2018

Neural correlates of nonverbal social communication in high-risk infants

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Neural Correlates of Nonverbal Social Communication in High-Risk Infants

by

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Thesis

Submitted to the Department of Psychology

Eastern Michigan University

in partial fulfillment of the requirements

for the degree of

DOCTOR OF PHILOSOPHY

in

Clinical Psychology

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December 17, 2018

Ypsilanti, Michigan

Abstract

The aim of this study was to replicate and extend a study by Grossmann and colleagues (2008), examining infant neural responses to gaze in 5-month-olds, to older and high-risk infants. Participants were 9-month-old infants (5 preterm, [3 female]; 12 full term [7 female]) who underwent fNIRS while viewing gaze paradigms. Findings revealed that hemisphere predicted peak oxygenated hemoglobin (HbO_2) across groups and conditions, with higher activation in the left hemisphere across groups. Interaction of group by condition predicted peak HbO_2 value, with an increase in activation in the high-risk group during the averted condition. Participants as random effects accounted for a significant amount of the variance, highlighting the importance of individual variability in infant studies. Lower activation in left frontal regions was related to higher expressive language while lower activation in right frontal and temporal regions was related to higher receptive language. Overall, higher activation was related to reduced language performance, negative affect, and behavior problems at 12 months.

Keywords: social communication, infancy, gaze, preterm, fNIRS

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Introduction to Social Neuroscience and Social Cognition

The field of neuroscience is broadly interested in the structure and function of the human brain (Cacioppo & Decety, 2011). Neuroscience encompasses the study of anatomy, physiology, biochemistry, and molecular biology of nerves and nervous tissue particularly as it relates to behavior and learning (Neuroscience, n.d.). One subfield of neuroscience that remains heavily studied is cognitive neuroscience. Cognitive neuroscience is interested in the study of the brain as an information processing organ and seeks to understand processes like attention, memory, executive functioning and the neural mechanisms that underlie these processes (Cacioppo & Decety, 2011). The field of social neuroscience first came to be studied and understood as its own entity only two decades ago (Cacioppo & Cacioppo, 2013). Because the field of cognitive neuroscience is interested broadly in cognitive processes, an argument had to be made as to the purpose of defining social neuroscience as its own field. Social neuroscience is the study of the neuroanatomy, neurochemistry, and neurophysiological mechanisms underlying social processes and aspects of social cognition like attachment, temperament, social communication, social perspective, and social learning (Cacioppo et al., 2000).

One of the major differences that has emerged between social neuroscience and cognitive neuroscience is that social neuroscience does not view each individual's brain as its own computing and processing organ, rather social neuroscience views the brains of individuals as being very much connected to others and defines cognitive processes from a social perspective (Cacioppo et al., 2000). Cacioppo and Cacioppo (2013) demonstrate these differences by comparing the perspective of cognitive neuroscience as viewing each individual's brain as a desktop computer, as opposed to social neuroscience, which views each individual's brain as something more comparable to a cell phone, something that relies on and is concerned with communication from others. For example, from the perspective of cognitive neuroscience, language is a tool for processing information and developing meaningful representations of that information within the brain of an individual, whereas from the perspective of social neuroscience, language is a tool for sharing meaningful representations and information between brains, with the goal of promoting coordination and communication across beings (Cacioppo & Cacioppo, 2013).

As neuroscience and the study of the human brain have become more popular and widespread, many disciplines have developed interest in the structure and function of the brain in relation to their field of study. The field of social psychology has always sought to empirically understand the ways in which people think about one another and the ways in which they engage socially with the world (Landau et al., 2010). With the emergence of techniques to study the brain, social psychology began utilizing methods to understand the neural underpinnings of these social phenomena. The combination of the two fields gave rise to social cognition, an area of inquiry that is interested in understanding the cognitive processes that underlie social behavior (Landau et al., 2010).

Theories of Social Learning and Cognition

Social cognition has come from many branches of psychology and neuroscience, so there are several theories addressing the development and acquisition of social and communicative skills and how individuals ultimately achieve competence in social communication (Bandura, 1978). Piaget's (1936) theory of cognitive development is hierarchical and states that cognitive skills develop in order, so early stages must be met before moving onto more complex cognitive processes. Infants use their senses to learn about the world. Infants eventually develop sensory knowledge of their environment and begin to build meaningful representations of the world around them (Piaget, 1936). According to Piaget's (1936) theory, by 18 months of age, toddlers begin to engage in symbolic, imaginative play, indicating that they are able to use objects for something other than their intended use. From this perspective, the development of more complex forms of communication, such as social communication and pragmatic language, language that is used for a social purpose and that fits the particular social context in which it is used, are only possible if the earliest stages of cognitive development are mastered (Bishop, 2000).

Social learning theorists believe that learning occurs within the context of social and cultural interactions (Hwa-Froelich, 2015). Bandura's (1978) social cognitive theory states that learning occurs through imitation of others, with the expectation that outcomes of their interactions will be similar to those they have imitated. In contrast to Piaget's theory, Vygotsky (1978) believed that a child's understanding of the social world precedes cognitive development. This theory assumes that children use language as an internal tool to self-regulate as well as an external tool for social interactions that are mediated by caregivers (Hwa-Froelich, 2015; Vygotsky, 1978).

Another theory of social cognition is interaction theory (Gallagher, 2013). This theory states that social interaction is bidirectional so that the child can influence and is influenced by interactions with caregivers and that the exchange of these interactions is what determines developmental outcomes (Hwa-Froelich, 2015). Because both internal factors like temperament and biology and external factors related to the environment play an important role in these interactions, development is widely varied among individuals (Gallagher, 2013).

Because social behavior involves the integration of several complex cognitive skills like attention, language, and memory, theories have been specifically developed to address how complex cognitive processes lead to functional social communication. Information processing theory states that the course of appraising information has three stages: sensory memory, short-term or working memory, and long-term memory (Atkinson & Shiffrin, 1968). Information processing theory further states that individuals have the ability to process stimuli both top-down and bottom-up in the sensory register, meaning that an individual is able to perceive stimuli utilizing cognition and previous memories, as well as perceive stimuli utilizing the senses as it is processed (Atkinson & Shiffrin, 1968).

In contrast to Atkinson and Shiffrin, social information processing theories have also been developed that state that the processing of social stimuli occurs simultaneously, rather than sequentially and employs many brain regions working in concert, forming stronger connectivity among regions the more that they are employed (Hebb, 1949). Crick and Dodge (1994) stated that social information processing occurs through interactions with others by first encoding internal and external cues of the interaction, evaluating those cues in the context of the interaction to account for intentions and goals, and comparing the current situation to past situations and accessing previously learned social rules. Then, personal goals and goals of others involved in the interaction are clarified in order to begin the process of selecting behavioral responses and determining potential outcomes of the interaction (Crick & Dodge, 1994). The process of encoding social information and accessing previous social memories begins again when the individuals involved in the interaction respond.

Social learning, cognition, and interaction theories serve as foundations for understanding how social skills are learned. Information processing theory, among others that seek to understand the cognitive aspects of social behavior, give broad insight into the development and acquisition of social communication, but they do not necessarily address the wide person-to-person variability that exists in terms of social communication development and outcomes (Hwa-Froelich, 2015). Dynamic systems theory was developed to address this wide variability in many aspects of development, and it pulls together insights from biology, physics, and psychology (Thelen & Bates, 2003). According to Thelen and Bates (2003), dynamic systems theory views human development as a process that is nonlinear and dynamic and understands development as being impacted by internal and external factors like neurobiological development and biological predispositions, exposure to developmentally appropriate experiences, and interactions with the environment. Systems are organized within an individual and then are reorganized following these experiences and interactions, and the more stable a system within an individual, the harder it is to change, and vice versa (Thelen, 2005). According to Fogel (2011), development is a process that is not imposed by the environment or by a person's biological make up, rather development is a dynamic and ever-changing process, even when a behavior, like smiling is repeated because the behavior is always subtly impacted by the context. For example, learning to crawl indicates achievement of a motor milestone, but over time, motor milestones like crawling or walking have social implications, as well (Fogel, 2011). The wide range of possible combinations of the aforementioned mix of internal and external interactions results in the substantial variability in development, including the development of social skills and abilities.

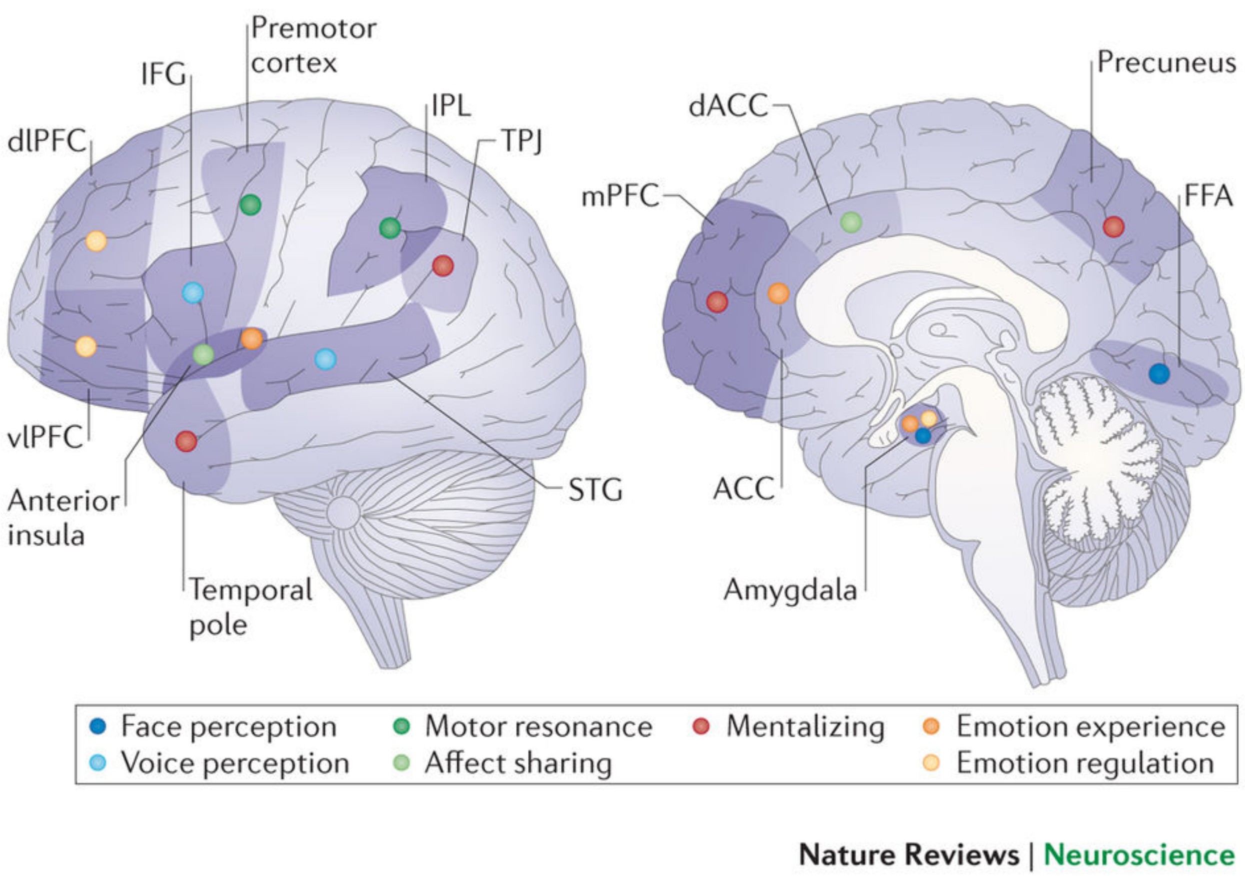
Theories of social learning and cognition have led to the study of the social brain. Neuroimaging and neuropsychological data on social cognition in adults have led to the understanding that there are several regions and purported networks of the brain that are involved in social information processing. Social cognition utilizes cortical and subcortical structures to integrate complex cognitive processes to facilitate social behavior. Although significant advances have been made in the understanding of the adult social brain, little is known about the development of social cognitive processes that lead to typical and atypical social functioning. Until recently, there have not been reliable methods for the study of social cognitive development in children, and even fewer studies have investigated social development in infancy.

Background

The Social Brain and Social Cognition

Figure 1

Brain Regions Associated with Social Processes



Note. From "Social Cognition in Scizophrenia," by M.F. Green, W. P. Horan, and J. Lee, 2015, *Nature Reviews Neuroscience,* 16(10), p. 625 (https://doi.org/10.1038/nrn4005). Copyright 2015 by Macmillan Publishers Limited.

Social functioning involves several complex cognitive processes and multiple brain regions. An extremely important social cognitive process is the experience of emotion. Studies have shown that several brain regions are responsible for the experience of emotion. These regions include the amygdala, anterior hippocampus, anterior insula, anterior cingulate cortex, brain stem nuclei, thalamus, ventral striatum, medial prefrontal cortex, posterior cingulate cortex, precuneus, lateral temporal cortex, and temporal poles (Green et al., 2015). The exact function of each of these regions in regard to the experience of emotion is still being investigated. The experience of emotions is vital to social cognition, but it is also important that emotions can be regulated. The regulation of emotions involves use of cognitive control strategies that engage the dorsolateral prefrontal cortex, ventrolateral prefrontal cortex, and the dorsomedial prefrontal cortex (see Figure 1; Green et al., 2015). The ability to experience, detect, and regulate emotions lay the groundwork for multiple social cognitive functions.

Perception of human faces also plays a key role in social cognition. The occipital face area, fusiform face area, and temporal regions like the superior temporal sulcus and superior temporal gyrus have all been implicated in the detection of human faces (Haxby et al., 2000). Each of these regions plays a specific role in the processing of faces. The occipital face area is critical for early detection and analysis of a face and relays information to the fusiform face area and superior temporal sulcus. The fusiform face area, located in the inferior temporal cortex, responds to faces more than any other stimuli, and it is critical for the detection of familiar faces. The fusiform face area is most sensitive to the stable, static aspects of faces (i.e., a person’s identity). Lesions isolated to the fusiform face area of the brain can lead to prosopagnosia, a condition that results in face blindness, or the inability to recognize familiar faces, including one’s own face (Kolb & Whishaw, 2015). The superior temporal sulcus has been implicated in visual processing of static aspects of human faces as well as dynamic aspects. Allison et al. (2000) hypothesized that the superior temporal sulcus is sensitive to implied motion and to any stimuli that signal the actions of another.

Though recognition of identity is important to social cognition, detection and understanding of dynamic changes in the face are absolutely critical to engage in meaningful social interactions (Haxby et al., 2000). As stated, the superior temporal sulcus is sensitive to both static and dynamic aspects of the human face. The superior temporal and middle temporal gyri have been implicated in visual processing of the dynamic aspects of the human face like facial expressions and eye gaze (Allison et al., 2000). The amygdala, superior temporal sulcus, orbitofrontal cortex, anterior cingulate cortex, ventral striatum, and multiple regions of the visual cortices have all been associated with the detection and recognition of human emotions (Utama et al., 2009). The ability to read human emotion and track another’s gaze are necessary skills that facilitate the understanding of the actions and intentions of another person and allow for two individuals to experience emotion together.

The ability to determine social and affective information from another’s tone of voice is vital to effective and meaningful communication. Schizophrenia is a disorder that results in deficits in social cognition (Green & Harvey, 2014). Neuroimaging studies including individuals with schizophrenia and healthy controls indicated that individuals with schizophrenia have difficulty identifying differences in pitch and rhythm related to emotional expression (Green et al., 2015). Deficits in affective speech perception in individuals with schizophrenia are characterized by hypoactivation in the left superior temporal and bilateral inferior frontal gyri (Green et al., 2015).

Another key social behavior is motor resonance. Motor resonance refers to a functional correspondence between the state in the motor system of an observer and that in the person actually carrying out the action (Zaki, 2014). Motor resonance is purported to be executed by the human mirror neuron system of the brain (Green et al., 2015). Neuroimaging studies with adults have identified the premotor cortex and inferior parietal regions as core regions for motor resonance (Green et al., 2005).

Theory of mind or mentalizing refers to the assumption that the behaviors of others are determined by their attitudes, desires, and beliefs (Frith & Frith, 2003). This ability likely requires a network of regions that operate together to infer the beliefs, desires, and attitudes of another. The medial prefrontal cortex, precuneus, temporoparietal junction, and superior temporal sulcus have been identified as core regions of interest in theory of mind, and several other regions may be engaged, depending on the specific task (Carrington & Bailey, 2009).

Studies have been carried out over the years that have elucidated social cognitive processes and the neuroanatomical regions that are responsible for social cognition in adulthood, but little is known about social cognition in children, and even less in the developing infant brain. The most important function of social cognitive processes, and arguably the reason that social cognition has evolved in humans is the ability to communicate with others. Communication is a complex process that integrates verbal and nonverbal social skills.

Social Communication

Communication involves the ability to understand others and express oneself verbally and without speech. Social communication refers to the ability to engage with others socially in a way that is appropriate and follows pragmatic rules of communication as well as receptive and expressive communication skills that are both verbal and nonverbal (Adams, 2005). Pragmatic language requires use of communication that fits its context (Bishop, 2000). Receptive skills include the ability to understand verbal and nonverbal communication, and expressive skills involve the ability to produce verbal and nonverbal communication (Hudry et al., 2010). Social communication involves the integration of several cognitive skills like language and attention within the context of social interactions and social functioning.

Fundamentals of Communication

Along with the ability to produce language using the appropriate motor sequences, the fundamental building blocks of spoken and written language include phonemes, individual units of sound that form words or parts of words, and morphemes, the smallest meaningful unit of a word that together form words (Liberman et al., 1974). Another important aspect of language is the mental lexicon, or the mental representation of what words sound like and what they mean (Marslen-Wilson et al., 1994). Syntax refers to the grammatical rules of language (Kolb & Wishaw, 2015). Phonemes, morphemes, the mental lexicon, and syntax are all fundamental to the expression and understanding of language, but as language serves a social function, it becomes more complex.

The meaning or understanding of a word or phrase is referred to as semantics (Kolb & Wishaw, 2015). In order to communicate, words must carry a meaning that can be understood and conveyed to others. One way to emphasize the meaning of words is through the use of varying tones of voice, or prosody (Cutler et al., 1997). Prosody can change the literal meaning of words and phrases by varying stress, pitch, and rhythm. At the highest level of language processing is discourse, the ability to string words together to produce a meaningful narrative. One must possess the ability to understand language and the use of changes in tone, as well as engage in discourse to produce language that can be used to communicate. For individuals with social communication deficits, it is likely that their ability to produce language is unimpaired. Instead, it is the integration of communication skills in a pragmatic, social context that is impaired, indicating that social language is something separate from fundamental language skills (Landa, 2000).

Pragmatic language involves the understanding of social aspects of language. Understanding the intention behind speech is an important part of pragmatic language. Individuals with pragmatic language impairment may be insensitive to innuendo or sarcasm and take a conversation too literally (Bishop, 2000). In order to successfully follow and contribute to a conversation, one must engage reciprocally, ensuring that one's conversation partner is also engaged and that one's responses are appropriate (Bishop, 2000). Pragmatic language is essential to the development of relationships formed from meaningful social interactions. Along with language and particularly pragmatic language, social communication also involves the use of nonverbal communication.

Nonverbal Communication. Nonverbal communication involves all of the ways in which we interact with others with or without the use of spoken language. Nonverbal communication includes facial expressions, eye gaze, and gestures, and these behaviors can be related to or independent of speech (Knapp et al., 2013). The integration of nonverbal and verbal behavior can add pragmatic meaning and context to a verbal statement. For example, a playful facial expression can indicate that an individual is using sarcasm (Knapp et al., 2013). Social communication disorders are characterized by pragmatic speech impairments, including deficits in verbal and nonverbal communication. Eye gaze is a fundamental nonverbal social communication behavior.

Awareness of where another is focusing their attention provides vital social information, and it can indicate where one should place his attention (Haxby et al., 2002). According to Haxby and colleagues (2002), averting gaze away from a social partner toward an object is an effective means of directing one's social partner to that same object. Attention to gaze is purported to develop very early in infancy, and for neurotypical individuals, gaze following in response to averted gaze is reflexive (Haxby et al., 2002; Nation & Penny, 2008). Eye gaze is a precursor to the development of the ability to integrate complex behaviors and cognitive processes to begin to infer the mental state of others, a critical social behavior (Nation & Penny, 2008). Because of the early emergence of these behaviors, thorough understanding of early neurodevelopment is critical to understanding social communication. The study of the emergence of nonverbal social communication skills has only begun to elucidate how social communication develops in the first years of life.

Development of Social Communication

There is a relative paucity of research aimed at elucidating the development of early social communication, even though processes like eye gaze are known to develop in infancy. As previously stated, social communication involves the integration of several complex cognitive skills like language and attention. Recent studies utilizing brain imaging methods have attempted to determine the neural underpinnings of social communication in infancy.

Early Brain Development. The first years of life are critical for the development of the brain, and growth is rapid. The brain develops from back to front, and the frontal cortices are the last to develop (Dunbar, 2014). Prenatal, perinatal, and postnatal environments are all extremely important for the developing infant brain. Prenatal exposure to toxins, poor nutrition, and stress have all been shown to have significant, negative effects on infant development that can persist through adulthood (Hwa-Froelich et al., 2012). From birth, infants are equipped with neurons that rapidly build associations through Hebbian learning (Hebb, 1949; Keysers & Perrett, 2004). This means that neurons that fire together become connected, and the more that they fire together, the stronger the connections between the neurons become (Munakata & Pfaffly, 2004). Early development is also a period of refinement of neural networks by pruning the associations that are weaker (Chechik et al., 1998). Early experiences contribute to the process of pruning, as the type and frequency of events leads to more or fewer associations. This means that early exposure to adverse events, stress, toxins, poor nutrition, etc., can lead to risk for poorer cognitive development and outcomes like poorer self-regulation and inhibition, problems sustaining attention, social skills deficits, difficulty with memory, and poor executive functioning skills (Elzinga et al., 2008).

