FOCUSED ATTENTION AND HEART RATE DURING EXPLORATORY PLAY IN HEALTHY PRETERM AND TERM-BORN INFANTS

by

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ABSTRACT

Focused Attention and Heart Rate during Exploratory Play in Healthy Preterm and Term-born Infants

Infant attention is central to early development. Previous research has linked focused attention during infant exploratory play to preschool cognition. Importantly, focused attention and information processing have been related to sustained decreases in heart rate (HR), which show developmental changes in infancy. Few studies have examined the relationship between focused attention, heart rate and development in very preterm infants, who are vulnerable to cognitive and attention problems. Participants were 35 extremely low gestational age (ELGA; ≤28 weeks), 48 very low gestational age (VLGA; 29-32 weeks) and 46 healthy term-born infants seen at 8-months corrected age. Focused attention was timed and global focused attention was rated using a toy exploration paradigm. Heart rate was recorded continuously during attention testing. Mean HR and heart rate variability (HRV) were assessed during infant exploration. Additionally, change in mean HR for all focused episodes, and the mean and greatest HR change for the peak focus were calculated. Bayley Scales of Infant Development (BSID-II, Mental Development Index [MDI]) were administered.

Term-born infants were rated higher on global focused attention than VLGA, and marginally higher than ELGA infants. For all infants, greater HRV suppression during exploration and magnitude of HR deceleration during the peak focus were related to greater attentiveness. No group differences were seen in HRV suppression. However, ELGA infants showed greater HR deceleration during focused attention compared to VLGA and Term-born infants. Furthermore, after controlling for perinatal risk, infant peak focus and degree of HR deceleration predicted 8-month MDI for the ELGA (49% of the total variance), but not VLGA infants. This may reflect enhanced attentional effort to compensate for information processing deficits among the highest risk infants. These findings extend research on attention and heart rate during exploratory play to understanding the links between attention regulation, heart rate and cognitive development in very preterm infants. Further knowledge in this area will facilitate the development of effective methods to identify infants very early in life who are at-risk for attention and cognitive problems, and may lead to interventions that can improve developmental outcomes for vulnerable infants.

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List of Abbreviations / Definition of Key Terms

AGA	Appropriate for gestational age (based on statistical norms, weight within 10th and 90th percentile range for given gestational age)
Apgar score	Evaluated postnatally at 1 and 5 minutes based on heart rate, breathing, muscle tone, reflexes and colour (Score 1-10).
Apnea	Lapse of breath for a period of 20 seconds or more
BPD	Bronchopulmonary dysplasia (injury, inflammation, or scarring of the lungs due to oxygen, prematurity, infection, and/or ventilators).
BSID II	Bayley Scales of Infant Development, 2nd Edition
CCA	Corrected age (adjusted age of the infant if born on the projected due date for a term birth)
CNS	Central nervous system
ELGA	Extremely Low Gestational Age (<29 weeks gestation)
ELBW	Extremely Low Birthweight (<800grams or <1000grams, depending on the studies)
GA	Gestational age, as determined by second trimester ultrasound or from the first day of the mother's last normal menstrual period to date of delivery
HR	Heart rate
HRV	Heart rate variability
HRSD	Standard deviation of heart rate
IVH	Intraventricular hemorrhage (Grades I to IV according to bleed around ventricles; increasing severity associated with long-term complications)
LGA	Large for gestational age
MDI	Mental Development Index, Bayley Scales of Infant Development, 2nd Edition (BSID II)
NICU	Neonatal Intensive Care Unit

NMI	Neonatal Medical Index, a risk score that stratifies preterm infants into risk groups for serious complications and the infant's condition during hospitalization
NIDCAP	Newborn Individualized Developmental Care and Assessment Program
RDS	Respiratory Distress Syndrome, difficulty with independent breathing, due to immaturity in the development of the lungs
PVL	Periventricular Leukomalacia
RSA	Respiratory Sinus Arrythmia
SGA	Small for gestational age, birthweight below the 10th percentile on a standard growth chart
SNAP II	Severity of Neonatal Acute Physiology,
Very Preterm	Gestational age less than 32 completed weeks (<259 days)
VLGA	Very Low Gestational Age (29-32 weeks gestation)
VLBW	Very Low Birthweight (<1500 grams)

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Dedication

As an acknowledgment of the support and encouragement I have always received from my mother and father, I dedicate this doctoral dissertation to my parents Franklin and Peggy Petrie. I express my deep appreciation to my husband Raul, for his patience and care throughout my doctoral program, interrupted by the premature birth of our beautiful twin girls, and subsequent challenge of completing both our graduate degrees with the responsibilities and joys of parenthood. This dissertation was also completed in memory of my brother Christopher Petrie, who was granted a BSc in Chemical Physics shortly after what would have been his twenty-first birthday, and who would have continued to excel academically.

CHAPTER 1: INTRODUCTION

Context for Program of Study and Research

This doctoral dissertation "Focused attention and heart rate in healthy preterm and term-born infants" was completed as part of my program of PhD studies through the Interdisciplinary Studies Graduate Program (ISGP) at the University of British Columbia (UBC). The ISGP at UBC is one of the only programs in North America to offer doctoral degrees to independently motivated individuals who complete a demanding and unique program of study. As my Supervisor and Committee, five highly accomplished faculty came together with different areas of expertise and subfields including attention, early development, education, prematurity and neonatology, and cardiac physiology (Psychology, Early Human Development, Education, Neonatology and Developmental Pediatrics). Students enter the program with proven capabilities and a compelling interdisciplinary research topic, which combines and expands existing disciplines to advance research. In my case this involved the study of the development and regulation of focused attention in very preterm and term-born infants from various vantage points and methods. My work was further inspired by research "communities" that as an interdisciplinary doctoral student, in effect constituted "home" departments, and in my estimation the most ideal contexts through which to complete doctoral research of this nature. Community Child Health Research (CCHR) at the Child and Family Research Institute of British Columbia, which partners both with UBC and the Children's and Women's Health Centre of British Columbia (C&W), is located on the C&W site. Thus there were opportunities, with onsite expertise, to gain knowledge about the medically high-risk infants born at extremely and very low-gestational ages, from the point of view of the infant's beginning of life in the Neonatal Intensive Care Unit, C&W as well as from the point of view of the infant's developmental and clinical course, as many of these infants were followed in outpatient clinics at C&W. The CCHR setting also allowed excellent mentorship and exposure to high-level research of early human development emphasizing various perspectives, including specific physiological measures and technology for detailed behavioural coding. This not only provided training and exposure to a variety of techniques currently used in bio-behavioural research but also enabled a well- rounded focus necessary for advancing understanding of early development of focused attention in this doctoral research. On a larger scale, the Human Early Learning Partnership (HELP) provided academic enrichment, through participation in HELP seminars, retreats and conferences. Through HELP, prominent researchers as well as graduate students from all Universities across British Columbia exchange ideas and contribute to a rich interdisciplinary environment. Through HELP findings of researchers together have prompted interest and investment in early child development in Canada, and HELP functions as an international voice for issues in early child development as a designated resource for the World Health Organization. Thus, as a doctoral student in Interdisciplinary Studies, UBC, both the CCHR and the HELP group provided ongoing examples and inspiration as researchers sought to examine important trans-disciplinary issues and questions regarding early developmental processes. As an emerging pediatric researcher, the HELP group has provided me not only with some of the best examples of research in early development, but also ample inspiration for future research that will address important contextual factors, and has the potential to make a difference in the lives of young at-risk infants and their families. It is my hope that findings from this doctoral research, which brought together a variety of areas of expertise, may signal the beginning of a career where, together with other interdisciplinary researchers, I can contribute to understanding the early development of the ability to regulate and focus attention as a key to cognitive development and perhaps ultimately as a foundation for early risk assessment in vulnerable populations.

