *et al.*, 2001), and may point to a mechanism to account for this socio-emotional risk in the ELBW group.

The finding that vagal tone (VT) did not account for variability in gaze engagement in this context is intriguing. It may be explained by a shared variance between brainstem integrity and VT (Porges *et al.*, 1996), and might extend current findings dealing with cardiac vagal break and social engagement to additional behavioral brainstem-mediated actions, such as sleep–wake regulation deficits (Feldman, 2006) and feeding–satiety regulation difficulties, thereby suggesting brainstem dysfunction as a more inclusive marker for social engagement deficits (Schmid *et al.*, 2010).

Finally, it is important to note that the premature gaze disengagement for a social target seen in infants born prematurely who had prolonged and/or atypical brainstem transmission times, may not necessarily represent a maladaptive response; it may serve in this initial phase of development to reduce stress. Further longitudinal follow-up studies may elucidate to the efficacy of this behavior in alleviating social stress. Retrospective analyses in larger samples may point to specific mechanisms involved in compromising the ABR.

Future studies may enable better targeting of individuals who might be more sensitive to experience social engagement difficulties already in the first months of life when early emotional bonds and initial face-to-face interactions are experienced, and may enable the examination of the manner and degree to which these findings may generalize across different paradigms and other socio-cultural contexts.

Overall, the findings point to the role of perinatal brainstem input in scaffolding social engagement, as well as offer a possible avenue to allow for targeting of infants who are at risk for social gaze aversion using neonatal ABR recording.

Conflict of Interest

None declared.

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