Joint Attention. Joint attention refers to the ability to coordinate attention with a social partner, like looking at the same object, to share a common perceptual experience (Mundy & Newell, 2007). The ability to engage in this process begins in the first nine months of life (Mundy et al., 2010). Mundy's model of joint attention (2010) proposes that joint attention involves integration of self-referenced information (i.e., information about the physiological state of the body and the physical actions of the body), information about the other person's attention, and information about the common object or event that is shared. This process and continued practice with engaging in joint attention engages frontal, temporal, and parietal cortices, and over time, this network serves a social-executive function that facilitates efficient and smooth coordination of attention to external events and objects in social interactions (Mundy et al., 2010). According to Mundy and colleagues (2010), the ability to engage in joint attention lays the groundwork for the later emergence of symbolic thought and social cognition.

According to the parallel and distributed processing model (PDPM), joint attention can be divided into two independent but parallel networks: response to joint attention and initiation of joint attention (Mundy et al., 2010). Response to joint attention refers to the ability to follow a social partner's directed gaze, gesture, or movement of the head toward a particular object or event, whereas initiation of joint attention refers to the ability to use eye contact and gestures (i.e., pointing or showing) to establish shared attention with a social partner on a particular object or event (Mundy et al., 1992). Per the PDPM, response to joint attention emerges first at about six months of age, while initiation of joint attention develops between 8 and 10 months of age (Mundy et al., 2010). According to Mundy and colleagues (2000), the ability and frequency of initiation of joint attention primarily involves left frontal regions.

There are several theories as to why left frontal activation is associated with initiation of joint attention. One theory is that initiation of joint attention requires that the infant is able to hold information about the object or event of interest while also attending to and engaging with a social partner, cognitive skills that also engage frontal regions (Mundy et al., 2000). Another theory is that frontal functioning may be involved in the development of infants' ability to inhibit responses, which may be necessary in order to attend to one object or event of interest in favor of other stimuli present in the environment (McEvoy et al., 1993). Finally, left frontal activation has been implicated in the mediation of positive social motivation, including positive affect and approach behaviors at 10 months of age and may play a role in the development of initiation of joint attention in infancy (Mundy et al., 2000).

In all, social communication development in a typically developing infant is dependent upon the interaction of several aspects of social cognition, including the recognition of facial expressions and vocal tone, development of joint attention, and development of self-regulatory processes (Hwa-Froelich, 2015). Successful development of effective social communication skills is also reliant upon a rearing environment that is enriched with positive social interactions that are rich with spoken language and positive affect (Sroufe, 1997). Though infant behavior is largely driven by egocentric desires (i.e., having physical needs met), infants tend to prefer to interact with humans, rather than objects (Dawson et al., 2002). In the first year of life, infants engage in joint attention to share attention to an object or event with a social partner, laying the foundation for the ability to learn that others may have different thoughts, perspectives, and knowledge about those objects and events than they do (Hwa-Froelich, 2015).

Attention to Human Faces. From birth, infants attend to objects and faces in their environment. Within the first six months of life, infants begin attending to faces and following gaze (Mundy & Newell, 2007). These skills are extremely important and serve as vital precursors to social behavior. Gaze following is not only important for the recognition of facial expressions, but the ability to attend to human faces in infancy is linked to the ability to discriminate and selectively attend to sounds and mouth and tongue movements from the infant's native language between five and eight months of age (Mundy et al., 2000). The ability to shift attention to the face of another and track the attentional focus of that person is a vital task of early social communication development (Corkum & Moore, 1998; D'Entremont, 2000; Url & Development, 1998).

Processing of human faces includes perceptual processing and conceptual processing. Perceptual processing relies on subcortical pathways to detect upright human faces and direct attention to them (Hwa-Froelich, 2015). Tomalski and colleagues (2009) found that orientation to faces in newborns is facilitated by the subcortical visual pathway. The ability to detect dynamic changes in faces is vital to the recognition of facial expressions and engaging in joint attention. Conceptual processing of human faces involves reading and interpreting facial expressions. Before an individual develops language, the ability to recognize faces is largely bilateral. Over time, facial recognition becomes right lateralized, while language skills become left lateralized (Rossion et al., 2003).

Regulation of Attention. Regulation of attention, emotions, and behavior are social processes that are refined early in infancy. For example, an infant learns whether to engage with an object by looking to facial expressions and cues from caregivers (Mundy & Sigman, 2006). Young children are also able to self-monitor and regulate their behavior in the presence of a caregiver by looking to cues like facial expressions before the development of receptive and expressive language skills (Bronson, 2000). Once expressive and receptive language skills have become more refined, children have the ability to self-monitor and regulate their behavior, even in the absence of a caregiver by talking out loud to remind themselves of rules (Bronson, 2000; Hwa-Froelich, 2015; Vygotsky, 1986).

Posner (1994) described the emergence of attention regulation as being anterior-posterior, with the posterior component of the system developing before the anterior portion. An essential part of this posterior portion is thought to include the ability to orient to an object or event by shifting attention from an immediate focus, and this process is purportedly regulated by regions of the parietal cortex, as well as regions in the midbrain and thalamus (Posner & Petersen, 1990). Mundy and colleagues (2000) found that response to joint attention was related to left parietal activation and right parietal deactivation in 14-month-old infants measured by electroencephalogram (EEG) and posited that the activation may be related to infants redirecting attention when engaged in response to joint attention, thereby activating the posterior portion of the attentional system proposed by Posner and colleagues.

Infant Neuroimaging. Developmental science has been interested in the study of the infant brain for decades, but it has been limited due to the nature of the imaging techniques that were available. Neuroimaging allows for the investigation of brain-behavior relationships and in conjunction with behavioral data, can elucidate the ways in which stimuli are being processed (Wilcox & Biondi, 2015). It can be particularly challenging to utilize neuroimaging techniques with infants because of increased motion and an inability to tolerate certain methods (i.e., fMRI) while awake. As such, sedation is often necessary to acquire imaging data, which results in a reliance on structural rather than functional data to advance the field in our understanding of these developmental brain-behavior relationships (Raschle et al., 2012).

Magnetic resonance imaging (MRI) has provided valuable structural data of infant brains that are critical for the localization of brain regions at various stages of growth and development during infancy. Unlike the adult brain, the infant brain is rapidly growing and changing, and localization of regions of interest rapidly changes as well. MRI images of infant brains have led to the development of infant brain atlases that assist with co-registration for functional methods like EEG and magnetoencephalography (MEG). Co-registration is the process by which anatomical brain regions are located in individual subjects by aligning them with appropriate brain atlases (Huhdanpaa et al., 2014).

MEG is an electrical functional imaging technique that is noninvasive and has excellent temporal resolution. Use of MEG with infants is relatively limited due to the small number of MEG labs in the nation, the expense of using this methodology, and the need for participants to remain very still during the imaging (Cheour et al., 2004). EEG is also a functional imaging technique that is noninvasive. EEG is more commonly used with infants because it is widely accessible, relatively inexpensive, and it is sometimes portable (Spitzmiller et al., 2007). Its portability and less stringent guidelines regarding motion make it better for use with paradigms that are more ecologically valid. Unfortunately, EEG has poorer spatial resolution than MEG (Cheour et al., 2004).

Functional Near Infrared Spectroscopy (fNIRS). FNIRS is an imaging method that has been used since the early 1990s ((Ferrari & Quaresima, 2012). It utilizes light in the near-infrared range (700-900 nm) to measure changes in optical properties of the cortex of the brain (Bunce et al., 2006). Quasi-infrared light is released by emitting optodes at the scalp that travel through the skull and into the brain while the test subject is engaged in an activity. Detecting optodes in the cap capture the varying light intensity resulting from the concentration change of chromophores (intravascular oxy-Hb [HbO_2] and deoxy-Hb [HbR]), following a banana-shaped path back to the surface of the skin (Bunce et al., 2006). FNIRS indirectly measures cortical activity on the basis that vascular response and neural activation are tightly coupled. Studies have illustrated that neural activity and hemodynamic response maintain a linear relationship, suggesting that changes in hemodynamic response provide a good marker for assessing neural activity (Arthurs & Boniface, 2003).

FNIRS is a useful imaging technique for infant work because it is safe, noninvasive, and in some cases, is portable, allowing for studies that are more ecologically valid (Bunce et al., 2006). Like EEG, fNIRS can be conducted with infants who are awake, and it can measure brain activation of infants while they are engaged in a task, as it is only necessary to wear a cap, as opposed to entering a machine like fMRI. FNIRS has better spatial resolution than EEG, and it has better temporal resolution and is less expensive than fMRI, and fNIRS is easier to operate than fMRI (Wilcox & Biondi, 2015).

Current Literature. A very limited number of studies have investigated nonverbal social communication in infants, in particular, the neural underpinnings of nonverbal social communication development. In adults, direct gaze is thought to modulate activity in the superior temporal sulcus, the anterior rostral medial prefrontal cortex, and the amygdala (Senju & Johnson, 2009). In a study with adults using MRI, Cavallo and colleagues (2015) found that mutual gaze with another resulted in activation in left-lateralized areas typically associated with production and comprehension of language and actions of others like the inferior frontal gyrus, the premotor cortex, the supplemental motor area, and the anterior rostral medial prefrontal cortex, while averted gaze was associated with activation in the anterior cingulate cortex and the ventral striatum (Cavallo et al., 2015).

An infant EEG study with 7-month-olds found that infants at this age show differential ERPs to tones of voice congruent versus incongruent with facial affect, demonstrating that 7-month-olds have the ability to integrate emotional information and have the ability to recognize affect in faces and tones of voice (Grossmann et al., 2006). In an EEG study of orienting and attention to happy and sad faces in infants 3 to 13 months of age, results showed that the right hemisphere plays an important role in modulating attention related to self-regulation (Martinos et al., 2012). This is in direct contrast to Mundy (2000) who identified the left hemisphere as being important for gaze following in 14-month-olds. Contrasted findings between these two studies highlight how little we know about social communication at varying stages of development in infancy.

A study using diffusion tensor imaging (DTI) by Elison and colleagues (2013) found that 9 to 10 months of age may be a period of particular individual variability in regard to response to joint attention, consistent with previous reports that response to joint attention is developing around this time. They also found that white matter connecting the right ventral medial prefrontal cortex, amygdala and temporal cortex at six months of age was predictive of differences in response to joint attention at nine months of age (Elison et al., 2013). An optical imaging study using near-infrared spectroscopy found that response to joint attention results in activation in the right and left frontal regions of the brain when compared to a non-joint attention condition in neurotypical adults (Zhu et al., 2009).

The prefrontal cortex, and more specifically, the medial prefrontal cortex, is a region of the brain that has been historically associated with adult social cognition, but it may also play an important role in social cognition in infancy (Grossmann, 2013). Tzourio-Mazoyer and colleagues (2002) found activation in the right medial prefrontal cortex in 2-month-old infants when they were shown human faces. This activation was only present in response to being shown human faces. Other objects did not result in the same activation. A study by Grossmann and colleagues (2008) using fNIRS found activation in the superior temporal cortex, as well as the medial prefrontal cortex, in 4-month-old infants in response to establishing eye contact with a human-life character when viewing a video where the human-like characters established eye contact or averted gaze. Another study by Grossmann and colleagues (2010) found that infants at 5 months of age recruit similar brain regions as adults when engaged in joint attention with a social partner and a specific object, namely a dorsal region of the right prefrontal cortex.

A fNIRS study of 5-month-old infants’ ability to determine whether a virtual social partner has followed their gaze to an object of interest indicated that infants are sensitive to whether their gaze has been followed, and when their gaze is followed, left prefrontal regions of the brain are activated (Grossmann et al., 2013). This finding is consistent with a previous study by Mundy and colleagues (2000) that also identified left frontal regions as being associated with gaze following.

Though there are consistencies among some imaging studies that identified left frontal activation in response to gaze following, there are other studies that found right frontal activation or both left and right frontal activation (Elison et al., 2013; Grossmann, 2010, 2013; Martinos et al., 2012). Neuroimaging studies aimed to elucidate neural processes underlying social communication in infancy are equivocal and vary in regard to age and stages of development in infancy. A clearly defined timeline and path to development of foundational social communication skills has not yet been achieved. With that, the aforementioned neuroimaging studies included typically developing infants. Even less is known about the development of social communication skills in infants at risk for atypical development.

High-Risk Development. As previously stated, little is known about the development of important social communication processes in infancy. Currently, diagnosis of disorders characterized by impaired social functioning like schizophrenia, ASD, and ADHD is reliant upon the emergence of aberrant social behaviors, which become evident later in childhood. Altered neural network development is thought to precede social behavioral deficits (Bedford et al., 2012), so a thorough characterization of early neural correlates of later social development is needed to provide a basis for early identification and intervention of abnormal neurodevelopment for those at risk for social disorders.

Perinatal Risk Factors. Over the last two decades, incidence of preterm and low birth weight infants has increased, in part due to the use of fertility treatments that have led to higher rates of multiple births (Kulkarni et al., 2017). Infants born preterm and low birth weight are at risk for a series of neurodevelopmental disorders, cognitive deficits, and social-emotional problems (Arpino et al., 2010). According to Arpino and colleagues (2010), preterm and low birth weight infants are also more likely to have problems with attention that persist over time.

In a study that followed up on very low birth weight infants, incidence of a later ASD diagnosis was nearly four times the rate in the general population (i.e., 1 in 21 versus 1 in 88) (Mohammed et al., 2016). Perinatal risk factors like preterm birth, low birth weight, and small for gestational age have been linked with higher incidence of intellectual disability and ASD (Schieve et al., 2015). Another investigation into perinatal risk factors also found that preterm birth and low birth weight status were related to later onset of ASD (Lampi et al., 2012). Lampi and colleagues (2012) suggested that prematurity and very low birth weight status (< 1500 g) may have similar developmental antecedents to ASD like exposure to infection, prenatal insults, and genetic predisposition.

In a study that followed up on infants born term and preterm at six and 18 months (age corrected for the preterm infants), researchers found that preterm infants had poorer performance on the personal-social domain of a cognitive measure (Forcada-Guex et al., 2006). Within the preterm group, Forcada-Guex and colleagues (2006) reported a more difficult, less responsive temperament was related to poorer social functioning as well as language functioning, suggesting that temperament likely plays an important role in the development of social communication skills.

Behavioral Indicators of Risk. For children with autism spectrum disorders (ASD), disorders characterized by social communication deficits and restricted and repetitive behavior, disruptions in the ability to follow another’s gaze can be an early marker of those at risk for later onset of ASD. Jones and Klin (2013) used eye-tracking technology to investigate differences between patterns of eye fixation for children aged 2 to 24 months at high risk (defined by having a biological sibling with ASD) and low risk for ASD. They found that initially, all infants in the study showed similar patterns of fixation on the eyes of others, but between 2 and 6 months, the children later diagnosed with ASD exhibited a decline in eye fixation, indicating that the switch from subcortical processing of faces in early infancy to later more cortically reliant processing of faces may pose a problem for those at risk for ASD (Jones & Klin, 2013).

Rationale for the Current Study

Eye gaze following and joint attention are important precursors to the development of symbolic thought and language. Despite the vital role of gaze processing and joint attention in the development of social communication, few investigations have examined gaze-processing and its neural underpinnings in infancy, and no studies have examined this process in low birth weight, high-risk infants. Recent studies using fNIRS suggest that typically developing infants at 4 and 5 months of age display similar activation in temporal and prefrontal cortices, as observed in adults while engaged in an eye gaze and joint attention paradigm (Grossmann et al., 2008). FNIRS investigations have also demonstrated activation in left PFC of 5-month-old infants in response to eye gaze with a social partner (Grossmann et al., 2008). These findings suggest early specialization of the neural network involved in the perception of social communication cues. Identification of early specialization of this network could assist in the development of methods for detecting aberrant network activity in infants at risk for the development of social communication impairment before the emergence of impaired social behavior. Studies of eye gaze processing and joint attention have not yet explored relationships between cortical activation and performance on developmental measures, or with social development over time.

In this study, we sought to replicate and extend the findings by Grossman and colleagues (2008) with typically developing and high-risk nine-month-old infants using fNIRS. The paradigm, published by Grossmann and colleagues (2008), includes social (i.e., human-like figures) and nonsocial (i.e., nonhuman figures like a train) stimuli. When social stimuli are presented, the human-like figures either avert or maintain their gaze on the infant. Because aspects of joint attention develop between 6 and 10 months of age, this study examined gaze processing as a proxy for joint attention during the emergence of this important social milestone, as well as examined brain-behavior relationships between cortical activation in response to a joint attention paradigm and developmental measures.

Aims and Hypotheses of the Current Study

The current study included both retrospective data and a subset of participants who were recruited and sought to examine difference in regional cortical activation, as measured by oxygenated hemoglobin (HbO_2) concentration, during a nonverbal social communication task (i.e. response to gaze) in high- and low-risk infants measured with fNIRS and relationships between HbO_2 concentration and developmental and behavioral functioning.

Aim 1: This first aim of the study attempted to extend the work of Grossmann and colleagues (2008) and examine differences in HbO_2 concentration between high- and low-risk 9-month-old infants in response to social and nonsocial stimuli as well as between mutual and averted gaze conditions.

Hypothesis 1: It was hypothesized that there would be significant differences in regional cortical activation in response to the social compared to nonsocial condition in low-, but not high-risk infants.

Hypothesis 2: It was hypothesized that low-risk infants would demonstrate higher HbO_2 concentration in right frontal and posterior temporal regions in response to the social conditions, as opposed to the nonsocial, control condition.

Hypothesis 3: It was hypothesized that there would be a significant difference in HbO_2 concentration between mutual and averted gaze in the low-, but not high-risk infants. Consistent with Grossman et al. (2008), it was hypothesized that the low risk infants would demonstrate increased HbO_2 concentrations in right frontal and posterior temporal regions in response to the mutual gaze condition. It was hypothesized that low-risk infants would show higher HbO_2 concentration in right posterior temporal rather than frontal regions during the averted gaze condition.

Aim 2: The second aim of the study was to examine differences in development, temperament, and social competence between high- and low-risk infants as demonstrated on the Mullen Scales of Early Learning (MSEL; Mullen, 1995) and Infant Behavior Questionnaire-Revised (IBQ-R; Gartstein & Rothbart, 2003) at 9 months of age, and the Brief Infant Toddler Social Emotional Assessment (BITSEA; Briggs-Gowan et al., 2004) at 12 months of age.

Hypothesis 4: It was hypothesized that the high-risk infants would demonstrate lower extraversion/surgency and orienting/regulation and higher negative affectivity on the IBQ-R, overall lower developmental quotient on the MSEL at 9 months, and poorer social competence and more reported behavioral problems on the BITSEA at 12 months.

Aim 3: The third aim of the study was to examine the relationships between HbO_2 concentration in the aforementioned regions of interest and performance on the MSEL and parent/caregiver reports of temperament and behavior (IBQ-R and the BITSEA).

Hypothesis 5: Right frontal and posterior temporal HbO_2 in response to the social stimuli will be positively correlated with overall higher developmental quotient on the MSEL, higher extraversion/surgency, higher orienting/regulation, and lower negative affectivity on the IBQ-R, and better social competence and fewer social problems on the BITSEA.

Aim 4: The fourth aim of the study was exploratory and examined relationships between regional HbO_2 concentration at 9 months and social functioning, as measured with the BITSEA at 12 months in high- and low-risk infants.

Methods

The current study was quasi-experimental and investigated differences between two groups: infants at low- and high-risk for the development of social communication problems. Participants for this study included infants who are from both a retrospective cohort and a subset was enrolled prospectively.

Participants

Following institutional review board approval, caregivers and infants were either recruited from the obstetrics registry (OR) or from the neonatal intensive care unit (NICU) from the University of Michigan (see Appendix A). Low-risk infants were recruited from the OR in Psychiatry while the high-risk cohort were recruited from the NICU. There were initially 24 infants recruited and enrolled in the low-risk sample. Data for 10 of the infants were not used in these analyses due to an inability to tolerate the procedure, substantial motion artifact, or poor data quality. The final sample consisted of 12 infants (seven females) aged between 38 and 42 weeks at the time of the study (M = 40.85; SD = 1.46). All low risk infants were born full-term (37-42 weeks gestation) and at a normal birth weight (> 2500 g). No participating caregivers had a history of prenatal or intrapartum complications, and no infants had any brain injuries, neurological illnesses (e.g., seizures) or known genetic disorders. Furthermore, infant participants did not have any first or second-degree relatives with a diagnosis of ASD or any other social communication disorder, therefore suggesting low risk for ASD, a disorder characterized by aberrant social behavior.

The high-risk sample consisted of five infants (three female) aged between 39-44 weeks (M = 42.4; SD = 2.0) at time of study enrollment, born preterm (27-34 weeks gestation), but without any history of intraventricular hemorrhage (IVH) seen by ultrasound (grades III and IV), bronchopulmonary dysplasia (BPD) (on oxygen supplement at 28 days), retinopathy of prematurity (ROP), or sepsis (March of Dimes, 2014). The high-risk sample did not include any infant participants with first or second-degree relatives with a diagnosis of ASD or any other social communication disorder.