Focused Attention in Infants

One of the most important advances in infant development is acquisition of the ability to focus on and sustain attention to objects and events. In the second half of the first year of life, there are significant developments in the infant's regulation of attention, which consist of allocating and controlling attention to various stimuli, as a function of the infant's internal processes (Colombo & Cheatham, 2006). Maturational changes include increases in "endogenous attention," which is qualitatively and developmentally differentiated from other forms of attention such as simple orienting or the more reflexive "attentional capture" to objects and events that are evident much earlier in the infant's repertoire. As a form of attention that requires relatively more cognitive interest or effort (Kahneman, 1973), endogenous attention involves a more sustained interest or prolonged focused attention that enables infants to process information and resist distraction (Colombo et al., 2006). A number of researchers have identified the period between 7 and 10 months of age as potentially a very useful time for the detection of attention problems because endogenous attention increases markedly at this time of infant development (Colombo, 2001; Colombo, Harlan, & Mitchell, 1999; Lawson & Ruff, 2004b). Interestingly, it is also during this developmental phase of infancy that attention associated with information processing using measures of habituation and recognition memory, have traditionally been assessed to successfully predict childhood cognitive outcomes (e.g., McCall & Carriger, 1993; Rose, Feldman, & Wallace, 1988; Rose & Orlian, 2001).

During the second half of the first year of life, infants show a rapid and strong response to novel events, and, with the development of grasping, an intense interest in manually exploring novel objects (Graham, Anthony, & Zeigler, 1983; Ruff, McCarton, Kurtzberg, & Vaughan, 1984). Thus, independent exploration of novel objects becomes a predominant activity over this period (Smith, Pretzel, & Landry, 2001). Numerous researchers have observed and quantified the natural tendency to explore during this phase of infancy, in particular detailing the nature of infants' attention to 3-dimensional novel objects. In the paradigm of exploratory play with novel objects, measures of concentrated examining and focused attention reflect the cognitively active phase of attention (e.g., Lansink & Richards, 1997n; Lawson & Ruff, 2001; Oakes & Tellinghuisen, 1994; Ruff, Capozzoli, & Saltarelli, 1996a; Ruff & Lawson, 1991). Additionally, researchers have used measures of focused attention during exploratory play to predict later behaviour and cognition. In fact, numerous studies have found that infant examining behaviours during exploratory play are related to concurrent as well as later cognition and attention outcomes throughout infancy and the toddler and preschool ages in both full-term infants (Ruff, Lawson, Parrinello, & Weissberg, 1990a) and preterm infants (Lawson et al., 2001; Lawson & Ruff, 2004a; Ruff, Lawson, Parrinello, & Weissberg, 1990b).

It is particularly important to study early attention regulation in vulnerable or "at-risk" populations, such as those born very preterm. Children born at very low birthweight (<1500g; VLBW) or very low gestational ages (<32 weeks; VLGA) experience a higher incidence of attention-related problems and learning and cognitive difficulties at school age than their healthy term-born counterparts (e.g., Pharoah, Stevenson, Cooke, & Stevenson, 1994; Rose & Feldman, 2000; Taylor, Klein, Minich, & Hack, 2000a). Relatively poorer attention may result in less adequate acquisition of relevant information, and, over time, may contribute to deficits in cognitive development. For those children who are born at extremely low birthweight (<1000 or <800 grams; ELBW) or extremely low gestational ages (≤28 weeks; ELGA), outcome problems are generally greater than for children born at later gestations (e.g., Anderson & Doyle, 2003a; Grunau, Whitfield, & Davis, 2002a; Taylor, Hack, & Klein, 1998). Additionally, few studies compare sex differences in outcomes of very preterm infants, despite the recognition that in relation to perinatal illness and learning problems, that preterm boys are at higher risk than girls for neurodevelopmental problems (e.g., Whitfield, Grunau, & Holsti, 1997a). Further knowledge of early attention regulation in biologically vulnerable infants born very preterm can potentially help to identify specific characteristics of early focused attention behaviours which are essential to understanding the etiology of the attention, learning, and cognitive deficits so prevalent in this population.

Given the significance of studying focused attention in the earliest years, this dissertation research was undertaken to compare the specific attributes of focused attention during exploratory play at 8 months of age in two groups of very preterm infants defined by gestational age, to those in a group of healthy term-born infants. Focused attention was studied during infants' independent exploration of 3-dimensional novel objects, using a paradigm of exploratory play as described in numerous studies of infants in the second half of the first year of life (Ruff et al., 1991). To replicate previous research behavioural indices of focused attention including duration, frequency, and latency of focus, were examined during independent exploration of novel objects by preterm and term-born infants. To add to existing knowledge related to preterm birth and risk of problems in early attention regulation, clearly defined groups of preterm infants were compared, based on gestational age (GA) at birth and sex. This dissertation research also compared 5-point global ratings of focused attention (Lawson et al., 2001) across infant groups. These global ratings of focused attention represent a potentially useful measure in the clinical assessment of "at-risk" infants very early in life and were formerly validated with very preterm infants at 7 and 12 months of age (Lawson et al., 2001); however, these ratings have not previously been compared to a control group of healthy term-born infants. Thus, along with a number of focused attention measures, this current study uses Lawson and Ruff's (2001) 5-point global ratings of focused attention to assess three groups of infants at age 8 months corrected chronological age (CCA), including those born at extremely low gestational age (ELGA, <28 weeks GA), very low gestational age (VLGA, 29 to 32 weeks GA), and term-born.

Regulation of Heart Rate as Related to Focused Attention

A second aim of this research was to compare heart rate response in preterm versus term-born infants during their independent exploration of novel objects and during behaviourally identified periods of focused attention. Indices of heart rate or heart rate variability can provide additional information on the infant's level of engagement and attention regulation. Heart rate indices are indirect measures of central nervous system organization and status, and they provide information about the responses and adaptations of the autonomic and central nervous systems to behavioural demands that arise from cognitive interest or challenge (Grossman, 1992b). Heart rate response during exploratory play has received very little attention in preterm infants. This dissertation research extends the body of research on behaviourally defined focused attention in term-born infants as related to specific patterns of heart rate response.

Term-born infants have been shown to exhibit a developmental increase in the organization of attention during the exploration of objects across ages 6, 9, and 12 months, as related to phases of heart rate that are thought to reflect focused attention and information processing (i.e. sustained decreases in heart rate) (Lansink, Mintz, & Richards, 2000). In another study of term-born infants, Lansink et al. (1997m) examined the relationship of heart rate change to changes in behaviour including focused and more "casual" attention across these same ages. To assess degree of engagement according to behaviour or heart rate, they presented infants with distracting stimuli during periods where the infant showed focused attention (as defined by Holly Ruff and colleagues), or during phases of heart-rate that showed prolonged deceleration, compared to periods where the infant was casually engaged with the object or during other phases of heart rate (phases showing that the heart rate was returning to pre-stimulus levels). Since infants were found to be less distractible during focused behavioural attention or during the phase when heart rate indicated sustained deceleration, they suggested that these periods reflect active processing. Furthermore, in this study, infants were found to have the longest distraction latencies when stimuli were presented, both when heart rate showed prolonged deceleration, and when behavioural attention was focused. Importantly, these results indicated that greater neural integrity is achieved when focused attention behaviour and sustained deceleration in heart rate are temporally overlapped.

Research previously conducted in this area has explored heart rate and heart rate variability in relation to exploratory play compared to free play and problem solving in term-born toddlers (Hughes & Hutt, 1979a). No differences were found in heart rate across tasks. However, heart rate variability (as indexed by standard deviation of heart rate) was lowest during problem solving and was found to be lower in exploratory play than in free play. Compared to free play, it appears that exploratory play recruits and engages systems that reflect greater regulation of heart rate and a more intense level of engagement.

In one of the few studies of preterm infants to examine the relationship of heart rate variability to exploratory play, 8-month-old infants were classified according to whether their vagal tone increased or decreased (an index of parasympathetic cardiac response) in response to a surprise stimulus (DiPietro, Porges, & Uhly, 1992). Preterm infants spent less time examining objects than term-born infants, and their vagal tone tended to decrease in response to surprise. Overall, infants in both groups whose vagal tone increased in response to surprise were found to have higher developmental scores at the 8-month assessment and showed more sophisticated exploratory play. Recent Russian studies examined preterm versus term-born infants regulation of sinus cardiac rhythm (a measure that reflects parasympathetic effects) during two types of attention tasks, one that elicited a reflexive "exogenous" attention versus another that elicited a more effortful "endogenous" attention (Stroganova, Posikera, & Pisarevskii, 2005a; Stroganova, Posikera, Pisarevskii, & Tsetlin, 2006d). Preterm infants were less able to maintain endogenous attention and showed poorer regulation of sinus cardiac rhythm (i.e., lower parasympathetic effects) during the endogenous attention task. Both of these studies suggest that the preterm infant's regulation of attention and heart rate in response to various visual stimuli may be compromised or altered in comparison to that of term-born infants.

Further, there is a body of literature that suggests that very preterm infants show differences in arousal regulation or altered bio-behavioural responses as compared to healthy term-born infants. Studies have linked altered reactivity or poor regulation of arousal in the newborn period to poorer learning during and beyond the newborn period (e.g., Krafchuk, Tronick, & Clifton, 1983). Furthermore, studies of preterm infants, particularly ELGA infants, who experience prolonged neonatal intensive care, have also shown altered regulation of physiological arousal and reactivity in infancy (Grunau et al., 2007a; Grunau et al., 2001; Oberlander et al., 2000b). On the basis of these studies, one would expect preterm infants to show not only less regulation of behavioural attention (i.e. endogenous attention as reflected by the ability to focus attention) but also altered patterns of heart rate response that reflect less integrity of attention and cardiac systems.

Thus the second aim of this current dissertation study was to examine patterns of heart rate response at 8 months of age during exploratory play, as related to premature birth status and sex. To my knowledge, there are no previous studies of preterm infants that have examined overall changes in heart rate during exploratory play. Furthermore, there have been no studies of preterm infants that have examined changes in heart rate response coincident with specific periods of behavioural focus during exploratory play, or changes in heart rate related to focused attention that compared specifically defined degrees of prematurity in infants born very (<32 weeks GA) or extremely preterm (≤28 weeks GA). Thus, important questions remain as to whether very preterm infants differ from term-born infants in their patterns of heart rate response during behavioural focused attention that would suggest altered integrity or regulation of attention response. Based on previous behavioural research comparing high-risk with lower-risk preterm infants and preterm with term-born infants, it was expected that Preterm ELGA infants, compared to preterm VLGA and Term-born infants would show less and poorer focused attention during independent exploratory play, including lower global focused attention using, for the first time, a published 5-point global rating scale (Lawson et al., 2001). Additionally, Preterm boys (both ELGA and VLGA) were expected to show greater negative effects compared to preterm girls.

This dissertation research will add to findings presented in the studies discussed above by comparing overall heart rate response and the direction and intensity of heart rate deceleration during focused attention in preterm infants at 8 months of age CCA versus controls at 8-months chronological age, using a paradigm of exploratory play with objects. Additionally, this dissertation research will add to the existing literature by determining whether there are different effects for the relatively higher risk ELGA preterm compared to VLGA preterm infants. Difficulties in attention regulation and attention problems associated with later learning and cognitive problems are higher in very preterm male infants, therefore this dissertation research will also add to knowledge in this area by examining sex differences. Based on the Canadian Institutes of Health Research guidelines, sex refers to the biological characteristics that distinguish males and females, and sex differences may occur at the genetic/molecular, cellular, organ or organism level, which originate in the genetic and intrauterine environment (Spitzer, 2008); thus the term sex will be used throughout this dissertation study.

In summary, this dissertation research was undertaken to further elucidate the nature of early focused attention and patterns of heart rate response during exploratory play in biologically vulnerable very preterm infants compared to healthy term-born infants. This research addresses gaps in the literature by examining the interplay of biological and physiological factors associated with the regulation of focused attention in preterm born 8-month infants compared to term-born controls, using a relatively naturalistic paradigm of exploratory play with 3-dimensional novel objects. Findings may shed light on the underlying problems in attention regulation and later outcome problems in the preterm population, of which little is known. The early identification of infants who are "at risk" for later attention and cognitive outcome problems is critical. Early interventions can potentially change the developmental trajectories and improve outcomes for this increasing population of preterm infants, who place significant demands on medical and educational resources.