Recruitment

Low-risk infants were recruited through the University of Michigan OR. The OR study coordinator sent names and contact information of caregivers with infants between the ages of 6 and 12 months to the study team. An identified graduate assistant (doctoral fellow) then contacted the potential recruits via email or phone to set up a phone screening and to further explain the study. The phone screen included eligibility questions to determine whether the infant met inclusion criteria for the study (see Appendix B and C). If the child passed the screening and the parent/caregivers remained interested in the study, the caregiver/infant dyad was scheduled for the study.

High-risk infants were recruited from the University of Michigan NICU follow-up clinic. The NICU Clinical Care Coordinator distributed flyers to caregivers with infants who were attending follow-up appointments around 6 months of age (see Appendix D). If a caregiver indicated that she was interested in participating in the study, the caregiver’s name and contact information were sent to the doctoral fellow on the project. The fellow contacted the potential recruits via email or phone to conduct the phone screen and to further explain the study (see Appendix E and F). The phone screen included questions to determine whether the infant met inclusion criteria for the study. If the child passed the screening and the parent/caregivers remained interested in the study, the caregiver/infant dyad was scheduled for the study.

Informed Consent

The testing sessions took place at the University of Michigan Center for Human Growth and Development. Sessions were scheduled for two hours to complete the informed consent, fNIRS imaging, and developmental testing. Parents/caregivers were met in a waiting room to complete the informed consent (see Appendix G). A research assistant explained the purpose of the study, study procedures, potential risks/benefits of participation, and ensured them that they could discontinue at any time without penalty. Parents/caregivers were given a subject payment of $35 dollars for participating in the study.

Behavioral Assessment

Once informed consent was obtained, infant participants underwent a neurodevelopmental assessment and fNIRS optical brain imaging with a gaze processing paradigm. Caregivers also completed questionnaires about their infants' development at 9 and 12 months.

Developmental

A trained research assistant or a PhD level neuropsychologist assessed the infants' developmental functioning using the Mullen Scales of Early Learning (MSEL; Mullen, 1995). The MSEL is a standardized test for children starting at birth to age 5 years, 3 months. The MSEL yields T-scores and age equivalents for five domains, including visual reception, gross motor, fine motor, receptive language, and expressive language. Test-retest reliability for the MSEL is reported to be 0.85 to 0.96 for the gross motor, visual reception, and expressive language domains for infants aged 1 to 24 months and below 0.85 for receptive language and fine motor (Mullen, 1995). Internal reliability ranges from 0.75 to 0.83 for the domains, and was reported to be 0.91 for the overall developmental score (Mullen, 1995). Inter-rater reliability ranges from 0.94 to 0.98 (Mullen, 1995).

Infant Temperament

To assess infant temperament and social-emotional development at 9 months, the Infant Behavior Questionnaire- Revised (IBQ-R; Gartstein & Rothbart, 2003) was completed by caregivers (see Appendix H). The questionnaire is comprised of 191 items with a 7-point Likert scale, in which 0 is *not applicable*, 1 is *my infant never engages in the behavior*, and 7 is *my infant always engages in the behavior*. The IBQ-R yields 14 subscales and three higher-order factors of Surgency/Extraversion, Negative Affectivity, and Orienting/Regulation. Gartstein and Rothbart (2003) reported that inter-rater reliability for the subscales on the IBQ-R ranges from 0.70 to 0.90 for infants aged 3 to 9 months of age. Convergent validity of the IBQ-R has yet to be investigated, and exploration of discriminant validity indicated that there are intercorrelations between the temperament constructs, but that the inter-correlations were expected given that they occurred between constructs that have some overlap (Gartstein & Rothbart, 2003).

Brief Infant-Toddler Social Emotional Assessment

To assess social emotional problems and competencies, the Brief Infant-Toddler Social Emotional assessment, Parent Form (BITSEA; (Briggs-Gowan et al., 2004) was completed by caregivers at the 12-month follow-up over the phone (see Appendix I). The BITSEA is a standardized norm referenced instrument that was developed to examine social emotional problems and competencies of children 12 to 35 months, 30 days. The BITSEA yields Problem and Competence total scores. Investigation of the sensitivity of the BITSEA to diagnosis of ASD revealed that 100% of children with a diagnosis of ASD had BITSEA competence scores at or below the 15th percentile, and specificity of the BITSEA problem score was 97% at the 25th percentile (i.e., the cut point for *Possible Problems*) for the norm sample aged 12 to 35 months (Briggs-Gowan et al., 2004). Test-retest reliability for the problem and competence scores were .92 and .82, respectively, and inter-rater reliability for the problem and competence scores were .74 and .63, respectively for the norm sample aged 12 to 35 months (Briggs-Gowan et al., 2004).

Demographic Questionnaire

Infant caregivers also completed a demographic questionnaire as part of the PediaTrac™ Nine Month Module (see Appendix J). PediaTrac™ is an online questionnaire that includes questions about pregnancy, birth, caregiver characteristics, the infant's home environment, and development at nine months.

fNIRS Optical Imaging

To investigate cortical activation during the gaze following paradigm, infants underwent fNIRS imaging with a continuous wave fNIRS system (TechEn Inc., Boston, MA). FNIRS uses low power, near-infrared lights embedded into a cap to measure the neuroactivation coupled oxygen level in the brain. The international 10-10 system (Chatrian et al., 1985) was used to assist fNIRS probe co-registration. Co-registration is the process by which anatomical brain regions are located in individual subjects by aligning them with appropriate brain atlases (Huhdanpaa et al., 2014). Received signals from detectors are transferred to HOMER2, a software that was developed to examine oxygenated and deoxygenated hemoglobin concentration changes in the brain using a series of MATLAB scripts.

Gaze Processing Paradigm

The paradigm that was utilized is a replication of the design published by Grossmann and colleagues (2008). Two experimental conditions were developed: social (human) and nonsocial (animated non-social scenes). The human condition was generated with Poser (*Poser Digital Hybrid*, 2013). The paradigm consisted of several five-second long clips showing photorealistic, human-like cartoons either averting or maintaining their eye gaze on the infant (see Figure 2), who watched on a computer monitor while seated on his/her caregiver's lap.

In both the averted and mutual gaze conditions, the human animations were shown with their heads oriented 20 degrees to the left or to the right. In the mutual gaze condition, the human-like cartoon's face was shown on the screen for 1000 ms, then he/she moved his/her eyes towards the infant (100 ms gaze shift), without change in head orientation, where he/she remained for 900 ms. The cartoon's expression was then changed from neutral into a closed-mouth smile plus eyebrow raise within 100 ms and then the person continued smiling for 900 ms. The facial expression returned to the neutral position (1000 ms) followed by a second eyebrow raise and smile (duration 1000 ms) while gaze direction was held constant. The averted gaze condition differed from the mutual gaze condition in that the person on the screen moved his/her eyes away from (averted) rather than towards (mutual) the infant. The human-like cartoons were comprised of male and female, and child and adult variations. The faces presented subtended to $38X25^{o}$ and each eye subtended to $3X5^{o}$.

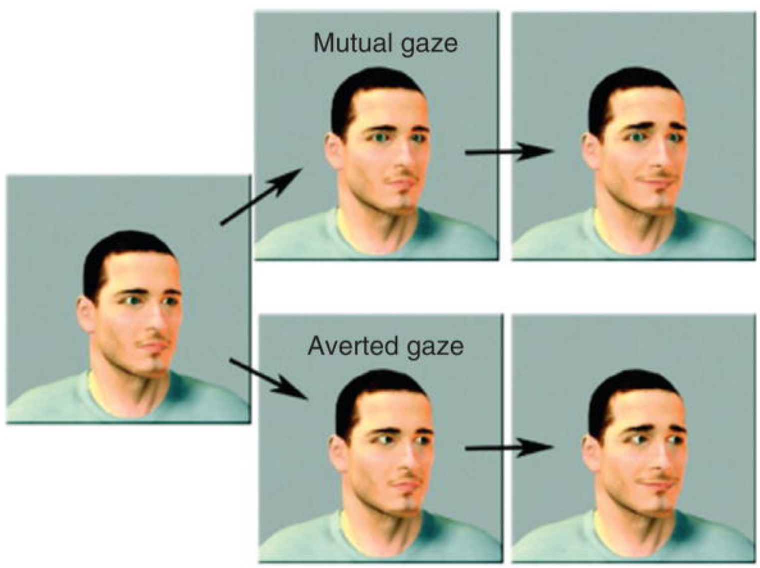
Animated non-social stimuli were interspersed between the social, human cartoon stimuli in order to increase attention to the task and to serve as a control condition. The control animations consisted of non-social moving stimuli, such as an airplane or train that engendered vertical or horizontal gaze shifts similar to those elicited by the human-like cartoons. Each 15-second trial consisted of a 5-second-long social condition (averted or mutual gaze, child or adult, male or female) that was followed by a 10-second long non-social, control condition (see Figures

2 and 3). The social face stimuli conditions were presented in a pseudo-random order, with no more than two presentations of the same condition (i.e., mutual or averted) in a row.

The duration of the paradigm was 5 minutes. The paradigm was shown on a 23-inch monitor at a distance of approximately 100 cm. Infant participants wore the fNIRS cap while sitting on the lap on their caregiver for the duration of the paradigm. Stimuli were presented via E-Prime 2.0 (Psychology Software Tools, Inc., Sharpsburg, PA). A video camera was utilized to capture the infant's face and record his/her gaze and behavior through the duration of the task.

Figure 2

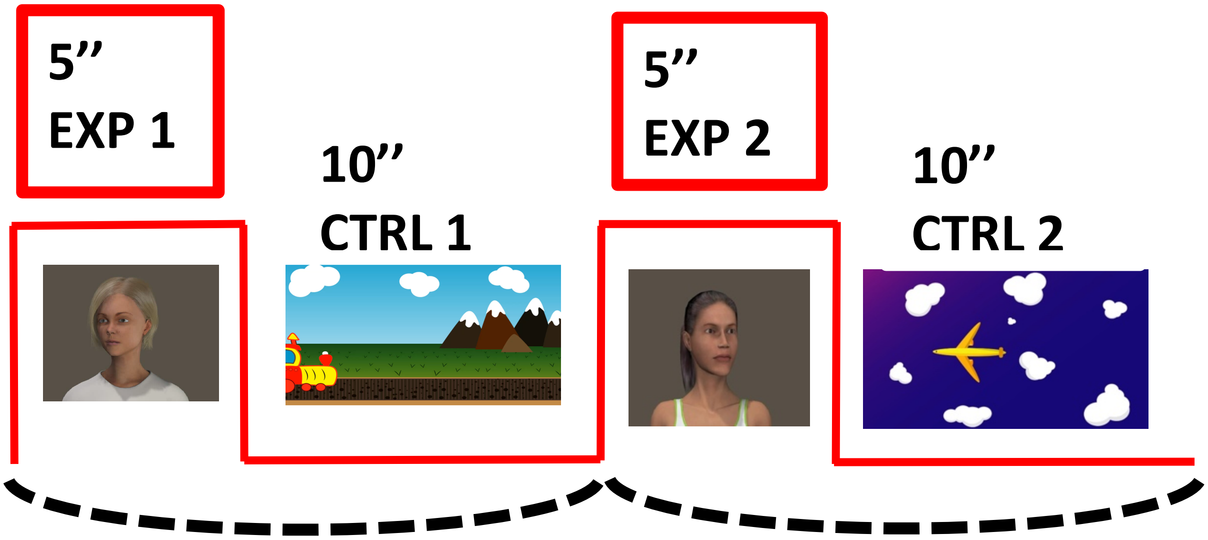
Human-Like Cartoon Maintaining or Averting Gaze



Note. From "Early Cortical Specialization for Face-to-Face Communication in Human Infants," by T. Grossmann, M.H. Johnson, S. Lloyd-Fox, A. Blasi, F.Deligianni, C. Elwell, & G. Csibra, 2008, *Proceedings of the Royal Society of London B: Biological Sciences*, *275*(1653), p. 2804 (https://doi.org/10.1098/rspb.2008.0986). Copyright 2008 by The Royal Society.

Figure 3

Schematic of the Experimental Paradigm



Note. From "Early Cortical Specialization for Face-to-Face Communication in Human Infants," by T. Grossmann, M.H. Johnson, S. Lloyd-Fox, A. Blasi, F.Deligianni, C. Elwell, & G. Csibra, 2008, *Proceedings of the Royal Society of London B: Biological Sciences*, *275*(1653), p. 2804 (https://doi.org/10.1098/rspb.2008.0986). Copyright 2008 by The Royal Society.

Imaging Data Acquisition and Extraction

The data were acquired using wavelengths of 690 nm and 830 nm, which are considered to be the optical window for studying cognitive functioning in humans (León-Carrión & León-Domínguez, 2012). The sampling rate was 50 Hz, which determines the range of frequencies that are measured during the imaging. E-prune channels is a pre-processing option in the HOMER2 software that allows for automatic exclusion of a channel if it is too noisy due to motion artifact or oversaturation. Parameters for channel exclusion were set at a minimum threshold of 80 and a maximum of 120.

A custom-built array and headgear with thirty source-detector pairs was used to measure HbO_2 and HbR in frontal and temporal cortices (see Figures 4 and 5). Grossmann and colleagues (2008) also used a custom-built array that had probe locations over the frontal and temporal cortices. Since they identified areas of activation in these regions, and research has indicated that these are regions implicated in social cognition in adults, our probe configuration was also designed to capture activation in the frontal and temporal cortices. There were eight emitters and 16 detectors. The inter-optode distance was set to 2.5 cm, just slightly larger than the Grossmann and colleagues (2008), whose inter-optode distance was 20 cm. This increased distance was to account for a larger head circumference at 9 versus 4 months of age. Eighteen channels (source-detector pair) covered the frontal cortex (FP) and six channels covered the left and six covered the right temporal cortex. Because MRI images of the infants' brains were not acquired, co-registration of anatomical regions could not be established. To address this, the International 10-10 System for EEG electrode placement, was used to determine anchor points that separated the frontal and temporal regions (Hosseini et al., 2015). T3 and T4 (see Figure 6) were used to differentiate frontal and temporal regions. The probe configuration resulted in four regions of interest (source-detector pair locations): left and right frontal, left and right temporal. We also conducted analyses which distinguished anterior compared to posterior temporal cortices (i.e., two anterior temporal pairs and four posterior temporal pairs for each hemisphere).

Prior to the start of imaging data collection, measurements of the head circumference, lateral semi-circumference from ear to ear, and the semi-circumference from nasion to inion were taken. Measurements from the low-risk infants revealed an average head circumference of 45.9 cm (*SD* = 1.0 cm), and measurements from the high-risk infants had an average head circumference of 42 cm (*SD* = 1.0 cm). Photographs of frontal, left, and right views were taken after the fNIRS headgear was placed. The photographs were used to record the positioning of the fNIRS headgear relative to the nasion, ears, and other fiducials. Information from the head measurements and photographs as well as measurements that correspond to the International 10-10 System for EEG electrode placement were used to approximate the cortical regions underlying the channels that revealed significant responses. Channel 29 is positioned approximately over T4, equal distance between channels 25 and 1 lies over FP, and channel 5 is positioned over T3. The distance between Source D and FP was 1.5 cm. To identify if the probe/optode array has moved during testing, the positions of the T3 and T4 were inspected before and after data acquisition.

Figure 4

Infant Participant Wearing Our Custom-Built Cap During Imaging Session

Figure 5

Custom Probe Configuration

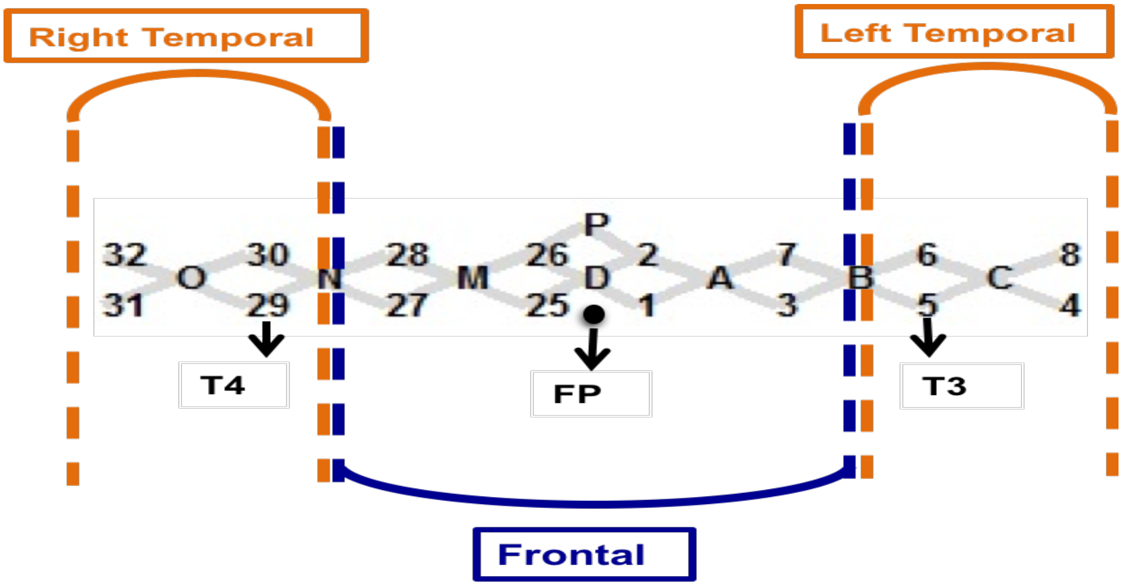
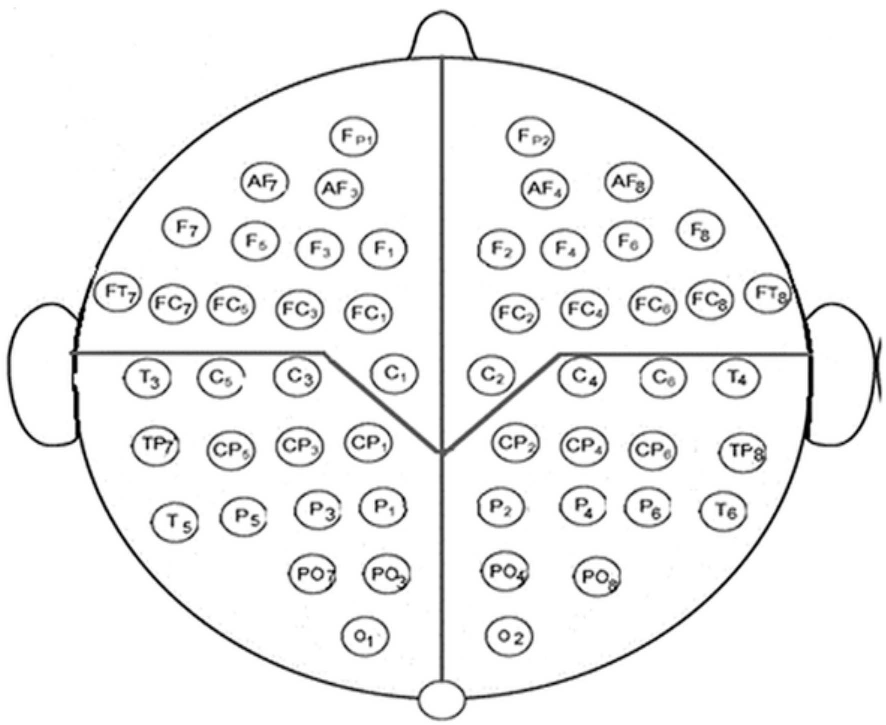


Figure 6

International 10-10 System for EEG Electrode Placement



Note. EEG = Electroencephalogram. From "Event-Related Brain Potentials During Picture Naming, Using Early and Late Acquired Words," S. H. Hosseini, A. R. Khatoonabadi, H. Dadgar, M. Saadati, & G. H. Zade, 2015, *Middle East Journal of Rehabilitation and Health*, 2(2), p. 3 (https://doi.org/0.17795/mejrh-26717). Copyright 2015 by Semnan University of Medical Sciences.

The fNIRS data was processed using NIRS-toolbox at individual level (Santosa et al., 2018). Finite impulse response (FIR) basis function was used to deconvolve the data collected from each fNIRS data and extracted the estimated hemodynamic responses for the social (averted and mutual conditions) and non-social conditions. Briefly, we first downsampled the signal to 2 Hz. Then we modeled a series of 30 distinct unit-magnitude impulse, each of which was delayed in time by 1 sec (FIR model). We used autoregressive, iteratively reweighted least squares in the toolbox to estimate model coefficients (Barker et al., 2013). The FIR basis model makes no assumptions about the shape of the hemodynamic response function (HRF)-the weight applied to each basis function can take any value–which allows the model to capture a wide range of HRF. The dependent variables for the analysis were extracted beta values for the HbO_2 peak concentration at each channel location.

Video Coding and Data Rejection

To assess attention to the visual stimuli, infants were videotaped throughout the duration of the fNIRS assessment. Non-looking times were coded off-line and extracted using Datavyu, a Java-based video coding and data visualization tool. The videos were coded by two raters who were blind to the coding results of the other rater. Based on a study with 4-month-old, typically developing infants, trials were considered valid if the infants attended to the task for a minimum of 60% of the entire duration of a trial (Lloyd-Fox et al., 2015). The data were examined to determine appropriate looking time for the study sample, as 9-month-old infants are significantly more mobile than 4-month-olds, and this study includes high risk infants.

Data Analysis

The current study is quasi-experimental.

Hypothesis 1: It was hypothesized that there would be significant difference in HbO_2 concentration in response to the social compared to nonsocial condition in low-, but not high-risk infants.