Overview and Organization of Chapters

This dissertation is structured according to the respective aims of examining the regulation of behaviour (focused attention) and changes in heart rate response during exploratory play as related to preterm versus term-born birth status and sex. The literature review comprises two main sections, 1) a general review of the literature on exploratory play and behavioural focused attention, and 2) a review of the literature on focused attention in relation to regulation of heart rate and heart rate response. Each section includes relevant studies of preterm infants. The review sections are followed by the methodology in chapter three. Results in the fourth chapter are presented according to findings related first to behavioural focused attention, which validate and extend previous focused attention studies, and second to the heart rate response of infants during exploratory play and specifically identified periods of behavioural focused attention. Attention and heart rate change, as predictors of concurrent cognitive function are also examined. A summary and discussion of the results is presented in chapter five, where the findings are situated within a larger body of literature and their implications for focused attention are discussed in relation to basic and applied research.

CHAPTER 2: LITERATURE REVIEW

Focused Attention and Exploration of Novel Objects

Theoretical Perspectives for Studying Infant Attention during Exploration

Through the last century, and particularly over past 50 years, since Fantz first conducted his studies of infant looking (1958; 1964), theorists have emphasized various perspectives on attention. For example, attention has been viewed as a perceptual process, an arousal state, or an elementary cognitive function, with further distinctions made according to whether attention is inherently active and internally driven or more reflexive in nature. The difficulty in specifying what attention is can be traced to the view that attention is involved in multiple systems of development and is generally inferred indirectly (Heitz, Unsworth, & Engle, 2004), using cognitive tasks or observing behaviours during perceptual tasks. With the exception of William James (1890), who is well known for his pioneering work on the "varieties" of attention, and who is cited frequently for his statement "everyone knows what attention is," conceptualizing and clearly defining attention has challenged many generations of psychologists. Theoretical frameworks that have related attention to information processing have emphasized different aspects of the process of selectivity, and, as Enns and Burack (1997) note, the definition of attention can vary dramatically according to differing standpoints, for example, whether attention is viewed primarily from the perspective of the perceiver, who has a limited sensory and perceptual capacity to filter incoming stimuli, or from the perspective of that which is perceived. Colombo (2001; 2002) notes that the role of attention in the first years of life must be considered in the context of multiple developmental systems and that, based on the idea that the acquisition of cognitive and memory skills all require attention, infant attention can be seen as a "primary cognitive function".

Developmental Theories

Developmental psychologists have long emphasized the importance of infant attention to features and events during active exploration in the development of cognition (Bruner, 1973b; Gibson, 1969; Piaget, 1952; White, 1959e). In a landmark paper "The concept of competence", Robert White (1959d) presented his theory of competence, which emphasized that the organism's motivation and competence is acquired through the selective, persistent, and effective capacity to interact with its environment. He also provided an extensive review of various theories and approaches that argued against the backdrop of psychoanalytic drive-reduction theories such as those of Freud, and upon which he supported his ideas. White's theory was biologically rooted and based on animal studies, such as those of Zimbardo and Miller in the late 1950's, where "the opportunity to explore a 'novel' environment or to effect a stimulus change was a reinforcing agent" (as cited in White, 1959c, p. 298). Infants were seen as acquiring competence through interactions with their environment, as manifested in developmental processes such as play and investigatory behaviour. Support for this theory is found in the work of researchers such as Charlotte Buhler (as cited in White, 1959b, p. 315), who emphasized the responsive and adaptive behaviours of newborns and later exploratory tendencies of infants. A review of developmental theorists of this period (1940's to 1950's) such as Goldstein, French and Maslow emphasized the infant's intrinsic mental needs, self-actualization or growth motivation (as cited in White, 1959a, p. 312, 313) Importantly, White also surveyed work on focal attention by Schachtel (as cited in White, 1959f, p. 315), where acts of focal attention exclude the rest of the field and are aimed at mentally grasping the nature of a particular object. Thus the many theories that White reviewed of his contemporaries, and the ideas that he put forth almost 50 years ago are relevant to, and emphasize the significance of infant attention during exploratory play.

Piaget's (1952) theory of learning and development emphasized that infants' active and continued exploration of and actions with objects, which lay the foundation for acquiring understanding and knowledge of the world. In his writings, Piaget (1954) described sequences in which the infant visually follows and recognizes objects in the first few months of life. He outlined these skills as developing further between 3 and 6 months of age, when infants grasp and bring objects in view, and when they look at the locations of objects as they disappear from view. At 8 months of age, Piaget provided detailed descriptions of infants' great interest in and visual examination of objects and partially hidden objects, prior to their establishing object permanence.

In a different theoretical perspective, Eleanor Gibson (1969) viewed infant attention and exploratory behaviours as inherent features of perceptual development. Specifically, the infant was seen as choosing stimulus properties that were meaningful and detecting features that distinguished objects, all of which reduced the infant's uncertainty. Thus exploration was seen as a process of selective gathering or seeking information about distinctive features, invariants, and structure. Exploratory development over the first year of life was described as "a sequences of phases that build the infant's knowledge of the permanent features of the world, of the predictable relations between events, and of its own capacities for acting on objects and intervening in events" (Gibson, 1988, p. 7). During the second phase, which extended from 5 months to about 9 months of age, infants were seen as attending to distinctive features and "affordances" of objects which, enabled them to the learn about the functional possibilities and classification of things in the world.

Jerome Bruner studied the development of skilled actions in infants and described intention, feedback, and the actions that mediated them as central to the growth of infant competence (Bruner, 1973a). Competencies in the first year of life were seen as consisting of five broad behaviours, which included feeding, perceiving and attention, manipulating objects, locomotion, and interacting with other persons. As an added component, Bruner also highlighted the infant's control of his/her internal state. He saw objects as threshold phenomena that operated like triggers and aroused "intentionality," prolonging orienting on the part of the infant and triggering anticipation of activity, a "loosely ordered sequence of constituent acts" that became more organized throughout development (Bruner, 1973c, p. 2).

From a theoretical perspective that emphasized the neurological correlates of learning, Hebb (1949) saw sustained interest as a neurological state, where complex "phase sequences" enabled the process of establishing new internal relations (i.e., distinguishing familiar with novel stimuli). This mental comparison model, as the basis for acquiring and processing novel information has been one of the most widely applied theories in the field of infant attention. In models of information processing, it is thought that perceptual processes such as attention are basic across development and that concepts are constructed from relatively simple to increasingly more complex levels (Johnson, 2004). More specifically, in information processing models, developmental changes are described as occurring incrementally with respect to information content, beginning with the accessing of simple units of information and proceeding to the integrating of higher-level units in an increasingly complex bottom-up process as infants mature.

Hebb and Donderi (1987) also emphasized the concept that regulation of behaviour is intrinsic to developmental processes. Because of its occurrence in many species across the evolutionary scale, "exploratory motivation" was seen as a biologically primitive behaviour and as having survival value. Using the laboratory rat as a model, Hebb maintained that strange rather than familiar objects or events increased arousal of cortical activity, which produced a point of balance between opposing motivations of exploration and fear. Providing "ambivalence" would result in arousal that was not too high; thus the animal would continue to explore. Hebb saw low to moderate arousal as having an organizing effect on behaviour and that high arousal could be decreased by discontinuing exploration. Posner and Rothbart (2007) maintain that the connections among neural networks, genes, and the environment provide a common approach to all aspects of human emotion and cognition. They salute Hebb for having proposed a unified common network approach to psychological science over 50 years ago which can be applied to questions of today regarding genes, learning, perception, motivation, and development.