Hypothesis 1 Methods: Multilevel linear modeling was planned to investigate differences in HbO_2 concentration in response to the social compared to the nonsocial condition in the low- and high-risk infants.

Hypothesis 2: It was hypothesized that low-risk infants, but not the high-risk infants, would demonstrate higher HbO_2 concentration in right frontal and posterior temporal regions in response to the social conditions, as opposed the nonsocial, control condition.

Hypothesis 2 Methods: Multilevel linear modeling was planned to examine statistically significant changes in HbO_2 concentration in the social and nonsocial conditions over the hemispheres (right vs. left) and lobar regions (frontal vs. temporal).

Hypothesis 3: It was hypothesized that there would be a significant difference in regional HbO_2 between mutual and averted gaze in the low-, but not high-risk infants. Consistent with Grossmann et al. (2008), it was hypothesized that the low-risk infants would demonstrate increased HbO_2 concentration in right frontal and posterior temporal regions in response to the mutual gaze condition. It was hypothesized that low risk infants would show greater activation in right posterior temporal, rather than frontal regions during the averted gaze condition.

Hypothesis 3 Methods: Multilevel linear modeling was utilized to examine statistically significant changes in HbO_2 concentration in the mutual and averted conditions over the hemispheres (right vs. left) and lobar regions (frontal vs. temporal).

Hypothesis 4: It was hypothesized that the high-risk infants would demonstrate lower extraversion/surgency and orienting/regulation, and higher negative affectivity on the IBQ-R, overall lower language skills on the MSEL at 9 months, and poorer social competence and more reported behavioral problems on the BITSEA at 12 months.

Hypothesis 4 Methods: Mann-Whitney U tests were used to examine group differences in performance on the MSEL and IBQ-R at 9 months and the BITSEA at 12 months in the low- and high-risk groups.

Hypothesis 5: It was hypothesized that right frontal and posterior temporal activation in response to the social stimuli would be positively correlated with overall higher language on the MSEL, higher extraversion/surgency, higher orienting/regulation, and lower negative affectivity on the IBQ-R, and better social competence and fewer social problems on the BITSEA.

Hypothesis 5 Methods: Kendal Tau correlation coefficients were calculated to examine relationships between HbO_2 concentration and performance on the MSEL, IBQ-R and BITSEA.

Results

Behavioral Data

Results and mean differences on the Mullen Scales of Early Learning, Infant Behavior Questionnaire-Revised, and Brief Infant Toddler Social Emotional Assessment are noted in Table 1. On subscales of receptive and expressive language of MSEL, infants in the low-risk group performed in the average range while infants in the high-risk group performed in the low average range. Similarly, the low-risk group performed in the average range or higher on all of the scales of IBQ-R and BITSEA. The high-risk group demonstrated high average negative affect, as measured by the IBQ-R and high average problem behaviors on the BITSEA, suggesting more negative affect and problem behaviors in high-risk infants.

A Mann-Whitney test was conducted to examine differences between the high- and low-risk groups on the MSEL and caregiver reported behaviors on the IBQ-R and BITSEA. Given the small sample size of the high-risk group, in addition to conducting non-parametric testing, effect sizes were also computed to examine the magnitude or clinical significance of the difference. The high-risk group exhibited poorer receptive language ($U = 9.00$, $p = .03$, $d = 1.47$) and expressive language ($U = 8.00$, $p = .02$, $d = 1.27$) than the low-risk group, both with large effect sizes. On the IBQ-R, high-risk infants were reported to display more negative affect ($U =$

25.00, $p = .04$, $d = 1.59$) than the low-risk group, again with a large effect size. Finally, the high-risk group were reported to exhibit more problem behaviors ($U = 26.00$, $p = .02$, $d = 3.33$) than the low-risk group, with a large effect size.

Table 1

Behavioral Data

	MSEL-EL	MSEL-RL	IBQ-R-NEG	IBQ-R-REG	IBQ-R SUR	BITSEA-Prob	BITSEA-Comp
	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)
Low-Risk	53.36 (11.74)	49.55 (7.52)	3.02 (.71)	5.17 (.55)	5.64 (.46)	5.71 (3.15)	16.57 (3.69)
High-Risk	40.2 (5.50)	39.4 (8.56)	4.28 (.33)	5.61 (.09)	5.59 (.13)	12.00 (4.08)	19 (2.16)
U	8.00*	9.00*	25.00*	19.5	15	26*	19.5

Note. EL = Expressive Language; RL = Receptive Language; NEG = negative affect; REG = orienting/regulation; SUR = surgency/extraversion; Prob = problem; Comp = Competency. U = Mann-Whitney U Score.

* $p < .05$

fNIRS Analyses

Nonsocial Condition

Hypotheses 1 and 2. With regard to the nonsocial condition, it was hypothesized that there would be a significant difference in HbO_2 concentration in response to the social compared to nonsocial condition in low-, but not high-risk infants. It was also hypothesized that low-risk infants, but not the high-risk infants, would demonstrate higher HbO_2 concentration in right frontal and posterior temporal regions in response to the social conditions, as opposed the nonsocial, control condition. Due to the short duration of the social condition (5 seconds), there was collinearity between the hemodynamic response to the social and nonsocial conditions. As such, we were unable to examine HbO_2 activation in regions of interest during the nonsocial condition.

Social Conditions

Group membership (high- vs. low-risk) did not predict peak HbO_2 activation across the averted and mutual conditions, $F(1, 1020) = .88$, $p = .35$. In addition, condition (averted vs. mutual) did not significantly predict peak HbO_2, $F(1, 1020) = .09$, $p = .76$. Lobar brain region (frontal vs. temporal) did not significantly predict mean HbO_2 activation, $F(1, 1020) = .02$, $p = .88$. Anterior and posterior temporal regions also did not predict peak HbO_2 activation, $F(1, 391) = .93$, $p = .34$. In contrast, hemisphere (right vs. left) significantly predicted peak HbO_2 activation, $F(1, 1020) = 4.78$, $p = .03$, with higher HbO_2 activation noted in the left compared to the right hemisphere across conditions. The beta weight predicting peak HbO_2 value for the right hemisphere across conditions was 8.05. The beta weight predicting peak HbO_2 value for the left hemisphere was 19.94.

When assessing the amount of variance in peak HbO_2 accounted for by the random effect, participants, it was necessary to examine two models that included group, condition, and hemisphere and a second model that included group, condition, and lobar region, as hemisphere and lobar regions did not have independent regions. The relationships among group, condition, and hemisphere showed significant variance in intercepts across participants, $\mathrm{Var}(u_{oj}) = 487.54$, $\chi^2(1) = 40.75$, $p = 0.01$. In addition, the relationships among group, condition, and lobar region also showed significant variance in intercepts across participants, $\mathrm{Var}(u_{oj}) = 486.89$, $\chi^2(1) = 40.38$, $p = 0.01$. Therefore, a very substantial part of the variance in the peak HbO_2 value is accounted for by individual differences in the cortical values of each infant. Additional multilevel analyses examining the interactions of our predictor variables were conducted to further model this variance.

The interaction of group (high- vs. low-risk) by condition (averted vs. mutual) significantly predicted peak HbO_2, $F(1, 1020) = 4.50$, $p = .03$. The difference in peak HbO_2 activation was primarily accounted for by higher activation in the high-risk group during the averted condition. That is, the interaction therefore reflects the differences in slopes for condition as a predictor of peak HbO_2 activation in the low compared to high-risk group. The interaction for group (high-risk vs. low-risk) by lobar region (frontal vs. temporal) did not significantly predict peak HbO_2, $F(1, 1020) = .35$, $p = .56$. The interaction for group (high- vs. low-risk) by anterior and posterior temporal regions was also not significant, $F(1, 391) = .61$, $p = .43$. Similarly, the interaction for condition (averted vs. mutual) by hemisphere (right vs. left) was not significant, $F(1, 1020) = .83$, $p = .36$. The interaction for condition (averted vs. mutual) by lobar region (frontal vs. temporal) was also not significant, $F(1, 1020) = .79$, $p = .38$. The interaction for condition (averted vs. mutual) by anterior and posterior temporal regions was not significant, $F(1, 391) = .003$, $p = .96$. The interaction for group (high- vs. low-risk) by hemisphere (right vs. left) did not significantly predict peak HbO_2, $F(1, 1020) = 1.56$, $p = .21$.

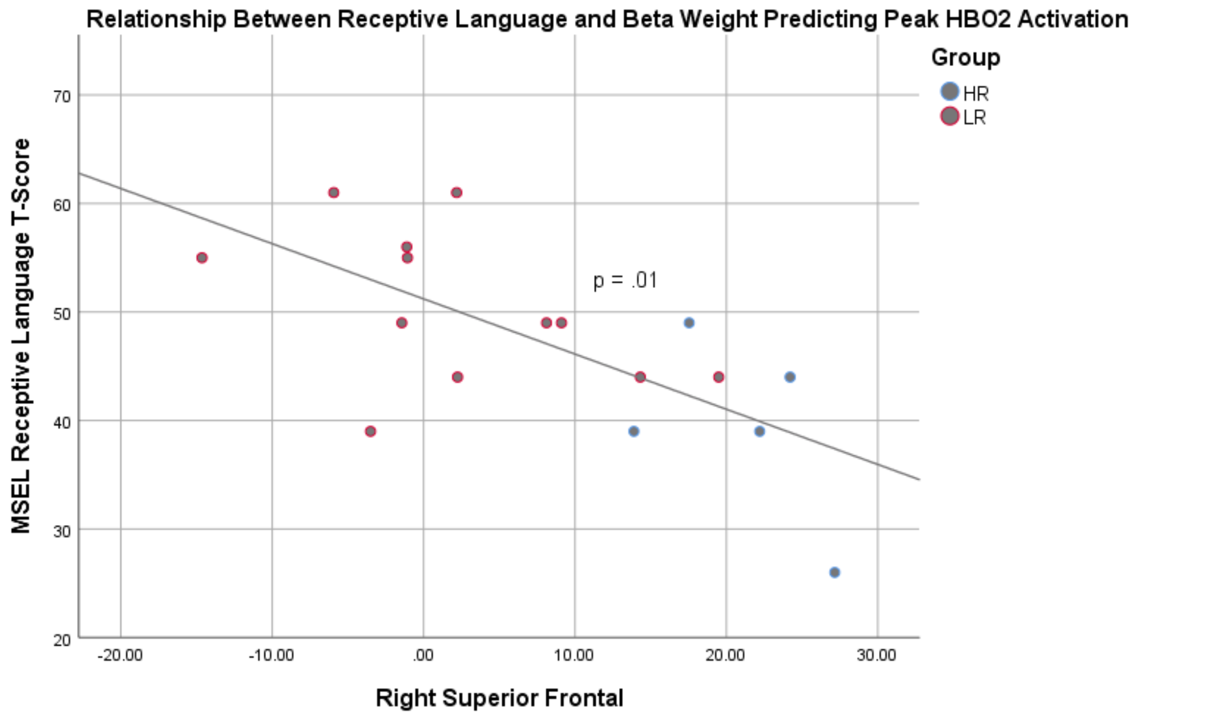
Brain-Behavior Relationships

Relationships between peak HbO_2 activation with communication and social competency were examined. Given the small sample size of the high-risk cohort, we first describe the relationships between HbO_2 activation with communication and social within the low-risk group independently and then with the low- and high-risk groups collapsed. Mean differences between groups on the MSEL, IBQ-R and BITSEA can be found in Table 1.

Within the low-risk group, higher HbO_2 activation in right frontal (τ = -.65, *p* = .005, *d* = 1.30 [channel M25]) and right posterior temporal regions (τ = -.58, *p* = .012, *d* = 1.24 [channel O31]) during the averted condition was related to lower receptive language on the MSEL at 9 months of age. Correspondingly, across groups, higher HbO_2 activation in right superior frontal (τ = -.50, *p* = .01, *d* = 1.16 [channel N28]) and right posterior temporal regions (τ =-.54, *p* = .01, *d* = 1.20 [channel O31]) during the averted condition was related to lower receptive language performance on the MSEL at 9 months of age (see Figure 7). An alternative description is that lower HbO_2 activation in right fronto-temporal regions when comparing high and low risk cohorts during the averted condition is related to higher receptive language at 9 months of age.

Figure 7

Correlation Between Receptive Language on the MSEL and Beta Weight Predicting Peak HbO_2 Activation Across Groups

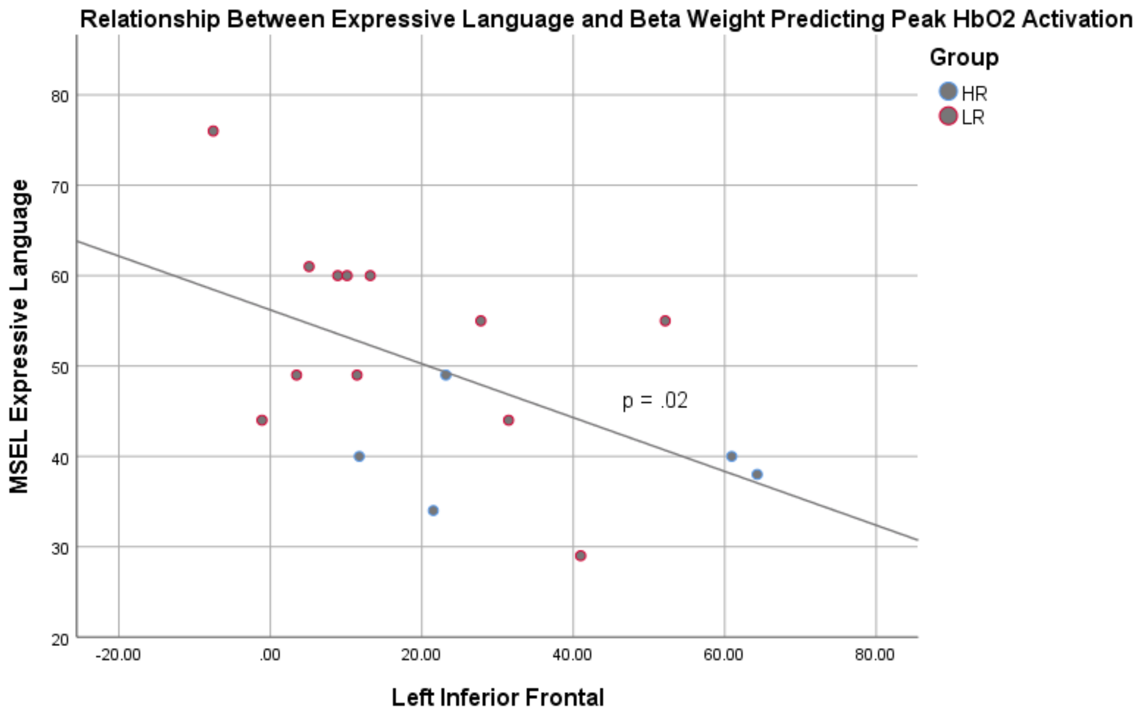


Note. MSEL = Mullen Scales of Early Learning.

Similarly, across groups, lower HbO_2 activation in left inferior frontal regions was related to higher expressive language performance on the MSEL at 9 months of age (τ = -.43, p = .018, d = 1.07 [channel D1; see Figure 8]).

Figure 8

Correlation Between Expressive Language on the MSEL and Beta Weight Predicting Peak HbO_2 Activation Across Groups



Note. MSEL = Mullen Scales of Early Learning.

Within the low-risk group, higher right temporal HbO2 activation during the averted condition was related to longer parent-reported duration of orienting (attention) on the IBQ-R at 9 months of age ($\tau = .67$, $p = .01$, $d = 3.53$). Across the groups, higher HbO2 activation in right frontal regions during the averted condition was related to higher parent-reported negative affect on the IBQ-R at 9 months of age ($\tau = .58$, $p = .01$, $d = 2.58$ [channel D25]). In other words, lower HbO2 activation in right frontal regions during the averted condition is related to a more flexible orienting response and less negative affect at 9 months of age.

Within the low-risk group, higher HbO_2 activation in left posterior temporal regions during the mutual condition was related to higher parent-reported negative affect on the IBQ-R at

9 months ($\tau = .67$, $p = .012$, $d = 3.53$). In contrast, within the low-risk group, higher HbO_2 activation in right posterior temporal regions during the mutual condition was related to lower parent-reported negative affect on the IBQ-R ($\tau = -.67$, $p = .012$, $d = 1.31$). Across groups, during the mutual condition, lower HbO_2 activation in left anterior temporal regions at 9 months was related to higher parent-reported problems on the BITSEA at 12 months of age ($\tau = -.61$, $p = .01$, $d = 1.27$ [channel B5]). In contrast, across groups, higher peak HbO_2 concentration in right posterior temporal regions during the averted condition at 9 months was related to higher parent-reported problems on the BITSEA at 12 months of age ($\tau = .65$, $p = .01$, $d = 3.23$ [channel O31]).

Discussion

This primary aim of the study was to replicate and extend the work of Grossmann and colleagues (2008), and examine differences in blood oxygenation (HbO2) between high- and low-risk 9-month-old infants in response to social and nonsocial stimuli as well as between mutual and averted gaze conditions. It was hypothesized that there would be a significant difference in regional cortical activation in response to the social compared to nonsocial condition in low-, but not high-risk infants. Unfortunately, we were unable to examine this, as there was collinearity in our results between the conditions due to too short of a duration of the social epoch, despite this being a replication of a previously established paradigm (Grossmann et al., 2008). That is, the social condition was 5 seconds followed by a nonsocial condition of 10 seconds. After the social stimulus was presented, the interval of time for the hemodynamic response resolution (i.e., ramping down) occurred at the intersection of the social and nonsocial epoch, making it impossible to detect an independent nonsocial peak signal. This brings into question the conclusions from the Grossmann findings, as the nonsocial condition was not able to serve as a valid control condition in the original nor the present study. It was also hypothesized that low-risk infants would demonstrate higher HbO_2 concentration in right frontal and posterior temporal regions in response to the social (averted and mutual) conditions, as opposed the nonsocial, control condition. Again, this hypothesis was not able to be examined given the short time window between conditions in the paradigm. These hypotheses were based on previous findings from Lloyd-Fox and colleagues (Lloyd-Fox et al., 2009) that suggested that 4- to 8-month-old infants show distinguishable responses to social rather than nonsocial stimuli.

For the third hypothesis, it was suggested that there would be a significant difference in regional cortical activation between mutual and averted gaze in the low-, but not high-risk infants. Consistent with Grossmann and colleagues (2008), it was hypothesized that the low-risk infants would demonstrate increased HbO_2 concentrations in right frontal and posterior temporal regions in response to the mutual gaze condition, and it was hypothesized that low-risk infants would show greater activation in right posterior temporal, rather than frontal regions during the averted gaze condition. Multilevel modeling revealed that lobar brain region (frontal vs. temporal) did not significantly predict peak HbO_2 activation. In contrast, with respect to hemispheric differences, hemisphere was found to predict peak HbO_2 activation such that overall, across groups during the gaze processing, greater HbO_2 activation was noted in the left hemisphere, as opposed to the right. These findings were inconsistent with hypothesis three.

There are several possible reasons that this hypothesis was not supported. As stated, the infants in this study were 9 months of age, versus 4 months of age in Grossmann's (2008) original study. Again, infant imaging studies investigating social processes have been equivocal with regard to when hemispheric specialization for the "social neural network" (SNN) emerges in low-risk development, not to mention high-risk. Recent investigations have reported that bilateral and right hemispheric regions are activated in response to social stimuli in infants from

5 to 8 months of age (Braukmann et al., 2018; Lloyd-Fox et al., 2009; van der Kant et al., 2018). Before an individual develops language, the ability to recognize faces is purported to have bilateral representation. Over time, facial recognition becomes right lateralized, while language skills become left lateralized (Rossion et al., 2003).

Nine months of age could be a time when hemispheric specialization of language is a priority, and thus information related to language processing may be more salient and recruit regions associated with this process. Mundy and colleagues (2000) found that response to joint attention was related to left parietal activation and right parietal deactivation as measured by EEG at 14 months. Though our findings did not reveal that there was more posterior activation, the left hemisphere was more active during the social (mutual and averted gaze) tasks, even at 9 months. Perhaps our infants are responding more similarly to 14-month-old infants than 5-month-olds. In adults, activation measured by MRI has revealed that mutual gaze is related to activation in left-lateralized regions responsible for language production and comprehension, while averted gaze was related to activation in the right anterior cingulate and ventral striatum, regions thought to be involved in social motivation and reward (Cavallo et al., 2015). The fact remains that a clear developmental time course has not been established for lateralization of processes involved in social communication, like response to gaze cueing and joint attention and as such, our findings were different than those recently published on infants younger than 9 months of age.

It was hypothesized that activation would be higher in right frontal and temporal regions during the social condition. Though increased activation in right hemispheric regions may have been expected given the developmental unfolding of joint attention in which response to joint attention emerges before initiation of joint attention, between 6 and 9 months (Mundy & Jarrold, 2010; Mundy & Newell, 2007; Paparella et al., 2011), and depends on more right lateralized and posterior temporoparietal regions (Gillespie-Lynch et al., 2012), our paradigm elicited a response rather than an initiation of joint attention. At this point, the nature of lobar and hemispheric involvement and the developmental integration of frontal and temporal regions during infant gaze processing remains unresolved.

It was hypothesized that the low risk but not high-risk infants would show differential cortical activation to the mutual and averted conditions. While group membership alone (high- vs. low risk) did not predict peak HbO_2 activation across the social conditions (averted and mutual), the interaction of group (high- vs. low risk) by condition (averted vs. mutual) significantly predicted peak HbO_2. This difference in peak HbO_2 activation was primarily accounted for by higher activation during the averted condition in the high-risk group. The possible relevance of how and when infants process averted gaze may be best understood by examining what has recently been reported in ASD and social anxiety in children and adults (Ford et al., 2010; Lajiness-O'Neill et al., 2014; Salmelin & Kujala, 2006; Urakawa et al., 2015). As noted, the medial prefrontal cortex has been shown to activate when responding to direct (mutual) relative to averted gaze in typically developing adults; however, a gaze direction by group interaction has been reported in ASD such that the pattern of cortical activation to both mutual and averted gaze is reversed in brain regions that underlie the social neural network and theory-of-mind, including frontal regions (anterior medial frontal cortex (arMFC), temporoparietal junction (TPJ), posterior superior temporal sulcus (pSTS) and amygdala) (Urakawa et al., 2015). Adults with ASD demonstrate an averted $>$ direct activation pattern, whereas typically developing adults reveal a direct $>$ averted pattern. Similar averted $>$ direct gaze patterns of activation have been revealed in investigations of children with ASD using magnetoencephalography (Lajiness-O'Neill et al., 2014), in adults with ASD using fMRI (Salmelin & Kujala, 2006), and in adults with anxiety using EEG, suggesting a possible attentional processing bias to averted gaze. Of note, our high-risk sample included those at risk for ASD due to preterm birth, rather than familial risk of ASD. Few studies to date have examined social communication development in other at-risk populations. Further investigations of gaze-following and development of joint attention must be pursued to generalize to this population, who, as stated are at higher risk for a host of developmental disorders like ASD, and are growing in numbers.

The second aim of the study was to examine differences in development, temperament, and social competence between high- and low-risk infants as demonstrated on the Mullen Scales of Early Learning (MSEL; Mullen, 1995) and Infant Behavior Questionnaire-Revised (IBQ-R; (Gartstein & Rothbart, 2003) at 9 months of age, and the Brief Infant Toddler Social Emotional Assessment (BITSEA; Briggs-Gowan et al., 2004) at 12 months of age. It was hypothesized that the high-risk infants would demonstrate lower extraversion/surgency and orienting/regulation, and higher negative affectivity on the IBQ-R, overall lower language skills on the MSEL at 9 months, and poorer social competence and more reported behavioral problems on the BITSEA at 12 months. Examination of group differences revealed that the high-risk group exhibited lower receptive and expressive language skills on the MSEL, as hypothesized. With that, the high-risk group was reported to have higher negative affectivity on the IBQ-R at 9 months. There was not a significant difference between groups with regard to parent-reported extraversion/surgency or orienting/regulation on the IBQ-R. Finally, the groups differed significantly with regard to problem behaviors, such that a significantly higher number of problem behaviors were reported in the high- compared to the low-risk group, but there was not a significant difference with regard to social competency at 12 months.

The third aim of the study was to examine the relationships between HbO_2 concentrations in the aforementioned regions of interest and performance on the MSEL and parent/caregiver reports of temperament and behavior (IBQ-R and the BITSEA). It was hypothesized that right frontal and posterior temporal activation in response to the social stimuli would be positively correlated with overall higher language performance on the MSEL, higher extraversion/surgency, higher orienting/regulation, and lower negative affectivity on the IBQ-R, and better social competence and fewer social problems on the BITSEA. With regard to brain-behavior relationships, regardless of group membership (high- vs. low-risk), higher HbO_2 activation in right superior frontal and right posterior temporal regions during the averted condition was related to lower receptive language performance on the MSEL at 9 months. Similarly, across groups, lower HbO_2 activation in left inferior frontal regions was related to higher expressive language performance on the MSEL at 9 months. Taken together, these findings suggest that higher activation may be related to more inefficient cortical processing of gaze at 9 months of age. Investigations into brain activation in children with traumatic brain injury and ADHD have demonstrated that higher cortical activation can be compensatory (Caeyenberghs et al., 2009; Ma et al., 2012; Westfall et al., 2015). A recent review of fNIRS infant studies concluded that the size of the hemodynamic response is related to cognitive effort, such that new and emerging skills can lead to increased activation (Issard & Gervain, 2018).

With regard to the relationships between temperament and cortical activation, within the low-risk group, higher right temporal HbO_2 activation during the averted condition was related to longer parent-reported duration of orienting (attention) on the IBQ-R at nine months. Longer duration of orienting may suggest a more immature attentional system; that is, a more inflexible attentional system (Harman et al., 1994). Consistent with the MSEL, across the groups, higher HbO_2 activation in right frontal regions during the averted condition was related to higher parent-reported negative affect on the IBQ-R at 9 months.

During the mutual gaze condition, in the low-risk group, higher HbO_2 activation in left posterior temporal regions was related to higher parent-reported negative affect, while higher HbO_2 activation in right posterior temporal regions during the mutual condition was related to lower parent-reported negative affect on the IBQ-R at 9 months.

Taken together, mutual gaze was related to expressive language, while averted gaze was related to receptive language in both high- and low-risk 9-month-olds. Morales and colleagues (2000) found that response to joint attention, as elicited by our averted gaze paradigm, was related to expressive language in a longitudinal study examining relationships between joint attention and language from 6 to 24 months. Of note, very few brain imaging studies include behavioral data to derive brain-behavior relationships. This finding warrants further study and replication in the future.

The fourth aim of the study was to examine relationships between regional HbO_2 concentration at 9 months with social functioning as measured with the BITSEA at 12-month follow-up in high- and low-risk infants. At the 12-month follow-up, across groups, higher HbO_2 activation in left anterior temporal regions during the mutual condition at 9 months was related to fewer parent-reported problems on the BITSEA at 12 months. Green and colleagues (2015) identified the anterior temporal lobe as an important region for understanding and inferring another's perspective (i.e., mentalizing) in adulthood. Anterior temporal lobe functioning in infancy is not well-known, and this finding warrants future study. In contrast, across groups, higher peak HbO_2 concentration in right posterior temporal regions during the averted condition at 9 months was related to higher parent-reported problems on the BITSEA at 12 months. This finding was consistent with the above, such that increased cortical activation was related to poorer behavioral outcomes, even at the 12-month follow-up.

There are several clinical implications that could be derived from the present study. First, 9 to 10 months is a period of great variability with regard to skill acquisition, behavior, and emerging network development (Bosl et al., 2011; Elison et al., 2013). Bosl and colleagues (2011) used resting state EEG network activity to predict later diagnosis of ASD in siblings of children with ASD. They reported that differences in network activity at 9 to 12 months of age was the most accurate period, and in fact, at 9 months, they predicted later ASD diagnosis with 80% accuracy. This highlights that 9 months may be a particularly important time for network development and identification of risk.

Again, the findings with regard to cortical activation in infants in response to gaze cues are equivocal. There is little consistency across study findings which indicates that there is more work to be done to clarify gaze processing in infancy in low-risk development, not to mention infants at risk for atypical development due to prematurity. Of note, few studies use behavioral data through developmental assessment or parent report to derive meaningful brain-behavior relationships. This makes clinical application of infant neuroimaging studies extremely difficult. In order to move the field forward with regard to identifying early markers of risk, brain-behavior relationships must be examined and replicated to establish an evidence base for future intervention development and implementation.

A study by Elsabbagh and colleagues (2009) examined a high-risk, ASD sibling group of 10- month-olds to examine differences between them and a control group with regard to latency of responding to gaze stimuli using ERP. Findings indicated that differential response latency to the averted condition distinguished the groups. The authors noted that they had MSEL data on the sibling group only to demonstrate average cognitive development. Though they collected these data, Elsabbagh and colleagues (2009) did not include MSEL data in the analyses. Perhaps inclusion of behavioral data in conjunction with the imaging data could have yielded more robust findings.

While Bosl and colleagues (2011) were able to use imaging methods to predict later onset of ASD in infant siblings of children with ASD at 9 months, others have indicated that the ability to predict later diagnosis based on imaging alone in infancy may not be reliable. Braukmann and colleagues (2018) reported that not all ASD siblings go on to develop ASD, even if they demonstrate altered cortical activation compared to the control groups. It appears as though the between-group differences (high- vs. low-risk) are larger than the within-group differences among the high-risk infants. In contrast, Lloyd-Fox and colleagues (2018) found that they were able to distinguish which high-risk infants went on to develop ASD from those who did not. For future studies aimed at predicting outcomes based on cortical activity in infancy, perhaps it would be helpful to include behavioral markers to further differentiate the within-group differences. With that, ASD is considered to be a spectrum disorder, and those at familial risk of ASD may not go on to meet full criteria for a diagnosis, but they might exhibit features of the broader autism phenotype (Constantino et al., 2010; Ozonoff et al., 2011). Behavioral data might be helpful to clarify the combination of cortical activation patterns and behavior in infancy that lead to later diagnosis.

FNIRS has been established as a functional imaging method that has utility in infant populations. The current study sought to add to the growing infant brain imaging work focused on identifying early markers of atypical development. As previously stated, few studies have investigated social communication development in preterm infants. Greisen and colleagues (2011) suggested that fNIRS could be used clinically to identify and manage preterm infants at risk for circulatory insufficiency. They suggested a large-scale, longitudinal RCT to determine whether use of fNIRS to identify stroke risk in high-risk infants could lead to better outcomes overall.

Though there were several clinical implications to be drawn from the present study, there were also limitations. First, though it is not uncommon to see small sample sizes in imaging studies, the high-risk group was particularly small and was likely under-powered. We were unable to collect all IBQ-R and BITSEA data from our participants in both groups. The attrition rate for the IBQ-R data at 9 months was 29% and increased to 35% at the 12-month follow-up.

Recruitment of high-risk infants was also a barrier. One problem was that families from across the state travel to our recruitment site for specialty care. As such, they would have had to travel to complete our study, making it more difficult for high-risk infants and their families to participate. With that, medical follow-up of preterm infants is burdensome, and it was difficult to find families who were willing to participate.

Multilevel linear modeling revealed that individual differences among our participants accounted for a significant amount of the variance in outcome. Elison and colleagues (2013) found that 9 to 10 months may be a period of particular individual variability with regard to joint attention. As such, it may be that individual differences, as noted in our findings, especially in small sample sizes, makes it difficult to find meaningful group differences between our high- and low-risk groups using a paradigm that elicits response to joint attention.

The current study was a replication of Grossmann and colleagues' (2008) and included a replicated paradigm. As stated, analyses examining differences in cortical activation to social versus nonsocial stimuli across our groups were not possible due to collinearity as a result of the social condition duration being too short. The hemodynamic response occurs over several seconds and thus infants' hemodynamic response to the social condition carried over into the nonsocial condition. Because of this, only results from the social conditions were able to be examined.

In conclusion, the present study contributed to the infant brain imaging literature despite some limitations. A particular strength of this study was the integration of neuroimaging and behavioral data to examine brain-behavior relationships at a critical period for the development of joint attention, a pivotal social communication skill. Relationships between gaze processing and language were highlighted, with a clear link between mutual gaze and expressive language and averted gaze and receptive language. This finding deserves further investigation and replication. Overall, higher activation across conditions was related to reduced language performance, more negative affect, and more behavior problems at the 12-month follow-up. This could indicate that higher activation does not necessarily mean more efficient processing and could in fact indicate the opposite. Another key finding of the current study was that individual differences among participants accounted for a significant amount of the variance in cortical activation across groups, conditions, and regions of interest. This may have been due, in part to the age of our participants, as 9 months is a time when key social behaviors, like joint attention, are emerging.

The findings of the current study added to the inconclusive body of research on infant social network development. Our findings suggest that 4- and 5-month-old infants respond differently to social stimuli than do 9-month-old infants. Contrary to Grossmann's findings (2008), our 9-month-old sample did not respond to the social stimuli in a way that was consistent with adult gaze processing either. As such, 9 months may be a developmental period of interest for future studies aimed at elucidating early markers for aberrant social behavior.

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Appendices

Appendix A: University of Michigan IRB Approval

UNIVERSITY OF MICHIGAN
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Medical School Institutional Review Board (IRBMED) • 2800 Plymouth Road, Building 520, Suite 3214, Ann Arbor, MI 48109-2800 • phone (734) 763 4768 • fax (734) 763 9603 • irbmed@umich.edu

To: Dr. Elise Hodges

From:
Michael Geisser
Alan Sugar

Cc:
Renee Lajiness-O'Neill
William Thacker
Tristin Nyman
Elise Hodges
Casey Swick
Tiffany Andersen
Prachi Shah
Ana-Mercedes Flores
Salam Taraben
Ann Iatrow
Ioulia Kovelman
Kaitlyn McFarlane
Annette Richard
Neelima Wagley
Kimberly Brink
Ketrin Lengu

Subject: Scheduled Continuing Review [CR00057528] Approved for [HUM00079033]

SUBMISSION INFORMATION:
Study Title: Neural Correlates of Nonverbal and Verbal Social Communication in High Risk Infants
Full Study Title (if applicable): Neural Correlates of Nonverbal and Verbal Social Communication in High Risk Infants: Relationship to Caregiver Observations of Behavior using Pediatrac™

Study eResearch ID: HUM00079033
SCR eResearch ID: CR00057528
SCR Title: HUM00079033_Continuing Review - Thu Sep 29 19:39:17 EDT 2016
Date of this Notification from IRB:10/3/2016
Review: Expedited
Date Approval for this SCR: 10/3/2016
Current IRB Approval Period: 10/3/2016 - 10/2/2017
Expiration Date: Approval for this expires **at 11:59 p.m. on 10/2/2017**
UM Federalwide Assurance:FWA00004969 (For the current FWA expiration date, please visit the UM HRPP Webpage)
OHRP IRB Registration Number(s): IRB00000244

Approved Risk Level(s) as of this Continuing Report:

Name	Risk Level
HUM00079033	No more than minimal risk

NOTICE OF IRB APPROVAL AND CONDITIONS:
The IRBMED has reviewed and approved the scheduled continuing review (SCR) submitted for the study referenced above. The IRB determined that the proposed research continues to conform with applicable guidelines, State and federal regulations, and the University of Michigan's Federalwide Assurance (FWA) with the Department of Health and Human Services (HHS). You must conduct this study in accordance with the description and information provided in the approved application and associated documents.

APPROVAL PERIOD AND EXPIRATION DATE:
The updated approval period for this study is listed above. Please note the expiration date. If the approval lapses, you may not conduct work on this study until appropriate approval has been re-established, except as necessary to eliminate apparent immediate hazards to research subjects or others. Should the latter occur, you must notify the IRB Office as soon as possible.

IMPORTANT REMINDERS AND ADDITIONAL INFORMATION FOR INVESTIGATORS

APPROVED STUDY DOCUMENTS:
You must use any date-stamped versions of recruitment materials and informed consent documents available in the eResearch workspace (referenced above). Date-stamped materials are available in the "Currently Approved Documents" section on the "Documents" tab.

In accordance with 45 CFR 46.111 and IRB practice, consent document(s) and process are considered as part of Continuing Review to ensure accuracy and completeness. The dates on the consent documents, if applicable, have been updated to reflect the date of Continuing Review approval.

RENEWAL/TERMINATION:
At least two months prior to the expiration date, you should submit a continuing review application either to renew or terminate the study. Failure to allow sufficient time for IRB review may result in a lapse of approval that may also affect any funding associated with the study.

AMENDMENTS:
All proposed changes to the study (e.g., personnel, procedures, or documents), must be approved in advance by the IRB through the amendment process, except as necessary to eliminate apparent immediate hazards to research subjects or others. Should the latter occur, you must notify the IRB Office as soon as possible.

AEs/ORIOs:
You must continue to inform the IRB of all unanticipated events, adverse events (AEs), and other reportable information and occurrences (ORIOs). These include but are not limited to events and/or information that may have physical, psychological, social, legal, or economic impact on the research subjects or others.

Investigators and research staff are responsible for reporting information concerning the approved research to the IRB in a timely fashion, understanding and adhering to the reporting guidance (http://medicine.umich.edu/medschool/research/office-research/institutional-review-boards/guidance/adverse-events-aes-other-reportable-information-and-occurrences-orios-and-other-required-reporting), and not implementing any changes to the research without IRB approval of the change via an amendment submission. When changes are necessary to eliminate apparent immediate hazards to the subject, implement the change and report via an ORIO and/or amendment submission within 7 days after the action is taken. This includes all information with the potential to impact the risk or benefit assessments of the research.

SUBMITTING VIA eRESEARCH:
You can access the online forms for continuing review, amendments, and AE/ORIO reporting in the eResearch workspace for this approved study, referenced above.

MORE INFORMATION:
You can find additional information about UM's Human Research Protection Program (HRPP) in the Operations Manual and other documents available at: http://research-compliance.umich.edu/human-subjects.

Michael Geisser
Co-chair, IRBMED

Alan Sugar
Co-chair, IRBMED

Appendix B: Low-Risk Recruitment Call Script

Recommended script for calling Registry participants

Hi this is __________________ from the University of Michigan. I have your name because when you were pregnant with your xx old child, you indicated on a form at your OB's office that you were willing to be contacted about future research studies during pregnancy or postpartum, after the birth of your child. I have a study that you may qualify for that I would like to tell you about. Are you interested in hearing about it?

[If YES] Is this a good time to talk? Explain study.
In this study we are interested in understanding how the brain works when infants listen to speech and when they pay attention to social communication cues, for example looking at eye gaze. To study these abilities, we use functional near-infrared spectroscopy (fNIRS). This technique is very safe and allows us to see easily how the brain is involved in the activities the infants are performing. Please see the attached PowerPoint for more details. The reason we are doing this is because we are trying to figure if we can identify infants who are at risk for developmental disorders like Autism earlier than we currently are. We will be asking you to complete three brief questionnaires about your baby's development. 2 are paper and we will send you a URL for one. At the end, your baby will receive a small gift. Additionally, you will receive a $15 VISA card if he/she completes the session.

If you are interested in the study and you plan to come with a sibling, please let us know in advance and a member of our research team will be there to supervise her/him in the reception room, which has toys, books, and coloring activities.

[If NO (not a good time to talk)] Is there a better time for me to call you back? Great. I will call you back later. (Note: Date/Time _________________) Thank you!

*If NO (don't want to hear about study)+ Okay, thank you for your time. Might you still be interested in participating in other studies, or would you rather I remove you from our list of those interested in participating in research projects?
* If they want to be removed, make note in Excel file to give to Stephanie to update the Registry

Appendix C: Low-Risk Phone Screen

fNIRS Infant Study Subject ID: ______________________

- Inclusion/Exclusion Criteria
  - Does your baby have a full biological sibling with Autism Spectrum Disorder? YES or **NO**
    - If YES, how was the child diagnosed? _____________ (ADOS or ADI?)
  - Does your child have any first degree relatives with ASD? YES or **NO** ___________________________
  - Was your baby born at 37-42 weeks gestation? **YES** or NO __________________
  - Was your baby at least 2500g, 5 lbs, 5 oz? **YES** or NO ___________________
  - Do you have a history of prenatal or intrapartum complications? YES or **NO** __________________
  - Does your baby have a brain injury? YES or **NO** __________________
  - Does your baby have seizures? YES or **NO** ____________________
  - Does your baby have any other neurological illness? YES or **NO** ____________________
  - Is the primary language spoken in your home English? **YES** or NO

Appendix D: NICU Recruitment Flyer

Study ID: HUM00079033 IRB: IRBMED Date Approved: 10/3/2016 Expiration Date: 10/2/2017

Would you like to find out how your baby communicates? So would we!

Participate with your baby in a study on the development of language and social communication! We are looking for infants ages **6-12 months**.

Why participate? Researchers at the University of Michigan and Eastern Michigan University are studying how infants learn to communicate and we invite healthy infants as well as infants at risk for social/communication disorders. During the study, we will explore your child's language and social development!

What will the study involve? During the one time visit, infants will undergo a brief developmental assessment. We will also record infants' brain activity with fNIRS optical imaging, which is safe for infants and consist of a soft head band with small and safe low-intensity lights embedded into it. Infants will sit comfortably on the caregiver's lap watching videos and listening to sounds. The study will take about one hour.

When and Where? Appointments are flexible and can be scheduled at a time that is convenient for you. The study takes place at the Center for Human Growth and Development, 300 North Ingalls, Ann Arbor.

Contact: If you would like to help improve our understanding of infant's social communication, please let us know.

________ Yes, I would like to participate.

________ No, I am not interested.

________ I'm not sure; please give me more information.

If interested in participating or if you would like more information, please fill out the following:
Caregiver Name: ____

Phone number or email address: ______________________________

Best time to reach me: _____________________________________

IRB Human Subjects Approval- HUM00079033

Appendix E: High-Risk Recruitment Call Script

Recommended script for calling high risk recruits

Hi this is __________________ from Eastern Michigan University in partnership with the University of Michigan. I have your name because at your recent neonatal follow-up visit with (child's name), you indicated on a form that you might be interested in a study we are currently conducting at the Center for Human Growth and Development. I would like to tell you about the study, if this is a good time for you….

[If YES, Explain study]

In this study we are interested in understanding how the brain works when infants listen to speech and when they pay attention to social communication cues, for example looking at eye gaze. To study these abilities, we use functional near-infrared spectroscopy (fNIRS). This technique is very safe and allows us to see easily how the brain is involved in the activities the infants are performing (introduce the powerpoint presentation if they want more written information – offer to send to their email).

The reason we are doing this is because we are trying to figure if we can identify infants who are at risk for developmental disorders like Autism earlier than we currently are. If you agree to participate, we will invite you for a one time visit at the Center for Human Growth and Development close the UM Hospitals. At that time we will do brief developmental testing with your child, and we will also conduct neuroimaging. The visit takes about 1.5-2 hours. In addition, we will be asking you to complete three brief questionnaires about your baby's development. 2 are paper and we will send you a URL for one. At the end, you will receive a $15 VISA card and $20 cash for your time and efforts in our study.