In summary, many developmental theorists have stressed that infants' active exploration of their environment is central to early development. Numerous developmental theories and frameworks support the study of focused attention as a critical construct in the study of infant development. Researchers and theorists, who have described specific characteristics of infant behaviours during exploratory play, underscore the importance of the more effortful, focused endogenous attention, as related to cognitive processing. Thus, converging evidence supports focused attention as a critical measure of early encoding that can inform developmental theory and cognitive science.

Exploratory Play as a Framework for Studying Infant Focused Attention

Infant exploratory play with 3-dimensional objects constitutes a set of inherent and spontaneous behaviours that predominate in the second half of the first year of life (e.g., McCall, 1974; Ruff et al., 1991; Ruff & Rothbart, 1996b). During this period of development, infants show a typical repertoire of exploratory behaviours that can be readily observed when a novel object or toy is placed within their reach. In the second half of the first year of life, characteristic exploratory behaviours include orienting, looking, reaching, grasping, and mouthing objects of interest, as well as waving, banging, or throwing objects. Intermittently, the infant may also show a more sustained and focused visual interest in a novel object or toy, while carefully examining, fingering, or rotating the object to inspect its specific properties or features (Ruff, 1984; Ruff, 1986u; Ruff & Lawson, 1990). As noted in the overview, focused attention is thought to reflect an effortful or cognitively active engagement on behalf of the infant, which constitutes endogenous attention, and is differentiated from earlier more reflexive forms of attention (Colombo et al., 2006). That infants' focused interest in objects or events can be recognized in their repertoire of exploratory and examining behaviours using characteristic facial expressions and body postures is well established in the literature. In the mid-1980s, Holly Ruff quantified specific infant examining behaviours, such as fingering or turning the object while looking at it, that had previously been qualitatively described by other researchers in the 1960's and 1970's such as Collard, Hutt, Kopp and Uzgiris (as cited in Ruff, 1984). Carefully identified behaviours of infant examining, including multiple cues such as body postures, use of hands and facial expressions, allowed observers to make judgements as to whether examining was occurring or not. As a construct, "focused attention" was then derived from studies of infants examining toys, and was characterized as the "duration of looking that occurs simultaneously with a deliberate manipulation of the object and serious facial expression" (often furrowed brow), and "postures oriented toward the object of interest" with a "general decrease in extraneous body movements" (e.g., Ruff, 1986t; Ruff et al., 1990). Thus, based on established guidelines, infant examining behaviours such as duration of focused attention have been quantified.

Specifically, focused attention has been quantified using global categorical ratings, which account for the number, duration, and quality of specific examining behaviours that reflect focused attention in a single score. Global ratings of focused attention have been found to be reliable and significantly correlated with duration of focused attention (Lawson et al., 2001). Ruff, Lawson, Parrinello, and Weissberg, (1990c) have used global ratings for overall attentiveness on a 3-point scale, which they found to be stable predictors of later attention behaviours at ages of 1, 2, and 3.5 years in both preterm and full-term infants. More recently, 3-point global ratings have been used in conjunction with ratings of negative emotionality at 1 and 2 years of age to predict both cognition and behaviour at 3.5 years of age in full-term infants (Lawson & Ruff, 2004c). Furthermore, Lawson and Ruff (2001) developed 5-point global ratings of focused attention, which differ from the formerly used 3-point ratings in that they provide more information and were designed to distinguish low from very low levels of attention in preterm infants. Ratings from 1 (relatively little engagement and no signs of concentration) to 5 (an exceptionally high level of object engagement, with clear and prolonged periods of absorption to the object) are based on multiple cues for determining the degree of infant's focused attention during exploratory play, including steadiness of gaze, facial expression and affect, position of toys relative to eyes (see Appendix A). Lawson and Ruff note in using the 5-point rating scale that global ratings are more readily generated in a clinical setting, provide unique information about the functional status of infants in the second half of the first year of life, and have clinical importance in the follow-up of very preterm infants.

In summary, exploration of objects is a spontaneous activity in infants, typical in the second half of the first year of life. At 8 months of age, exploratory play encapsulates the infant's natural behaviour in orienting towards the manipulation and examining of objects, providing an ideal arena in which to explore the infant's development of attention and organization. This dissertation research will compare 5-point ratings of focused attention in 8-month-old preterm versus healthy term-born infants during exploratory play, together with measures of other specific behaviours, such as the latency of focused attention following the presentation of the toy, and the overall duration of focused attention. These findings extend Lawson and Ruff's work (2001), which has validated and quantified 5-point global ratings of focused attention for 7- and 12-month-old very low birthweight preterm infants but has not compared ratings of preterm infants to a control term-born group.

Differentiating Attention Processes: Theories and Components of Attention

The infant's propensity to orient to objects or events and the ability to subsequently organize a response, which regulates and sustains attention to the details of those objects or events, is central to the development of information processing and cognition. Berlyne (1966) proposed that there are two types of exploration, one "specific" and the other "diversive", both of which are motivated by a need for knowledge. His work led to the development of further concepts associated with exploration, such as novelty (Hutt, 1970). Becoming alert to changes in the environment and information gathering about the physical, functional, and relational properties of objects and events has been characterized as serving both adaptive and preservative functions (McCall, 1974). The infant's interest in novelty has been seen to play a significant role both in initial orienting to the object and subsequent examining of the object's properties (sustaining of interest) (Berg & Sternberg, 1985; Berlyne, 1960; Hutt, 1970). The "orienting reaction," also known as an "investigating" or "what is it?" reaction, first described by the Russian physiologist Pavlov (1927), is characterized by changes in overall arousal involving alterations in sensory, motor, and physiological systems.

Researchers and theorists have described different psychological processes associated with the construct of attention. As early as James (1890), distinctions have been made between passive involuntary attention, seen as primarily reflexive and involving the sensory systems, and active voluntary attention directed toward sensory or representational objects, which has been associated with interest and selection. Researchers have attempted to parse out unique components or phases of attention based on different underlying processes. In a landmark paper, Cohen (1972a) differentiated the process by which the infant turns to attend to a stimulus (attention getting) and the process that determines the length of the fixation once the infant has attended (attention holding). Furthermore, he suggested that behaviours belonging to this 2-component model of "attention-getting" versus "attention-holding," such as duration or number of looks, represented different underlying mechanisms. Similarly, Mayes and Bornstein (1997) differentiated selective attention, which involves initial orienting and possibly discriminating novel from familiar, from sustained attention, which refers to attention of a longer duration where active encoding takes place. The distinction of orienting to an object versus sustaining interest in an object is supported by a large body of research measuring heart rate response (Porges, 1984; Porges, 1992a; Richards & Casey, 1992). As outlined in detail later in this review, infants show a significant drop in heart rate associated with orienting, which is followed by a phase of sustained lowered heart rate, provided the infant continues to show focused attention (Richards & Casey, 1991a).

Behavioural researchers who study infant examining and focused attention during exploratory play with novel objects distinguish between the reactive aspects of attention, which they maintain involve arousal, orienting, and interest in novelty, and focused attention, which they suggest reflects an interest in what could be learned or how the object of interest could be manipulated (Ruff, 1986s; Ruff et al., 1991). In this model, the "initial orienting is conceptualized as a reflexive response to novelty, whereas sustained interest reflects a greater degree of self-regulation and information processing." Ruff et al. (1996b) propose two attention systems in early development. The first is an orientation/investigative system and the second is an attention system that comes into play towards the end of the first year of life and is more self-generated, with goals influencing sustained and focused attention. They maintain that manipulative play with objects is strongly governed by the first attention system, as focused exploration involves orientation and recognition of objects. However, the extent to which infants in the second half of the first year of life actively focus their attention to obtain information about objects or events of interest can be seen as reflecting the development of brain networks associated with endogenous attention and motivated by internal cognitive processes. As such, infant attention has been differentiated according to whether it is motivated by external stimuli or by internal cognitive processes. The development of systems related to internally motivated attention, are thought to be a major component of cognitive processes in infants (Posner & Raichle, 1994).

Focused Attention as an Index of Information Processing and Cognitive Effort

Extensive work conducted in the area of infant exploratory play has distinguished between the infant's concentrated, focused attention to the object versus interacting with the object in a manner characterized by a "casual" attention to the object. This distinction has been made in order to identify attention associated with more cognitive effort (e.g., Ruff et al., 1991). Periods of focused attention during exploration involve the selective and intensive aspects of attention (Lawson et al., 2001). Periods of examining, characterized by a concentrated or intense focus, are thought to reflect the active uptake and processing of information. A number of studies show that infants process details of stimuli or events and are more likely to remember those events when attention is focused (e.g., Colombo, 2001; Colombo, Richman, Shaddy, Greenhoot, & Maikranz, 2001; Frick & Richards, 2001; Richards, 1997d). Evidence that supports focused attention as active processing comes from studies that have used a relative degree of distraction to indicate degree of cognitive engagement (i.e. "lack of distraction" or a "longer latency to distraction" compared to frequent or immediate distraction to stimuli presented in the periphery). During independent exploration of novel objects, infants between 6 and 12 months of age have been found to be less distractible or have longer distraction latencies during examining/focused attention as compared to non-examining or more casual attention (Lansink & Richards, 1997l; Oakes et al., 1994; Ruff et al., 1996a). A number of studies of term-born infants have predicted later developmental outcomes from early focused attention. Sustained attention has been linked to better learning in 12-month-old, full-term infants (Sullivan & Lewis, 1988) and to better developmental outcomes using the Bayley Scales of Infant Development (BSID II) in term-born toddlers of normal birth weight as well as in term-born toddlers born at birthweights that were low for gestational age (Choudhury & Gorman, 2000).

In summary, information processing can be inferred by the intensity or duration of the infant's visual exploration or the infant's examining objects of interest. Altogether, the infant's initial orientation and approach to objects and lack of focus, or, conversely intense interest in exploring novel objects, provides an ideal and natural framework for obtaining multiple and valuable sources of data, all of which reflect the infant's regulation of attention and tap important underlying processes (McCall, 1974; Ruff et al., 1991).

Focused Attention as Related to Development and Risk

Attention during Exploration as Reflecting Neurodevelopmental Change

Infants actively select, orient, and visually focus their attention on objects from the first days of life (e.g., Haith, 1980). In the months that follow, subsequent increases in visual scanning and duration of looking at objects (e.g., Bronson, 1990; Keller & Gauda, 1987; Keller, Scholmerich, Miranda, & Gauda, 1987) can be seen as reflecting a shift from subcortical mechanisms associated with orienting to the recruitment of different components of the visual network and greater cortical control (Johnson, Posner, & Rothbart, 1991; Ruff et al., 1996b). Thus, in neurodevelopmental models of visual attention, the newborn or very young infant has been viewed as responding primarily to movement, location, and peripheral visual information. However, over the first year of life, infants show a progressive increase in sensitivity to fine detail, objects, and forms (Bronson, 1974). Mark Johnson and colleagues (Johnson, 1990; Johnson et al., 1991) differentiated between visual behaviours that are primarily subcortical, mature at birth, and involve neural pathways for short-latency reflex, and other pathways that have various connections to cortical areas in the primary visual cortex, which develop rapidly over the first 6 months. The increase in cortical connections and control results in significantly improved flexibility of attention and allows the progressive encoding of increasingly more complex visual information (Colombo, 1995; Colombo, Mitchell, & Horowitz, 1988; Johnson et al., 1991; Ruff et al., 1996b).

In the first weeks of life, infants have also been observed to show early "swiping" movements of the hand and arm when attractive objects are suspended within their reach (Bower, 1982). While the extent of these behaviours in the first weeks of life has been a source of some debate (e.g., Ruff & Halton, 1978), the progression from these rudimentary behaviours to the increasingly integrated reaching actions seen by the middle of first year of life has been described. More recently, developmental sequences of these actions and the self-organizing nature of these motor processes have been emphasized. For example, from 3 to 7 months of age, reaching actions become more systematic, longer in duration, and more direct, with the number of action units decreasing towards a pattern that approaches a 2-phase structure of adult reaching (von Hofsten, 1991). As the baby develops more stable reaching, more effective behaviours are selected and integrated to form a new level of self-organization (Thelan & Smith, 1994). For these early motor competencies, self-initiated interactions between infants and their physical world rely heavily on vision prior to the age of 4 or 5 months, but from this time onward, active manipulation is coordinated with visual exploration (e.g., Field, 1977; Ruff, 1976). Thus, from 5 or 6 months of age, with this integration of visual exploration and increasing manual efficiency, a new world opens to infants as they examine and grasp objects within their reach. From this time and over the following months, there are significant increases in endogenous attention, which has been described as the process of controlling and allocating attention to stimuli, objects, or events as a function of the infant's internal processes (Colombo et al., 2006). The concept of endogenous attention is based on a limited capacity model of attention where the individual's focus on one feature assumes a lack of attention to other features in the environment, for example, holding one's interest and attention in the face of distraction (Colombo et al., 2006). As noted earlier, these significant increases in endogenous attention seen between 7 and 10 months, mark this developmental period as a potentially useful time for the detection of attention problems (Colombo, 2001; Colombo et al., 1999; Lawson et al., 2004c). It is also during this developmental phase that, in habituation and visual preference studies, indices of attention have traditionally been used in order to successfully predict later cognition (e.g., Rose et al., 2000).