Is this a study that you might be interested in? When would be a good time? [Make sure you ask to confirm DOB and determine when they will be about 9 months corrected so that we can schedule them around that time].

If you are interested in the study and you plan to come with a sibling, please let us know in advance and a member of our research team will be there to supervise her/him in the reception room, which has toys, books, and coloring activities.

[If NO (not a good time to talk)] Is there a better time for me to call you back? Great. I will call you back later. (Note: Date/Time _________________) Thank you!

*If NO (don't want to hear about study)+ Okay, thank you for your time. Might you still be interested in participating in other studies, or would you rather I remove you from our list of those interested in participating in research projects?
** Be sure to record all contact notes in the excel.

Appendix F: High-Risk Phone Screen

fNIRS Infant Study Subject ID: ______________________

- Inclusion/Exclusion Criteria
  - Was your baby born at fewer than 37 weeks gestation? **YES** or NO __________________
  - What was your baby's birth weight? ________________
  - Do you have a history of prenatal or intrapartum complications? YES or **NO** __________________
  - Does your baby have a brain injury? YES or **NO** __________________
  - Does your baby have seizures? YES or **NO** ____________________
  - Does your baby have any other neurological illness? YES or **NO** ____________________
  - Is the primary language spoken in your home English? **YES** or NO
- If recruitment is stalled, we may include infants with intraventricular hemorrhage (IVH) seen by ultrasound (grades III and IV), bronchopulminary dysplasia (BPD) (on oxygen supplement at 28 days), retinopathy of prematurity (ROP), and sepsis.

Appendix G: Parental Consent Form

Study ID: HUM00079033 IRB: IRBMED Date Approved: 10/3/2016 Expiration Date: 10/2/2017

UNIVERSITY OF MICHIGAN

CONSENT TO BE PART OF A RESEARCH STUDY

INFORMATION ABOUT THIS FORM

Your infant may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of the study, and the risks and possible benefits of participating in the study.

Please take time to review this information carefully. After you have finished, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or other doctors) about your infant's participation in this study. If you decide for your infant to take part in the study, you will be asked to sign this form. *Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.*

1. GENERAL INFORMATION ABOUT THIS STUDY AND THE RESEARCHERS

1.1 Study title:

Neural Correlates of Nonverbal and Verbal Social Communication in High Risk Infants

1.2 Company or agency sponsoring the study:

University of Michigan

1.3 Names, degrees, and affiliations of the researchers conducting the study:

Renee Lajiness-O'Neill, Ph.D., Associate Professor, Psychology Department, Eastern Michigan University
Ioulia Kovelman, Ph.D., Assistant Professor, Department of Psychology
Elise Hodges, Ph.D., Clinical Assistant Professor, Neuropsychology Section, Department of Psychiatry
Silvia Bisconti, Ph.D., Post-doctoral Research Fellow, Center for Human Growth and Development
Annette Richard, MS, Doctoral Student, Psychology Department, Eastern Michigan University

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

The purpose of this study is to discover how infants understand language and social communication. In particular, we are interested in understanding how the brain is involved in the processing of language and in decoding non-verbal communication cues. We are also interested in understanding any differences in language/communication between high risk siblings of children with autism spectrum disorder and low risk infants.

3. INFORMATION ABOUT STUDY PARTICIPANTS (SUBJECTS)

Taking part in this study is completely **voluntary**. You and your infant do not have to participate if you don't want to. You and your infant may also leave the study at any time. If your infant leaves the study before it is finished, there will be no penalty to you or your infant, and you and your infant will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

Infants with and without risk for autism spectrum disorder.

3.2 How many people (subjects) are expected to take part in this study?

60 infants are expected to participate.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

Visit 1

1) **Background Information.** First, we will ask you to complete questionnaires and answer questions about your infant's development. We will complete a brief screening of your child's development.

2) **Exploring your child's language and social development**. Your child will sit comfortably on your lap in front of a computer screen. The computer will display images and play sounds. Specifically, your infant will passively listen to language or watch a character communicating with eye gaze. The two types of experiments are randomized across participants, thus your child may experience the language experiment first and social experiment second visit, or vice versa.

We will record your infant's brain response to these images and sounds using functional Near Infrared Spectroscopy (fNIRS). fNIRS is safe for infants and children. It includes a comfortable hat with small plastic optodes (lights) imbedded into it. The optodes emit low-intensity near-infrared light, which is harmless. Your child's responses will be video recorded for later scoring and analysis.

Follow-Up

In addition to asking you to complete questionnaires when your child is 9 months and 12 months of age, when your child is between 2 and 3 years old, we will call you on the phone to ask questions about your child development.

4.2 How much of my time will be needed to take part in this study?

There will be 1 visit lasting up to 2 hours when your child is about 9 months old. About 1-2 years after the visit, when your child is between 2 and 3 years of age, we will contact you for an optional follow-up interview that can be completed via phone lasting about 30 minutes.

4.3 When will my participation in the study be over?

Your infant's participation in this study will be over once the follow-up phone interview is complete when your child is between 2 and 3 years of age.

5. INFORMATION ABOUT RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

Your infant may experience fatigue and frustration during this study. If this happens, we will address the situation right away. As with any research study, there may be additional risks that are unknown or unexpected.

fNIRS safety: fNIRS is a safe and non-invasive optical imaging technique used to study how the brain works. fNIRS uses light to measure brain activity. fNIRS does NOT use radiation or electricity. It is safe for babies, children and adults.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?

The researchers have taken steps to minimize the risks of this study. Even so, your child may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers, Drs. Renee Lajiness-O'Neill or Elise Hodges (rlajines@gmail.com, ekhodges@umich.edu or 734-763-9259) about any injuries, side effects, or other problems that your infant has during this study. You should also tell your regular doctors.

5.3 If I take part in this study, can I also participate in other studies?

Being in more than one research study at the same time, or even at different times, may increase the risks to your child. It may also affect the results of the studies. Your child should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?

Your infant may not receive any personal benefits from being in this study, but your infant's participation may help inform educators and clinicians on better methods of diagnosis and remediation of autism spectrum disorders.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?

Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. OTHER OPTIONS

6.1 If I decide not to take part in this study, what other options do I have?

Since participation in this study is entirely voluntary, you have the alternative option of not participating, in which case there will be no penalty.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?

You and your infant are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you or your infant. Neither you nor your infant will lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 "Contact Information" (below).

7.2 Could there be any harm to me if I decide to leave the study before it is finished?

You and your infant are free to leave the study at any time. Simply indicate your choice to the researcher. There are no dangers in leaving the study early.

7.3 Could the researchers take me out of the study even if I want to continue to participate?

Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- ✓ The researcher believes that it is not in your infant's best interest to stay in the study.
- ✓ Your infant becomes ineligible to participate.
- ✓ Your infant's condition changes and you need treatment that is not allowed while he or she is taking part in the study.
- ✓ You or your infant do not follow instructions from the researchers.
- ✓ The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?

The study will pay for research-related items or services that are provided only because your infant is in the study.

By signing this form, you do not give up your right to seek payment if your infant is harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?

Your infant will receive a toy or small gifts, and a photo of your child wearing the fNIRS cap. If you and your infant complete the study, you will be paid $35 for your participation with a visa gift card at the end of the session. If you choose to withdraw you and your child from the session, you will still be paid $35. Since participation in this study is entirely voluntary, you have the alternative option of not participating, in which case there will be no penalty, and your infant will still receive a small gift for participating. You will not receive the $35 incentive if you choose not to take part in the study. There is no compensation for completing the follow-up interview conducted when your infant is 2-3 years of age.

8.3 Who could profit or financially benefit from the study results?

No person or organization has a financial interest in the outcome of this study.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how your privacy and the confidentiality of your research records will be protected in this study.

9.1 How will the researchers protect my privacy?

Study records that contain subject names will have access limited to the Principal Investigator. Confidentiality will be preserved for participants by coding all study data, images, and test results data with an identifying number, and referring to this number in all analyses. You and your infant will not be identified in any reports on this study. Your infant's participation in this study is also kept completely confidential; any paperwork (such as this consent document) containing your name or other identifying information is stored in locked cabinets in locked offices, with access limited to the study team.

Although we assure you that everything you tell us will remain confidential, there are some circumstances where the law requires that we may need to break this assurance in order to prevent somebody from getting hurt. For example, if you tell us something that leads us to believe that harm may come to somebody in the future, e.g. ongoing abuse of a minor or vulnerable adult, then we may need to alert proper authorities. Furthermore, all study staff are trained in the proper handling and storage of confidential information and study records.

9.2 What information about me could be seen by the researchers or by other people? Why? Who might see it?

There are many reasons why information about your child may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University, Food and Drug Administration (FDA), and/or other government officials may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects
    - Analyze the results of the study
- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular UMHS medical record.

- If you receive any payments for taking part in this study, the University of Michigan accounting department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to your child or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who your child is.

9.3 What happens to information about me after the study is over or if I cancel my permission?

As a rule, the researchers will not continue to use or disclose information about your infant, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about your infant to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities (This information would not include your name, social security number, or anything else that could let others know who your child is.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan Notice of Privacy Practices. This information is also available on the web at http://www.med.umich.edu/hipaa/npp.htm. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal

Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission expire?

Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below).

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigators: Renee Lajiness-O'Neill, PhD or Elise Hodges, PhD

Mailing Address: University of Michigan Health Systems
Dept. of Psychiatry, Neuropsychology Section
2101 Commonwealth, Suite C

Study ID: HUM00079033 IRB: IRBMED Date Approved: 10/3/2016 Expiration Date: 10/2/2017

Ann Arbor, MI 48105
Phone: (734) 763-9259

E-mail: rlajines@gmail.com

You may also express a concern about a study by contacting the Institutional Review Board listed below.

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Road
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768 (For International Studies: US Country Code: 001)
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.

When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

Your signature in the next section means that you have received copies of all of the following documents:

- This "Parental Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*

12. SIGNATURES

Study ID: HUM00079033 IRB: IRBMED Date Approved: 10/3/2016 Expiration Date: 10/2/2017

Consent/Assent to Participate in the Research Study

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with ______________________. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Legal Name: ____

Signature: ____

Date of Signature (mm/dd/yy): ______________________

________ By providing my initials, I consent to allow researchers to contact me about future studies for which my child and I may be eligible to participate.

For use only if required by sponsor:

Date of Birth (mm/dd/yy): ________________________

ID Number: ________________________________

Legally Authorized Representative or Parent Permission

Legal Name: ____

Signature: ____

Address: ____

Date of Signature (mm/dd/yy): ______________________

Relationship to subject: ☐ Parent ☐ Spouse ☐ Child ☐ Sibling ☐ Legal guardian ☐ Other

If "Other," explain: ____

Reason subject is unable to consent: ________________________________

For use only if required by sponsor:

Date of Birth (mm/dd/yy): ________________________

ID Number: ________________________________

Principal Investigator or Designee

I have provided this participant and/or his/her legally authorized representative(s) with information about this study that I believe to be accurate and complete. The participant and/or his/her legally authorized representative(s) indicated that he or she understands the nature of the study, including risks and benefits of participating.

Legal Name: ______________________________

Title: ______________________________

Signature: ______________________________

Date of Signature (mm/dd/yy): ______________

Appendix H: Infant Behavior Questionnaire- Revised (IBQ-R)

Infant Behavior Questionnaire - Revised

Subject No. ______________ Date of Baby's Birth ______ ____ _____
month. day year

Today's Date ______________ Age of Child _____ _____
mos. weeks

Sex of Child ______________

INSTRUCTIONS:
Please read carefully before starting:

As you read each description of the baby's behavior below, please indicate how often the baby did this during the LAST WEEK (the past seven days) by circling one of the numbers in the left column. These numbers indicate how often you observed the behavior described during the last week.

(1) Never	(2) Very Rarely	(3) Less Than Half the Time	(4) About Half the Time	(5) More Than Half the Time	(6) Almost Always	(7) Always	(X) Does Not Apply

The "Does Not Apply" (X) column is used when you did not see the baby in the situation described during the last week. For example, if the situation mentions the baby having to wait for food or liquids and there was no time during the last week when the baby had to wait, circle the (X) column. "Does Not Apply" is different from "Never" (1). "Never" is used when you saw the baby in the situation but the baby never engaged in the behavior listed during the last week. For example, if the baby did have to wait for food or liquids at least once but never cried loudly while waiting, circle the (1) column.

Please be sure to circle a number for <u>every</u> item.

Feeding

During feeding, how often did the baby:
1 2 3 4 5 6 7 X . . . . (1) lie or sit quietly?
1 2 3 4 5 6 7 X . . . . (2) squirm or kick?
1 2 3 4 5 6 7 X . . . . (3) wave arms?
1 2 3 4 5 6 7 X . . . . (4) notice lumpy texture in food (e.g., oatmeal)?

In the last week, while being fed in your lap, how often did the baby:
1 2 3 4 5 6 7 X . . . . (5) seem to enjoy the closeness?
1 2 3 4 5 6 7 X . . . . (6) snuggle even after she was done?
1 2 3 4 5 6 7 X . . . . (7) seem eager to get away as soon as the feeding was over?

How often did your baby make talking sounds:
1 2 3 4 5 6 7 X . . . . (8) while waiting in a high chair for food?
1 2 3 4 5 6 7 X . . . . (9) when s/he was ready for more food?
1 2 3 4 5 6 7 X . . . . (10) when s/he has had enough to eat?

Sleeping

Before falling asleep at night during the last week, how often did the baby:
1 2 3 4 5 6 7 X . . . . (11) show no fussing or crying?

During sleep, how often did the baby:
1 2 3 4 5 6 7 X . . . . (12) toss about in the crib?
1 2 3 4 5 6 7 X . . . . (13) move from the middle to the end of the crib?
1 2 3 4 5 6 7 X . . . . (14) sleep in one position only?

After sleeping, how often did the baby:
1 2 3 4 5 6 7 X . . . . (15) fuss or cry immediately?
1 2 3 4 5 6 7 X . . . . (16) play quietly in the crib?
1 2 3 4 5 6 7 X . . . . (17) cry if someone doesn't come within a few minutes?

How often did the baby:
1 2 3 4 5 6 7 X . . . . (18) seem angry (crying and fussing) when you left her/him in the crib?
1 2 3 4 5 6 7 X . . . . (19) seem contented when left in the crib?
1 2 3 4 5 6 7 X . . . . (20) cry or fuss before going to sleep for naps?

When going to sleep at night, how often did your baby:
1 2 3 4 5 6 7 X . . . . (21) fall asleep within 10 minutes?
1 2 3 4 5 6 7 X . . . . (22) have a hard time settling down to sleep?
1 2 3 4 5 6 7 X . . . . (23) settle down to sleep easily?

When your baby awoke at night, how often did s/he:
1 2 3 4 5 6 7 X . . . . (24) have a hard time going back to sleep?
1 2 3 4 5 6 7 X . . . . (25) go back to sleep immediately?

When put down for a nap, how often did your baby:
1 2 3 4 5 6 7 X . . . . (26) stay awake for a long time?

1 2 3 4 5 6 7 X . . . . (27) go to sleep immediately?
1 2 3 4 5 6 7 X . . . . (28) settle down quickly?
1 2 3 4 5 6 7 X . . . . (29) have a hard time settling down?

When it was time for bed or a nap and your baby did not want to go, how often did s/he:
1 2 3 4 5 6 7 X . . . . (30) whimper or sob?
1 2 3 4 5 6 7 X . . . . (31) become tearful?

Bathing and Dressing

When being dressed or undressed during the last week, how often did the baby:
1 2 3 4 5 6 7 X . . . . (32) wave her/his arms and kick?
1 2 3 4 5 6 7 X . . . . (33) squirm and/or try to roll away?
1 2 3 4 5 6 7 X . . . . (34) smile or laugh?
1 2 3 4 5 6 7 X . . . . (35) coo or vocalize?

When put into the bath water, how often did the baby:
1 2 3 4 5 6 7 X . . . . (36) smile?
1 2 3 4 5 6 7 X . . . . (37) laugh?
1 2 3 4 5 6 7 X . . . . (38) splash or kick?
1 2 3 4 5 6 7 X . . . . (39) turn body and/or squirm?

When face was washed, how often did the baby:
1 2 3 4 5 6 7 X . . . . (40) smile or laugh?
1 2 3 4 5 6 7 X . . . . (41) fuss or cry?
1 2 3 4 5 6 7 X . . . . (42) coo?

When hair was washed, how often did the baby:
1 2 3 4 5 6 7 X . . . . (43) smile?
1 2 3 4 5 6 7 X . . . . (44) fuss or cry?
1 2 3 4 5 6 7 X . . . . (45) vocalize?

Play

How often during the last week did the baby:

1 2 3 4 5 6 7 X . . . . (46) look at pictures in books and/or magazines for 2-5 minutes at a time?
1 2 3 4 5 6 7 X . . . . (47) look at pictures in books and/or magazines for 5 minutes or longer at a time?
1 2 3 4 5 6 7 X . . . . (48) stare at a mobile, crib bumper or picture for 5 minutes or longer?
1 2 3 4 5 6 7 X . . . . (49) play with one toy or object for 5-10 minutes?
1 2 3 4 5 6 7 X . . . . (50) play with one toy or object for 10 minutes or longer?
1 2 3 4 5 6 7 X . . . . (51) spend time just looking at playthings?
1 2 3 4 5 6 7 X . . . . (52) repeat the same sounds over and over again?
1 2 3 4 5 6 7 X . . . . (53) laugh aloud in play?
1 2 3 4 5 6 7 X . . . . (54) repeat the same movement with an object for 2 minutes or longer (e.g., putting a block in a cup, kicking or hitting a mobile)?
1 2 3 4 5 6 7 X . . . . (55) pay attention to your reading during most of the story when looking at picture books?
1 2 3 4 5 6 7 X . . . . (56) smile or laugh after accomplishing something (e.g., stacking blocks, etc.)?
1 2 3 4 5 6 7 X . . . . (57) smile or laugh when given a toy?
1 2 3 4 5 6 7 X . . . . (58) smile or laugh when tickled?

How often during the last week did the baby enjoy:

1 2 3 4 5 6 7 X . . . . (59) being sung to?
1 2 3 4 5 6 7 X . . . . (60) being read to?
1 2 3 4 5 6 7 X . . . . (61) hearing the sound of words, as in nursery rhymes?
1 2 3 4 5 6 7 X . . . . (62) looking at picture books?
1 2 3 4 5 6 7 X . . . . (63) gentle rhythmic activities, such as rocking or swaying?
1 2 3 4 5 6 7 X . . . . (64) lying quietly and examining his/her fingers or toes?
1 2 3 4 5 6 7 X . . . . (65) being tickled by you or someone else in your family?
1 2 3 4 5 6 7 X . . . . (66) being involved in rambunctious play?
1 2 3 4 5 6 7 X . . . . (67) watching while you, or another adult, playfully made faces?
1 2 3 4 5 6 7 X . . . . (68) touching or lying next to stuffed animals?
1 2 3 4 5 6 7 X . . . . (69) the feel of soft blankets ?
1 2 3 4 5 6 7 X . . . . (70) being rolled up in a warm blanket?
1 2 3 4 5 6 7 X . . . . (71) listening to a musical toy in a crib?

When playing quietly with one of her/his favorite toys, how often did your baby:
1 2 3 4 5 6 7 X . . . . (72) show pleasure?
1 2 3 4 5 6 7 X . . . . (73) enjoy lying in the crib for more than 5 minutes?
1 2 3 4 5 6 7 X . . . . (74) enjoy lying in the crib for more than 10 minutes?

When something the baby was playing with had to be removed, how often did s/he:
1 2 3 4 5 6 7 X . . . . (75) cry or show distress for a time?
1 2 3 4 5 6 7 X . . . . (76) seem not bothered?

When tossed around playfully how often did the baby:
1 2 3 4 5 6 7 X . . . . (77) smile?
1 2 3 4 5 6 7 X . . . . (78) laugh?

During a peekaboo game, how often did the baby:
1 2 3 4 5 6 7 X . . . . (79) smile?
1 2 3 4 5 6 7 X . . . . (80) laugh?

How often did your baby enjoy bouncing up and down:
1 2 3 4 5 6 7 X . . . . (81) while on your lap?
1 2 3 4 5 6 7 X . . . . (82) on an object, such as a bed, bouncer chair, or toy?

How often did the infant look up from playing:
1 2 3 4 5 6 7 X . . . . (83) when the telephone rang?
1 2 3 4 5 6 7 X . . . . (84) when s/he heard voices in the next room?

When your baby saw a toy s/he wanted, how often did s/he:
1 2 3 4 5 6 7 X . . . . (85) get very excited about getting it?
1 2 3 4 5 6 7 X . . . . (86) immediately go after it?

When given a new toy, how often did your baby:
1 2 3 4 5 6 7 X . . . . (87) get very excited about getting it?
1 2 3 4 5 6 7 X . . . . (88) immediately go after it?
1 2 3 4 5 6 7 X . . . . (89) seem not to get very excited about it?

Daily Activities

How often during the last week did the baby:
1 2 3 4 5 6 7 X . . . . (90) cry or show distress at a change in parents' appearance, (glasses off, shower cap on, etc.)?
1 2 3 4 5 6 7 X . . . . (91) when in a position to see the television set, look at it for 2 to 5 minutes at a time?

How often during the last week did the baby:
1 2 3 4 5 6 7 X . . . . (92) when in a position to see the television set, look at it for 5 minutes or longer?
1 2 3 4 5 6 7 X . . . . (93) protest being placed in a confining place (infant seat, play pen, car seat, etc)?
1 2 3 4 5 6 7 X . . . . (94) startle at a sudden change in body position (for example, when moved suddenly)?
1 2 3 4 5 6 7 X . . . . (95) appear to listen to even very quiet sounds?
1 2 3 4 5 6 7 X . . . . (96) attend to sights or sounds when outdoors (for example, wind chimes or water sprinklers)?
1 2 3 4 5 6 7 X . . . . (97) move quickly toward new objects?
1 2 3 4 5 6 7 X . . . . (98) show a strong desire for something s/he wanted?
1 2 3 4 5 6 7 X . . . . (99) startle to a loud or sudden noise?
1 2 3 4 5 6 7 X . . . . (100) look at children playing in the park or on the playground for 5 minutes or longer?
1 2 3 4 5 6 7 X . . . . (101) watch adults performing household activities (e.g., cooking, etc.) for more than 5 minutes?
1 2 3 4 5 6 7 X . . . . (102) squeal or shout when excited?
1 2 3 4 5 6 7 X . . . . (103) imitate the sounds you made?
1 2 3 4 5 6 7 X . . . . (104) seem excited when you or other adults acted in an excited manner around him/her?

When being held, how often did the baby:
1 2 3 4 5 6 7 X . . . . (105) pull away or kick?
1 2 3 4 5 6 7 X . . . . (106) seem to enjoy him/herself?
1 2 3 4 5 6 7 X . . . . (107) mold to your body?
1 2 3 4 5 6 7 X . . . . (108) squirm?

When placed on his/her back, how often did the baby:
1 2 3 4 5 6 7 X . . . . (109) fuss or protest?
1 2 3 4 5 6 7 X . . . . (110) smile or laugh?
1 2 3 4 5 6 7 X . . . . (111) wave arms and kick?
1 2 3 4 5 6 7 X . . . . (112) squirm and/or turn body?

When the baby wanted something, how often did s/he:
1 2 3 4 5 6 7 X . . . . (113) become upset when s/he could not get what s/he wanted?
1 2 3 4 5 6 7 X . . . . (114) have tantrums (crying, screaming, face red, etc.) when s/he did not get what s/he wanted?

When placed in an infant seat or car seat, how often did the baby:
1 2 3 4 5 6 7 X . . . . (115) wave arms and kick?
1 2 3 4 5 6 7 X . . . . (116) squirm and turn body?
1 2 3 4 5 6 7 X . . . . (117) lie or sit quietly?
1 2 3 4 5 6 7 X . . . . (118) show distress at first; then quiet down?

When frustrated with something, how often did your baby:
1 2 3 4 5 6 7 X . . . . (119) calm down within 5 minutes?

When your baby was upset about something, how often did s/he:
1 2 3 4 5 6 7 X . . . . (120) stay upset for up to 10 minutes or longer?
1 2 3 4 5 6 7 X . . . . (121) stay upset for up to 20 minutes or longer?

1 2 3 4 5 6 7 X . . . . (122) soothe her/himself with other things (such as a stuffed animal, or blanket)?

When rocked or hugged, in the last week, how often did your baby:
1 2 3 4 5 6 7 X . . . . (123) seem to enjoy her/himself?
1 2 3 4 5 6 7 X . . . . (124) seemed eager to get away?
1 2 3 4 5 6 7 X . . . . (125) make protesting noises?

When reuniting after having been away during the last week how often did the baby:
1 2 3 4 5 6 7 X . . . . (126) seem to enjoy being held?
1 2 3 4 5 6 7 X . . . . (127) show interest in being close, but resisted being held?
1 2 3 4 5 6 7 X . . . . (128) show distress at being held?

When being carried, in the last week, how often did your baby:
1 2 3 4 5 6 7 X . . . . (129) seem to enjoy him/herself?
1 2 3 4 5 6 7 X . . . . (130) push against you until put down?

While sitting in your lap:
1 2 3 4 5 6 7 X . . . . (131) how often did your baby seem to enjoy her/himself?
1 2 3 4 5 6 7 X . . . . (132) how often would the baby not be content without moving around?

How often did your baby notice:
1 2 3 4 5 6 7 X . . . . (133) low-pitched noises, air conditioner, heating system, or refrigerator running or starting up?
1 2 3 4 5 6 7 X . . . . (134) sirens from fire trucks or ambulances at a distance?
1 2 3 4 5 6 7 X . . . . (135) a change in room temperature?
1 2 3 4 5 6 7 X . . . . (136) a change in light when a cloud passed over the sun?
1 2 3 4 5 6 7 X . . . . (137) sound of an airplane passing overhead?
1 2 3 4 5 6 7 X . . . . (138) a bird or a squirrel up in a tree?
1 2 3 4 5 6 7 X . . . . (139) fabrics with scratchy texture (e.g., wool)?

When tired, how often was your baby:
1 2 3 4 5 6 7 X . . . . (140) likely to cry?
1 2 3 4 5 6 7 X . . . . (141) show distress?

At the end of an exciting day, how often did your baby:
1 2 3 4 5 6 7 X . . . . (142) become tearful?
1 2 3 4 5 6 7 X . . . . (143) show distress?

For no apparent reason, how often did your baby:
1 2 3 4 5 6 7 X . . . . (144) appear sad?
1 2 3 4 5 6 7 X . . . . (145) seem unresponsive?

How often did your baby make talking sounds when:
1 2 3 4 5 6 7 X . . . . (146) riding in a car?
1 2 3 4 5 6 7 X . . . . (147) riding in a shopping cart?
1 2 3 4 5 6 7 X . . . . (148) you talked to her/him?

Two Week Time Span

When you returned from having been away and the baby was awake, how often did s/he:
1 2 3 4 5 6 7 X . . . . (149) smile or laugh?

When introduced to an unfamiliar adult, how often did the baby:
1 2 3 4 5 6 7 X . . . . (150) cling to a parent?
1 2 3 4 5 6 7 X . . . . (151) refuse to go to the unfamiliar person?
1 2 3 4 5 6 7 X . . . . (152) hang back from the adult?
1 2 3 4 5 6 7 X . . . . (153) never "warm up" to the unfamiliar adult?

When in the presence of several unfamiliar adults, how often did the baby:
1 2 3 4 5 6 7 X . . . . (154) cling to a parent?
1 2 3 4 5 6 7 X . . . . (155) cry?
1 2 3 4 5 6 7 X . . . . (156) continue to be upset for 10 minutes or longer?

When visiting a new place, how often did the baby:
1 2 3 4 5 6 7 X . . . . (157) show distress for the first few minutes?
1 2 3 4 5 6 7 X . . . . (158) continue to be upset for 10 minutes or more?
1 2 3 4 5 6 7 X . . . . (159) get excited about exploring new surroundings?
1 2 3 4 5 6 7 X . . . . (160) move about actively when s/he is exploring new surroundings?

When your baby was approached by an unfamiliar person when you and s/he were out (for example, shopping), how often did the baby:
1 2 3 4 5 6 7 X . . . . (161) show distress?
1 2 3 4 5 6 7 X . . . . (162) cry?

<u>When an unfamiliar adult came to your home or apartment, how often did your baby:</u>
1 2 3 4 5 6 7 X . . . . (163) allow her/himself to be picked up without protest?
1 2 3 4 5 6 7 X . . . . (164) cry when the visitor attempted to pick her/him up?

<u>When in a crowd of people, how often did the baby:</u>
1 2 3 4 5 6 7 X . . . . (165) seem to enjoy him/herself?

<u>Did the baby seem sad when:</u>
1 2 3 4 5 6 7 X . . . . (166) caregiver is gone for an unusually long period of time?
1 2 3 4 5 6 7 X . . . . (167) left alone/unattended in a crib or a playpen for an extended period of time?

<u>When you were busy with another activity, and your baby was not able to get your attention, how often did s/he:</u>
1 2 3 4 5 6 7 X . . . . (168) become sad?
1 2 3 4 5 6 7 X . . . . (169) cry?

<u>When your baby saw another baby crying, how often did s/he:</u>
1 2 3 4 5 6 7 X . . . . (170) become tearful?
1 2 3 4 5 6 7 X . . . . (171) show distress?

<u>When familiar relatives/friends came to visit, how often did your baby:</u>
1 2 3 4 5 6 7 X . . . . (172) get excited?
1 2 3 4 5 6 7 X . . . . (173) seem indifferent?

<u>Soothing Techniques</u>

Have you tried any of the following soothing techniques in the last two weeks? If so, how quickly did your baby soothe using each of these techniques? Circle (X) if you did not try the technique during the <u>LAST TWO WEEKS</u>.

<u>When rocking your baby, how often did s/he:</u>
1 2 3 4 5 6 7 X . . . . (174) soothe immediately?
1 2 3 4 5 6 7 X . . . . (175) not soothe immediately, but in the first two minutes?
1 2 3 4 5 6 7 X . . . . (176) take more than 10 minutes to soothe?

<u>When singing or talking to your baby, how often did s/he:</u>
1 2 3 4 5 6 7 X . . . . (177) soothe immediately?
1 2 3 4 5 6 7 X . . . . (178) not soothe immediately, but in the first two minutes?
1 2 3 4 5 6 7 X . . . . (179) take more than 10 minutes to soothe?

When walking with the baby, how often did s/he:
1 2 3 4 5 6 7 X . . . . (180) soothe immediately?
1 2 3 4 5 6 7 X . . . . (181) not soothe immediately, but in the first two minutes?
1 2 3 4 5 6 7 X . . . . (182) take more than 10 minutes to soothe?

When giving him/her a toy, how often did the baby:
1 2 3 4 5 6 7 X . . . . (183) soothe immediately?
1 2 3 4 5 6 7 X . . . . (184) not soothe immediately, but in the first two minutes?
1 2 3 4 5 6 7 X . . . . (185) take more than 10 minutes to soothe?

When showing the baby something to look at, how often did s/he:
1 2 3 4 5 6 7 X . . . . (186) soothe immediately?
1 2 3 4 5 6 7 X . . . . (187) not soothe immediately, but in the first two minutes?
1 2 3 4 5 6 7 X . . . . (188) take more than 10 minutes to soothe?

When patting or gently rubbing some part of the baby's body, how often did s/he:
1 2 3 4 5 6 7 X . . . . (189) soothe immediately?
1 2 3 4 5 6 7 X . . . . (190) not soothe immediately, but in the first two minutes?
1 2 3 4 5 6 7 X . . . . (191) take more than 10 minutes to soothe?

Appendix I: Brief Infant-Toddler Social and Emotional Assessment (BITSEA)

BITSEA™

Parent Form

Child's name ____________________ Sex ☐ Boy ☐ Girl Date of birth ____/____/____

Parent/Guardian's name ____________________ Date of test ____/____/____

Was your child born prematurely? ☐ No ☐ Yes If yes, what was the expected date of birth? ____/____/____

Instructions: Many statements describe normal feelings and behaviors, but some describe feelings and behaviors that may be problems. Please do your best to respond to every item. Please circle the ONE response that best describes your child's behavior in the LAST MONTH.

0 = Not true / Rarely 1 = Somewhat true / Sometimes 2 = Very true / Often

1. Shows pleasure when he or she succeeds (for example, claps for self).	0 1 2 *
2. Gets hurt so often that you can't take your eyes off him or her.	0 1 2
3. Seems nervous, tense, or fearful.	0 1 2
4. Is restless and can't sit still.	0 1 2
5. Follows rules.	0 1 2 *
6. Wakes up at night and needs help to fall asleep again.	0 1 2
7. Cries or has a tantrum until he or she is exhausted.	0 1 2
8. Is afraid of certain places, animals or things. *What is he or she afraid of?* ____________	0 1 2
9. Has less fun than other children.	0 1 2
10. Looks for you (or other parent) when upset.	0 1 2 *
11. Cries or hangs onto you when you try to leave.	0 1 2
12. Worries a lot or is very serious.	0 1 2
13. Looks right at you when you say his or her name.	0 1 2 *
14. Does not react when hurt.	0 1 2
15. Is affectionate with loved ones.	0 1 2 *
16. Won't touch some objects because of how they feel.	0 1 2
17. Has trouble falling asleep or staying asleep.	0 1 2
18. Runs away in public places.	0 1 2
19. Plays well with other children (not including brother/sister). (Circle N if there is no contact with other children)	N 0 1 2 *
20. Can pay attention for a long time (other than when watching TV).	0 1 2 *
21. Has trouble adjusting to changes.	0 1 2
22. Tries to help when someone is hurt (for example, gives a toy).	0 1 2 *
23. Often gets very upset.	0 1 2
24. Gags or chokes on food.	0 1 2
25. Imitates playful sounds when you ask him or her to.	0 1 2 *
26. Refuses to eat.	0 1 2
27. Hits, shoves, kicks, or bites children (not including brother/sister). (Circle N if there is no contact with other children)	N 0 1 2
28. Is destructive. Breaks or ruins things on purpose.	0 1 2
29. Points to show you something far away.	0 1 2 *
30. Hits, bites or kicks you (or other parent).	0 1 2
31. Hugs or feeds dolls or stuffed animals.	0 1 2 *
32. Seems very unhappy, sad, depressed, or withdrawn.	0 1 2
33. Purposely tries to hurt you (or other parent).	0 1 2
34. When upset, gets very still, freezes, or doesn't move.	0 1 2

The following statements describe feelings and behaviors that can be problems for young children. Some of the descriptions may be a bit hard to understand, especially if you have not seen the behavior in your child. Please do your best to respond to all statements. Please circle the ONE response that best describes your child's behavior in the LAST MONTH.

35. Puts things in a special order over and over and gets upset if he or she is interrupted.	0 1 2
36. Repeats the same action or phrase over and over without enjoyment. *Please give an example:* ____________	0 1 2
37. Repeats a particular movement over and over (like rocking, spinning). *Please give an example:* ____________	0 1 2
38. Spaces out. Is totally unaware of what's happening around him or her.	0 1 2
39. Does not make eye contact.	0 1 2
40. Avoids physical contact.	0 1 2
41. Hurts self on purpose (for example, bangs his or her head). *Please describe:* ____________	0 1 2
42. Eats or drinks things that are not edible (like paper or paint). *Please describe:* ____________	0 1 2

1 = Not at all worried 2 = A little worried 3 = Worried 4 = Very worried

A. How worried are you about your child's behavior, emotions, or relationships?	1 2 3 4
B. How worried are you about your child's language development?	1 2 3 4

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Appendix J: PediaTrac™ 9 Month and Demographic Questionnaire

PediaTrac Demographics + Month 9 fNIRS Study

Start of Block: Demographics

Q1.1 The first three letters of my infant's last name and first three of his/her first name are... (Ex: John Smith would be SmiJoh)

____

Q1.2 My infant's gender is...

○ Male (1)

○ Female (2)

JS

Q1.3 Please select your infant's date of birth from the calendar.

Q83 Tell us whether this is your first child, or whether there are other children in the family, by selecting the number of children (please select "1" if this infant your first child)

▼ 1 (1) ... More than 12 (13)

Q1.4 Select the biological mother's year of birth...

▼ 1960 (1) ... Unknown (55)

Q1.5 Select the biological father's year of birth...

▼ 1960 (1) ... Unknown (55)

Q1.6 The highest level of education of the mother is....

▼ Some high school (1) ... Unknown (8)

Q1.7 The highest level of education of the father is....

▼ Some high school (1) ... Unknown (8)

Q1.8 What is the occupation of the mother?

▼ Accommodation and Food Services (1) ... Unknown (25)

Q1.9 What is the occupation of the father?

▼ Accommodation and Food Services (1) ... Unknown (25)

Q1.10 Please specify the ethnic background of your infant, the mother and father...

	Infant (1)	Mother (2)	Father (3)
NO Spansih/Hispanic/Latino ethnic background (1)	☐	☐	☐
Yes Spanish / Hispanic / Latino (2)	☐	☐	☐
Yes Mexican American, Chicano (3)	☐	☐	☐
Yes Puerto Rican or Cuban (4)	☐	☐	☐
Yes Other Hispanic? (5)	☐	☐	☐

Q1.11 Please specify the race background of your infant, the mother and father...

	Infant	Mother	Father
	Yes (1)	Yes (1)	Yes (1)

White (1)	○	○	○
Black or African-American (2)	○	○	○
American Indian or Alaska Native (3)	○	○	○
Native Hawaiian (4)	○	○	○
Other Pacific Islander (5)	○	○	○
Asian Indian (6)	○	○	○
Chinese (7)	○	○	○
Filipino (8)	○	○	○
Japanses (9)	○	○	○
Korean (10)	○	○	○
Vietnamese (11)	○	○	○
Other Asian (12)	○	○	○
From multiple races (13)	○	○	○
Other (please specify) (14)	○	○	○

Q1.12 Please drag and drop the languages spoken in the home to their appropriate designation box...

Primary Language	Secondary Language
______ Arabic (1)	______ Arabic (1)
______ Bengali (2)	______ Bengali (2)
______ English (3)	______ English (3)
______ French (4)	______ French (4)
______ Hindustani (5)	______ Hindustani (5)
______ Malay - Indonesian (6)	______ Malay - Indonesian (6)
______ Mandarin (7)	______ Mandarin (7)
______ Portugese (8)	______ Portugese (8)
______ Russian (9)	______ Russian (9)
______ Spanish (10)	______ Spanish (10)
______ Other (please specify) (11)	______ Other (please specify) (11)

Q1.13 Please specify your marital status...

▼ Married (1) ... Single (6)

Q1.14 Please provide us with contact information for future study questionnaires, beginning by writing in your First Name.

○ Your First Name (1) ____

Q1.15 Please provide email and zip code for contact about survey questions ....

○ Email (required) (1) ____

○ Zip Code (required) (2) ____

Q1.16 Please provide your phone number for contact about survey questions (note: phone number is optional and not required) ....

○ Your phone number (xxx-xxx-xxxx) (1)
____

Q1.17 In which state in the USA, or other country or continent if not USA, do you live in?

▼ Africa (1) ... Wyoming (61)

Q1.18 Do you own or rent your home?

○ Own (1)

○ Rent (2)

○ Other specify (3) ____

Q1.19 Please indicate your current household income in U.S. dollars

▼ Under $10,000 (1) ... Rather not say (10)

Q1.20 Please evaluate the frequency of your experience of the following statements.

When holding or bathing my infant I get distracted and think about other things. (1)	
When out in nature I pay attention without being distracted. (2)	
I tend to withhold my feelings from others. (3)	
My thinking seems to run on automatic pilot. (4)	
When my infant is upset or fussy I take the time to listen and to comfort him/her. (5)	
When I am feeling anxious I turn my attention to doing one thing after another. (6)	
I forgive others and easily let go of wrongs. (7)	

Q1.21 Please rate the quality of the following items as your personal experience, in your home or in the environment near your home.... (if any item is not applicable to your experience, check N/A)

Categories	Happy	Somewhat Happy	Neutral	Somewhat Sad	Sad	N / A
Drinking water quality (1)	○	○	○	○	○	☐ N / A
Indoor air quality (2)	○	○	○	○	○	☐ N / A
Outdoor air quality (3)	○	○	○	○	○	☐ N / A
Heating and cooling system (4)	○	○	○	○	○	☐ N / A
Eating habits (5)	○	○	○	○	○	☐ N / A
Organic food (6)	○	○	○	○	○	☐ N / A
Sanitation, bathroom, waste removal (7)	○	○	○	○	○	☐ N / A
Extreme hot or cold temperatures (8)	○	○	○	○	○	☐ N / A
Noise (9)	○	○	○	○	○	☐ N / A
Personal stress (10)	○	○	○	○	○	☐ N / A

Personal safety and crime (11)	○	○	○	○	○	▢ N / A
Physical exercise habits (12)	○	○	○	○	○	▢ N / A
Farm fields with pesticides (13)	○	○	○	○	○	▢ N / A
Coal burning power plant (14)	○	○	○	○	○	▢ N / A
High power electrical lines (15)	○	○	○	○	○	▢ N / A
Microwave or cell phone towers (16)	○	○	○	○	○	▢ N / A
Nuclear power plant (17)	○	○	○	○	○	▢ N / A
Vehicles and highways nearby (18)	○	○	○	○	○	▢ N / A
Other environmental exposure (19)	○	○	○	○	○	▢ N / A

End of Block: Demographics

Start of Block: Month Nine

Q2.1 As you begin to fill out this Month Nine survey, please tell us how you are feeling about your infant (click tab and slide to select closest answer).

1 (1)
2 (2)
3 (3)
4 (4)
5 (5)

Q2.2 Is your infant's head circumference bigger than it was at 6 months of age?

- Yes (1)
- No (2)
- Unknown (3)

Q2.3 Has your infant received any vaccinations?

- Yes (1)
- No (2)
- Unsure (3)

Q2.4 If "Yes", please specify type...

- ☐ DTAP (1)
- ☐ Hib (2)
- ☐ IPV (3)
- ☐ Prevnar 13 (4)
- ☐ Hepatitis B (5)
- ☐ Influenza (6)
- ☐ Other (please specify) (7)

Q2.5 Does your infant have any teeth?

- ○ Yes (1)
- ○ No (2)

Q2.6 Did your infant have any medical problems since you last visited Pediatrac?

- ○ Yes (1)
- ○ No (2)

Q2.7 If "Yes", please specify...

____

____

____

____

____

Q2.8 Have you noticed any changes in your infant's skin? (e.g., dryness, red patches, hives)

○ Yes (1)

○ No (2)

Q2.9 Have you noticed any regression (loss) of skills in any of these areas?