In summary, individual differences in quality of focus and intensity of attention are reflections of differing degrees of infant neural maturity, coordination, and flexibility. These individual differences can be detected and can predict later cognitive outcomes, particularly from the 6- to 9-month-old period, which is one of the most rapid periods of the growth of endogenous attention (Colombo et al., 2006).

Individual Differences and Developmental Changes in Exploratory Play

Findings from previous studies have established that infants spontaneously explore and examine objects to varying degrees and show differences in exploratory play related to maturation. Heidi Keller et al. (1987) examined the development of exploratory behaviour from ages 2 weeks to 4 years and found that infants varied in the extent to which they relied on a particular sensory modality. Some infants showed high visual exploration together with cursive tactile exploration and few actions, whereas other infants showed prolonged and slow tactile exploration with many different actions (Keller et al., 1987, p. 138). In an early study, McCall (1974) examined a number of exploratory behaviours in 9-month-old infants. He characterized one group of infants as having a slow (but accurate) tempo, with sustained attention to toys and little mouthing, whereas other groups were characterized by less engagement, more mouthing, or a more rapid, superficial style of exploration. These individual differences in exploration were seen to reflect maturational changes, as McCall determined that the 9-month-old infants who sustained their attention were more similar in their behaviour to infants who were a few months older. In another study, Fenson and Kagan (1976) found a developmental progression of manipulative play in infants over the developmental course of 7, 9, 13, and 20 months. Belsky and Most (1981) developed and validated a developmental play scale for infants aged 7½ to 21 months of age. Infants showed a clear developmental sequence of exploratory play, from the last quarter of the first year of simple "undifferentiated" manipulation to the exploring of unique properties ("functional play"), whereby the infant's actions increasingly fit the specific properties of the object manipulated. Further work has verified that as infants mature over the second half of the first year of life, they increase their "examining" and "information-gathering" behaviours (Ruff, Saltarelli, Capozzoli, & Dubiner, 1992) and become less distractible while they examine objects (Oakes et al., 1994).

Notwithstanding the significance of focused attention as a neurodevelopmental measure in the second half of the first year of life, periods of focused attention during exploratory play are generally quite brief. At age 7 to 9 months, infants have been reported to demonstrate focused attention for an average of 12 to 16 seconds over a 90-second exposure of an individual object or toy (Ruff et al., 1991), with increased duration as infants mature, provided that stimuli are sufficiently complex. In normal infants at 5, 7, 9, and 11 months of age, periods of examining were reported to occupy 3.5%, 11%, 15%, and 20% of available time across these respective ages (Ruff et al., 1991), whereas casual looking did not increase with age (49%, 41%, 47% and 47% respectively). Additionally, a developmental trend has been reported with the occurrence of more examining in the first half relative to the second half of an exploratory session (Ruff et al., 1992). Temporally, focused attention is most often preceded and followed by a casual visual exploration or by simple looking without focus (Lansink et al., 2000), the latter of which proportionally occupies most of the infant's time in exploration.

Thus, the infant's exploration and engagement with 3-dimensional objects includes many variations of behaviours as well as distinct forms of attention. For normally developing infants in the second half of the first year of life, these behaviours are organized and show predictable temporal patterns. For example, careful observation has shown that there is a sequential hierarchy of adaptive behaviours in normally developing infants, for example, visually inspecting the object before mouthing or banging (Ruff, 1986r). These established parameters of infant exploration allow examination of executive behaviours related to exploration, such as the quality, duration, and organization or intensity of infant visual attention and the propensity to return to objects for re-examination, all of which can provide important information about the infant's maturity and development.

Vulnerability of Focused Attention in those at Biological Risk

There is much evidence to indicate that the processes involved in focused or sustained attention are particularly sensitive to biological adversity or risk. This is not surprising, as the capacity for focused concentration in situations that require information processing depends largely on the integrity of the neural recruitment that occurs in response to these situations, which require cognitive effort (Horn & Blankson, 2005). There are significant individual differences and variation in attention because the functional integrity of attention processes are mediated by multiple brain regions, networks, and circuitry (Mesulam, 1981; Posner & Petersen, 1990), thus ineffective signalling at any one level can lead to the poor regulation of attention (Casey, 2007). Posner et al. (1990) outlined three interactive attention brain networks, including the posterior system (orienting to external events), the anterior system (detection of stimuli and information-processing), and a vigilance network (optimizes arousal states); they note that the interdependence of each system is key to understanding variations in attention performance. Rothbart, Posner, and Rosicky (1994) suggest that attention processes are involved in early plasticity of brain development and hypothesize that the development of attention creates sensitive periods for change. They maintain that the focusing of attention can be a means for immediate changes in organization and function and is involved in problem solving that can affect long-term structural changes. Over the past 15 years, studies of attention brain networks have proliferated, and attention has been one of the fastest-growing fields within cognitive psychology and cognitive neuroscience (Posner & Rothbart, 2007). Studies of biologically "at-risk" infants, such as those born very preterm, are valuable in that they provide a basis for viewing attention as it changes through maturation and in conjunction with other developmental processes.

At the beginning of life, biologically adverse conditions and events such as fetal distress, delivery complications, and poor maternal health predispose infants to attention problems (Sprich-Buckminster, Biederman, Milberger, Faraone, & Lehman, 1993). The capacity for focused attention and concentration appears to be sensitive not only to biological adversity or risk in the beginnings of life but to risk throughout human development. Throughout the life span, clinical populations of individuals with various neurological disorders frequently show vulnerabilities on attention-related tasks that co-exist with identified cognitive deficits (Ward, 2004). Attention disorders can be seen as markers that reflect the vulnerability of an atypical nervous system maladapted to contextual demands and expectations (Gorski, 2002). During later human development, abilities that require obtaining and maintaining awareness of information, such as novel fluid reasoning, short-term memory, and cognitive speed show significant decline in the aging population and are believed to be vulnerable primarily because they require sustained focused attention (Horn et al., 2005).