	Yes (1)	No (2)
Eating (1)	○	○
Sleeping (2)	○	○
Movement (3)	○	○
Language (4)	○	○
Social-emotional (5)	○	○

Page Break

Q2.10 **Please answer these questions about your infant's feeding and nutrition...**

What is your infant's primary source of nutrition? (1)	○ Breast milk (1)	○ Formula (2)	○ Combination of breast milk and formula (3)
Overall, is your infant feeding well? (3)	○ Yes (1)	○ No (2)	○ Uncertain (3)

Q2.11 If receiving breast milk...

	Yes (1)	No (2)
Is your infant latching on with entire nipple in his/her mouth? (1)	○	○
Are your breasts softer after nursing? (2)	○	○

Q2.12 If receiving breast milk, is your infant nursing about every 4 hours?

○ Yes (1)

○ No (2)

○ If No, how often are you nursing? (3) ____

Q2.13 If receiving breast milk, is your infant nursing on each breast for 10 minutes at each feeding?

○ Yes (1)

○ No (2)

○ If No, how long are you nursing? (3) ____________________

Q2.14 If receiving formula, is your infant being fed organic formula?

○ Yes (1)

○ No (2)

Q2.15 Is your infant receiving 24 - 32 fluid ounces of formula in 24 hours?

○ Yes (1)

○ No (2)

○ If No, how many ounces of formula in 24 hours? (3) ____________________

Q2.16 If receiving combination of breast milk and formula, what percentage of your infant's intake is..... (Note: Total should equal to 100%)
Breast milk : _______ (1)
Formula : _______ (2)
Total : ________

Q2.17 If receiving combination of breast milk and formula...

	Yes (1)	No (2)
During breast feeding, is your infant latching on with entire nipple in his/her mouth? (1)	○	○
During breast feeding, are your breasts softer after nursing? (2)	○	○

Q2.18 If receiving combination of breast milk and formula, how frequently are you breast feeding?

- ○ Every 3 hours (3)
- ○ Every 4 hours (4)
- ○ Every 5 hours (5)
- ○ Every 6 hours (6)
- ○ Every 7 hours (1)
- ○ Every 8 hours (2)

Q2.19 If receiving combination of breast milk and formula, how long are you breast feeding each time?

- ○ Less than 5 minutes (1)
- ○ 5 - 10 minutes (2)
- ○ More than 10 minutes (3)

Q2.20 If receiving combination of breast milk and formula... Is your infant being fed organic formula?

- Yes (1)
- No (2)

Q2.21 If receiving combination of breast milk and formula, how frequently are you formula feeding?

- Every 3 hours (3)
- Every 4 hours (4)
- Every 5 hours (5)
- Every 6 hours (6)
- Every 7 hours (1)
- Every 8 hours (2)

Q2.22 If receiving combination of breast milk and formula, how much formula is your infant taking at each feeding?

- Less than 6 ounces (1)
- 6 - 8 ounces (2)
- More than 8 ounces (3)

Q2.23 My infant is CURRENTLY prescribed the following medications, vitamins and/or supplements...

◯ Known medications, vitamins or supplements, please specify: (1)
____

◯ None (2)

◯ Unknown (3)

Q2.24 How many wet diapers is your infant having per day?

▼ 1 (1) ... More than 8 (9)

Q2.25 How many bowel movements is your infant having per day?

▼ 1 (1) ... More than 12 (13)

Q2.26 **Please answer these questions about your infant's feeding and nutrition...**

	Yes (1)	No (2)
Is your infant drinking from a cup more often than a bottle? (1)	○	○
Is your infant eating at least 3 meals plus 2-3 snacks per day? (2)	○	○
Is your infant taking solid foods? (3)	○	○
Can your infant sit up in a high chair or on your lap? (4)	○	○

Q2.27 Does your infant like or accept these solid foods, or have an reaction to these solid foods?

	Likes / Accepts?		Reaction?
	Likes / Accepts (1)	No (2)	
Rice cereal (1)	○	○	▼ Skin (1) ... Diarrhea (4)
Oat cereal (2)	○	○	▼ Skin (1) ... Diarrhea (4)
Wheat cereal (3)	○	○	▼ Skin (1) ... Diarrhea (4)
Vegetables (4)	○	○	▼ Skin (1) ... Diarrhea (4)
Fruits (5)	○	○	▼ Skin (1) ... Diarrhea (4)

Q2.28 **Please answer these questions about your infant drinking water....**

	Drinking water?		If yes, which type?			How many fluid ounces of each?		
	Yes (1)	No (2)	Tap water (1)	Bottled water (2)	Well water (3)	Tap water (1)	Bottled water (2)	Well water (3)
Is your infant drinking water? (1)	○	○	○	○	○			

Q2.29 **Please answer these questions about your infant drinking juice....**

	Drinking juice?		If yes, which type?		How many fluid ounces of each?	
	Yes (1)	No (2)	100% juice (1)	Other juice drink (2)	100% juice (1)	Other juice drink (2)
Is your infant drinking juice? (1)	○	○	○	○		

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Q2.30 **Please answer these questions about your infant's sleep patterns....**

	Yes (1)	No (2)
Is your infant sleeping through the night? (1)	○	○
Is your infant able to soothe him/herself back to sleep? (2)	○	○
Is your infant sleeping in his/her own bed/crib? (3)	○	○
Has your infant developed a consistent bedtime routine? (4)	○	○
Does your child have difficulty with changes in the bedtime routine? (5)	○	○

Q2.31 How many naps does your infant take per day?

○ 0 (1)

○ 1 - 2 (2)

○ more than 2 (3)

Q2.32 How many continuous hours does your infant sleep at night?

▼ 1 (1) ... More than 12 (13)

Q2.33 **Please answer these questions about your infant's movement and motor development...**

	Yes (1)	No (2)
Can your infant get from sitting to crawling position on hands and knees? (1)	○	○
While lying will the infant hold onto an individual's fingers to pull him/herself into a sitting position? (2)	○	○
Can your infant sit unsupported? (3)	○	○
Can your infant pull up to a standing position by him/herself? (4)	○	○
Will your infant shift weight from foot to foot to reach for items when standing with support? (5)	○	○
Will your infant bang objects together with his/her hands? (6)	○	○
Does your infant pick up small objects (such as cheerios) with their first finger and thumb? (7)	○	○

Q2.34 **Please answer these questions about your infant's receptive communication and language development...**

	Yes (1)	No (2)
When you look at or point to an object, does your infant look at what you are looking at or pointing to? (1)		
Does your infant recognize familiar words and names? (2)		
Does your infant understand "No!"? (3)		

Q2.35 **Please answer these questions about your infant's expressive communication and language development...**

	Yes (1)	No (2)
Does your infant attempt to get you to look at an object across the room by eye contact, vocalizing or by gesture? (1)		
During play, does your infant repeat your actions? (2)		
Does your infant point to objects? (3)		
Does your infant use at least 3 consonant sounds such as /b/, /d/, /k/, /g/, /m/, /p/? (4)		
Does your infant vocalize 2-syllable sounds such as "baba" or "dada"? (5)		
Is your infant using single words? (6)		

Q2.36 **Please answer this question about your infant's receptive and expressive communication and language development...**

	Yes (1)	No (2)
Does your infant respond to your emotions by imitating them? For example, does your infant become sad when you are sad, or laugh when you laugh? (1)	○	○

Q2.37 **Please answer these questions about your infant's cognitive development...**

	Yes (1)	No (2)
Can your infant tell the difference between familiar caregivers (e.g. mother, father, grandparents, nanny) as opposed to strangers? (1)	○	○
Does your infant appear to be cautious with strangers? (2)	○	○
Does your infant search for a hidden object when it is moved out of sight? (3)	○	○
Does your infant rummage through drawers and cabinets? (4)	○	○
Does your infant enjoying putting this in containers? (5)	○	○
Does your infant enjoy taking things out of containers? (6)	○	○
Does your infant enjoy cause and effect toys, watching things drop and pop? (7)	○	○
Does your infant play interactive games like Paddy-cake, Peek-a-boo and Tickle? (8)	○	○

Q2.38 **Please answer these questions about your infant's attachment behavior and development...**

	Yes (1)	No (2)
Does your infant seek out parents? (1)	○	○
Does your infant explore his/her environment? (2)	○	○

Q2.39 **Please indicate WHO your infant responds to for eye contact (gazing), holding and calming... (please check as many as apply)**

	Mother (1)	Father (2)	Grandparents (3)	Daycare Provider (4)	Other (5)	Sibling (6)	No one (7)
Who does your infant look at when awake? (1)	☐	☐	☐	☐	☐	☐	☐
When they speak, who does your infant look at? (2)	☐	☐	☐	☐	☐	☐	☐
Who calms your infant by how they touch the infant? (3)	☐	☐	☐	☐	☐	☐	☐
Who can calm your infant by picking up or holding him / her? (4)	☐	☐	☐	☐	☐	☐	☐

Who can calm your infant by how they speak with their voice? (5)	▢	▢	▢	▢	▢	▢	▢

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Q2.40 **The following series of questions ask about the current weight and length of your infant. What type of measurement would you prefer to answer these questions?**

- ◯ British measurement (pounds and ounces for weight and inches for length) (1)
- ◯ Metric measurement (grams for weight and centimeters for length) (2)

Q2.41 What is your infant's CURRENT weight? (Fill in a number for both pounds and ounces).
________ lbs (1)
________ ounces (2)

JS

Q2.42 What is your infant's CURRENT length? (Fill in the number of inches)

- ◯ Length in Inches (1) ____

JS

Q2.43 What is your infant's CURRENT weight? (Fill in the number of grams)

____

JS

Q2.44 What is your infant's CURRENT length? (Fill in the number of centimeters)

____

Q2.45 **Please rate your level of concern with any domain of your infant's development (if you feel Uncertain about any domain, check the box)**

Domain	Sad	Somewhat Sad	Neutral	Somewhat Happy	Happy	Uncertain
Eating (1)	○	○	○	○	○	☐ Uncertain
Sleeping (2)	○	○	○	○	○	☐ Uncertain
Movement (3)	○	○	○	○	○	☐ Uncertain
Communication / Language (4)	○	○	○	○	○	☐ Uncertain
Social / Emotional (5)	○	○	○	○	○	☐ Uncertain

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Q2.46 **Please list 3-5 words that describe your relationship with your infant.**

____

____

____

____

____

Q2.47
Please list 3-5 words that describe your infant.

____

____

____

____

____

Q2.48
I think the words I listed above will probably describe my child for a long time.

- ○ Definitely Yes (6)
- ○ Maybe Yes (3)
- ○ Neither Yes or No (4)
- ○ Maybe No (5)
- ○ Definitely No (2)

Q2.49
Please indicate the degree to which you agree with the following statements about your baby. Click the tab and slide it to the area that most closely reflects how you feel. A tab closer to "7" indicates greater levels of agreement, while a tab closer to "1" indicates higher levels of disagreement.

My baby seems to have a pretty easy going nature. (1)	
While my baby shares some similarities with me and the other parent, s/he seems to have a unique personality. (2)	
When my infant cries or fusses, I think s/he is doing it on purpose to get a rise out of me. (3)	
My infant gets emotionally upset a lot. (4)	
My infant doesn't really need me that much because s/he is really independent. (5)	

Q2.50 **Please indicate the degree to which you agree with the following statements about your baby. Click the tab and slide it to the area that most closely reflects how you feel.**

My baby seems to have a lot of different feelings. (1)	
My baby feels the same way I do in most or all situations. (2)	
I often wonder about what my baby is thinking and feeling. (3)	
It's OK if my baby thinks differently than me. (4)	
I have no idea why my baby does certain behaviors. (5)	
I can understand what my baby is thinking or feeling by watching him/her. (6)	
I always know what my child is thinking and feeling. (7)	
I try to figure out what my child is thinking and feeling. (8)	

Q2.51
Please indicate how often you have the following thoughts and feelings about parenting your baby on a scale ranging from "Never" to "All of the Time." Click the tab and slide it to the area that most closely reflects how you feel.

Taking care of my baby is stressful. (1)	
Having a baby has really interfered with the other things I need or want to do. (2)	
Taking care of my baby is more difficult than I thought it would be. (3)	
Being a mother is a lot more stressful than I thought it would be. (4)	
My baby is harder to take care of than most other babies. (5)	
I worry about my infant. (6)	
The daily tasks involved in taking care of my baby overwhelm me. (7)	

Q2.52 **For each of the following statements about your baby, please indicate the degree to which you agree with that statement. Click the tab and slide it to the area that most closely reflects how you feel.**

Picking up my baby a lot will spoil him/her. (1)	
It is important to get the baby on my schedule/ routine as quickly as possible. (2)	
It is important to be available to my child if s/he needs me. (3)	

Q2.53 **Please indicate how often the following statements happen on a scale ranging from "Never" to "All of the Time." Click the tab and slide it to the area that most closely reflects how you feel.**

When my baby is upset, I pay attention to him/her. (1)	
I am affectionate with my baby. (2)	
I try to follow my baby's lead. (3)	
When my baby is crying, I ignore him/her. (4)	
My baby's needs come before my own needs. (5)	

Q2.54 **Please indicate how much of the time the following statements about you, your baby, and your parenting are true, on a scale ranging from "Never" to "All of the Time." Click the tab and slide it to the area that most closely reflects how you feel.**

My child is perfect. (1)	
I love being a parent. (2)	
My own childhood was perfect. (3)	

Q2.55 **For each of the following statements, please indicate the degree to which you agree with that statement. Click the tab and slide it to the area that most closely reflects how you feel.**

There is nothing I would change about my child or my parenting if I could. (1)	
There is nothing stressful about being a parent. (3)	

Q2.56 **Below are a list of statements that describe how people sometimes feel. Thinking over the past few weeks, on a scale ranging from "never" to "All of the Time," please rate how often you have felt the following statements:**

I have felt down, "blue," or sad. (1)	
I have been more tearful than usual. (2)	
I have felt anxious or "keyed-up." (3)	
I have felt irritable or easily annoyed (5)	
I have lost interest in things or don't feel like doing things that I usually enjoy. (6)	
I have a hard time controlling my worries. (7)	
I have not wanted to be around other people and prefer to be alone. (8)	

Q2.57 **Please tell us anything else you would like to share about your infant, and how things are going for you as a caregiver to your infant. Thank you for completing this Pediatrac survey.**

End of Block: Month Nine

Start of Block: Additional Demographics

Q990 The first three letters of my infants last name and first three letters of his/her first name are... (Ex: John Smith would be SmiJoh)

Q991 My infant's date of birth is...

____

Q992 Please describe your relationship with the newborn infant...

- ◯ Mother (biological) (1)
- ◯ Father (biological) (2)
- ◯ Mother (adopted or foster) (3)
- ◯ Father (adopted or foster) (4)
- ◯ Mother (Surrogate) (5)
- ◯ Grandparent (6)
- ◯ Other relative (for example, aunt, uncle, sibling) (7)
- ◯ Legal guardian (8)
- ◯ Other (specify) (9) ____

Q993 Tell us whether this is your first child, or whether there are other children in the family, by selecting the number of children (please select "1" if this infant your first child)

▼ 1 (1) ... More than 12 (13)

Q994 How many weeks of gestation was the mother pregnant, carrying your infant?

▼ Under 24 weeks (1) ... Uncerain (21)

Q995 Were any of the following aids used to conceive? (Check all that apply)

- ☐ Fertility medications (1)
- ☐ In vitro fertilization (2)
- ☐ Other methods (3)
- ☐ Did not use reproductive technologies (4)

Q996 How was your infant delivered?

▼ Vaginal (1) ... Unknown (3)

Q997 Where did your infant's birth take place?

▼ Hospital (1) ... Other (4)

Q998 Please answer these questions about the biological parent...

	Yes (1)	No (2)	Uncertain (3)
Did the biological mother and infant receive prenatal care? (1)	○	○	○
Did the parents receive genetic testing or counseling? (2)	○	○	○

Q999 Please answer these questions about the pregnancy and delivery ....

	Yes (1)	No (2)	Uncertain (3)
Were there any complications with the pregnancy? If Yes,specify (1)	○	○	○
Were there any complications with the delivery? If Yes, specify (2)	○	○	○
Was your infant a multiple birth? (for example, twin or triplet) (3)	○	○	○
Did your infant receive hepatitis B vaccination in the hospital? (4)	○	○	○
Did your infant spend any time in the NICU neonatal intensive care unit or special care nursery? (5)	○	○	○

Q1000 If "Yes" that your infant spent time in the NICU or special care nursery, how long?

○ 1 - 9 days (1)

○ 10 days or more (2)

Q1001 My infant has a medical / clinical diagnosis of...(please also specify if more than one diagnosis)

____

____

____

____

____

Q1002 Have you noticed any loss (regression) of skills in any of these areas since the birth of your infant?

	Yes (1)	No (2)
Eating (1)	○	○
Sleeping (2)	○	○
Movement (3)	○	○

Q1003 The MOTHER took the following medications or drugs, vitamins or supplements during pregnancy...

- ◯ Known medications or drugs, vitamins or supplements, please specify (1) ____
- ◯ None (2)
- ◯ Unknown (3)

Q1004 My INFANT is prescribed the following medications, vitamins and/or supplements...

- ◯ Known medications, vitamins or supplements, please specify (1) ____
- ◯ None (2)
- ◯ Unknown (3)

Q1005 Indicate your family history of medical, developmental, or psychiatric disorders on both mother's and father's side of the family... (please check all that apply).

	Mother (1)	Mother's Side (2)	Father (3)	Father's Side (4)	Sibling (5)
Cardiologic (heart / vascular) (1)	▢	▢	▢	▢	▢
Endocrinologic / glands (2)	▢	▢	▢	▢	▢
Gastroenterologic (stomach / intestines) (3)	▢	▢	▢	▢	▢
Hematologic (blood) (4)	▢	▢	▢	▢	▢
Hepatologic (liver / gall bladder) (5)	▢	▢	▢	▢	▢
Nephrologic (kidney) (6)	▢	▢	▢	▢	▢
Pulmonary / Respiratory (lungs) (7)	▢	▢	▢	▢	▢
Neurologic (brain) (8)	▢	▢	▢	▢	▢
Musculoskeletal (bones / joints) (9)	▢	▢	▢	▢	▢
Language delays (10)	▢	▢	▢	▢	▢
Motor delays (11)	▢	▢	▢	▢	▢
Cognitive delays / Mental retardation (12)	▢	▢	▢	▢	▢

Depression (13)	☐	☐	☐	☐	☐
Anxiety (14)	☐	☐	☐	☐	☐
Schizophrenia (15)	☐	☐	☐	☐	☐
Autism (16)	☐	☐	☐	☐	☐
Aspergerger's (or Pervasive developmental disorder) (17)	☐	☐	☐	☐	☐
Learning disabilty (18)	☐	☐	☐	☐	☐
Substance addiction (19)	☐	☐	☐	☐	☐
Eating disorder (20)	☐	☐	☐	☐	☐
Unknown (21)	☐	☐	☐	☐	☐
Other (please specify) (22)	☐	☐	☐	☐	☐
None of the above (23)	☐	☐	☐	☐	☐

Q1006 Please indicate if your infant has any unusual markings or malformations in these locations....

	Yes (1)	No (2)
Head (1)	○	○
Facial features (2)	○	○
Torso (3)	○	○
Hands / feet (4)	○	○
Skin (5)	○	○
Genitalia (6)	○	○

Q1007 Did your infant have any medical problems?

○ If yes, please specify (1) ____

○ No (2)

○ Uncetain (3)

Q1008 Did your infant pass their newborn hearing screen?

- Yes (1)
- No (2)
- Unertain (3)

Q1009 Did your infant have an abnormal newborn screening evaluation?

- Yes (1)
- No (2)
- Unknown (3)

Q1010 If "Yes", your infant had a abnormal newborn screening, specify which conditions were identified... (please check as many as apply)

- ☐ Biotinidase (1)
- ☐ Congenital hearing loss (2)
- ☐ Congenital Hypothyroidism (CH) (3)
- ☐ Congential adrenal hyperplasia (CAH) (4)
- ☐ Cystic fibrosis (5)
- ☐ CPS, carbamoylphosphate synthetase (6)
- ☐ G6PD, glucose 6 phosphate dehydrogenase (7)
- ☐ Galactosemia (8)
- ☐ HHH, hyperammonemia/ornithinemia/citrullinemia (ornithine transporter defect) (9)
- ☐ HIV (10)
- ☐ Homocystinuria (11)
- ☐ Maple syrup urine disease (12)
- ☐ MCAD deficiency (13)
- ☐ NKH, nonketotic hyperglycinemia (14)
- ☐ Phenylketonuria (PKU) (15)

- [ ] PRO, prolinemia (16)
- [ ] Sickle cell disease (17)
- [ ] Thalassemia (18)
- [ ] TOXO, toxoplasmosis (19)
- [ ] Tyrosinemia (20)
- [ ] 5-OXO, 5-oxoprolinuria (pyroglutamic aciduria) (21)
- [ ] Other, please specify (22) ____

Q1011 Is your infant receiving support services in the home? (please specify yes or no to the following list...)

	Yes (1)	No (2)
Nursing (1)	○	○
Dietetics / feeding specialist (2)	○	○
Social work (3)	○	○
Other support (specify) (4)	○	○

JS

Q1012 What was your infant's BIRTH length? (Fill in the number of inches)

○ Length in Inches (1) ____

JS

Q1013 What was your infant's BIRTH weight? (Fill in the number of grams)

____

JS

Q1014 What was your infant's BIRTH length? (Fill in the number of centimeters)

____

End of Block: Additional Demographics