Attention Problems in Children Born Very Preterm

Attention problems are the most commonly reported behavioural sequelae of prematurity (e.g., Botting, Powls, Cooke, & Marlow, 1997; Hack et al., 1992b; Ross, Lipper, & Auld, 1990b). For VLBW school-aged children, parent-reported rates of attention-related problems have been estimated at about 18% (e.g., Ross, Lipper, & Auld, 1991; Stjernqvist & Svenningsen, 1999; Taylor et al., 1998). For ELBW children, rates of attention-related problems have been reported as somewhat higher, in both parent ratings (26%) and teacher reports (42%) (e.g., Taylor et al., 1998). In a large prospective study of infants born <1000 grams, social, thought, and attention difficulties were 0.5 to 1.2 standard deviations higher than term controls, with similar behavioural problems across four countries, suggesting that these problems are not culturally specific (Hille et al., 2001). A meta-analysis of VLBW and ELBW behavioural school-age outcomes revealed that 81% of studies reported increased problem behaviours in preterm-born children (Bhutta, Cleves, Casey, Cradock, & Anand, 2002a). In their meta-analysis, Bhutta et al. reported that compared to their full-term peers, children born preterm have a 2.64 chance of developing attention deficit hyperactivity disorders, and a higher frequency of internalizing and externalizing behaviours during school age. Despite the large number of follow-up studies that report school-age outcome problems, the nature of and development of attention problems in children who were born very preterm needs to be more clearly specified. It has been suggested that deficits in attention found later in the preterm population, sometimes described as attention deficit hyperactivity disorder (Bhutta, Cleves, Casey, Cradock, & Anand, 2002b; Mick, Biederman, Prince, Fischer, & Faraone, 2002; Stjernqvist & Svenningsen, 1995b; Szatmari, Saigal, Rosenbaum, Campbell, & King, 1990), may in fact be more clearly understood as problems of self-regulation (Grunau, 2003; Robson & Cline, 1998; Robson & Pederson, 1997a) or of adaptive functioning (Schothorst & van Engeland, 1996b). Later attention problems in the very preterm population may reflect individual variation in the ability to sustain interest and inhibit distracting information that is evident very early in life (Lawson & Ruff, 2004d). In one follow-up study of very preterm (born <32 weeks GA) preschoolers, 23% of the children were deemed uncooperative for developmental assessment (Langkamp & Brazy, 1999a). Interestingly, by school age, these same children had significantly more attention problems and were twice as likely to receive remedial assistance than those who had been cooperative (Langkamp & Brazy, 1999b). Thus, in the preschool years, difficulties completing an assessment may represent difficulties in sustained attention, adapting to a novel situation, or learning difficulties rather than simple non-compliance. Consistent with this idea, many very preterm children have difficulty self-regulating in structured situations, need ongoing adult support and feedback in learning or evaluation settings, and show significantly more "backing off" behaviours during standard cognitive assessment (Grunau, 2003; Whitfield, Grunau, & Holsti, 1997b).

Further information about the nature and etiology of attention problems in the preterm population may be gleaned by examining the specific forms of attention that are vulnerable to risk. In a recent Russian study, preterm infants born between 28 and 32 weeks gestation were exposed to two different types of stimuli at age 5 months (adjusted for prematurity), and their responses were compared to those of full-term infants (Stroganova, Posikera, & Pisarevskii, 2005b). Each of the two types of stimuli was expected to elicit different types of attention. Soap bubbles were presented to attract the infant's attention as an exogenous attention task. Endogenous attention was measured using a visual expectation paradigm. In this sequence, a doll appeared and disappeared repeatedly from the infant's view. The infant's scanning of the location where a doll had disappeared and ability to maintain attention in anticipation of seeing the doll reappear was measured (attention maintained by internal mental processes). Interestingly, there were no significant differences between the preterm and full-term infants' exogenous attention abilities, but the preterm infants' ability to maintain endogenous attention in anticipation of a forthcoming stimulus was much lower. They interpreted their findings as a lack of effective control and maintenance of anticipatory attention. Subsequently, Stroganova, Posikera, Pisarevskii, and Tsetlin (2006c) presented further results from this study of 5-month-old infants, comparing the preterm and term-born infants' heart rate responses to the exogenous and endogenous attention tasks, and found that preterm infants showed less efficient autonomic regulation during shifts of attention.

Difficulties in particular forms of attention may underlie or be closely related to later difficulties in learning and cognition. Kopp and Vaughn (1982c) note that the concept of sustained attention has been linked to the study of learning disabilities, where there is consensus that control over attention is a fundamental process associated with learning problems (Keogh & Margolis, [1976] Kopp & Vaughn, 1982b p. 175). Longitudinal studies have shown that when ELGA infants are compared with full-term controls of the same age, they demonstrate a significantly higher incidence of childhood cognitive and learning problems (Anderson & Doyle, 2003b; Grunau, Whitfield, & Davis, 2002b; Taylor, Klein, & Hack, 2000; Taylor, Klein, Minich, & Hack, 2000b). Recent studies have found that these difficulties persist into adolescence (Grunau, Whitfield, & Fay, 2004; Hack et al., 2002; Saigal, Hoult, Streiner, Stoskopf, & Rosenbaum, 2000). Interestingly, for many very preterm school-age children, specific cognitive and learning problems are frequently related to relative weaknesses in visual perceptual processing, which may be linked to problems in early visual attention. Visual-motor and visual-spatial difficulties are the most commonly reported learning problems, as are other skills that require visually based problem solving and encoding such as written output and mathematics (e.g., Grunau, Whitfield, & Davis, 2002c; Klein, Hack, Gallagher, & Fanaroff, 1985; Luoma, Herrgard, & Martikainen, 1998; Olsen et al., 1998; Stjernqvist & Svenningsen, 1995a; Taylor, Klein, Schatschneider, & Hack, 1998; Waber & McCormick, 1995).

Most studies on outcomes of prematurity have not assessed sex effects, often due to sample size limitations. The additional risk of attention or cognitive problems in very preterm boys needs to be examined, since boys generally experience more serious neonatal complications, as evidenced by an increased vulnerability for intracranial hemorrhage (Raz et al., 1994) and a higher incidence of disability or handicap (Verloove-Vanhorick et al., 1994b; Whitfield, Grunau, & Holsti, 1997c). In a Dutch follow-up study of over 600 infants born less than 32 weeks gestation, the incidence of disability or handicap, using World Health Organization definitions, was three times greater in boys (21% versus 7% in girls) (Verloove-Vanhorick et al., 1994a). In a sample of ELBW infants from British Columbia, boys were found to experience substantially more learning problems than girls (Whitfield, Grunau, & Holsti, 1997d). In this study, ELBW survivors were three times more likely to have learning disorders, and 41% of the ELBW children had multiple areas of learning difficulty. Overall, only 26% of the ELBW group were intact, compared to 82% of the term group. When these numbers were analysed by sex, this figure was reduced to 12% for ELBW boys escaping disability compared to 35% of the ELBW girls. Furthermore, the increased incidence of behaviour problems in the preterm group was attributed to the preterm boys (Breslau, Klein, & Allen, 1988; Ross, Lipper, & Auld, 1990a). Another study found overall sex differences, with boys showing more externalizing and attention problems in both their preterm and control groups (Schothorst & van Engeland, 1996a).

In summary, there is a high preponderance of outcome problems in the preterm population related to attention processing, with possible increased risk for boys. Defining the nature of attention behaviours most sensitive to risk very early in life has the potential to contribute to our scant knowledge of the underlying mechanisms and developmental course of attention, learning, and cognitive problems of children born very preterm.

Focused Attention during Exploratory Play in Infants born Very Preterm

Biologically vulnerable groups of infants, such as those born very preterm, differ in their exploratory play when compared to healthy term-born infants. In studies of exploratory play conducted in the second half of the first year of life, high-risk preterm infants have been found to differ from lower-risk and term-born infants in that they are less organized in their approach to exploration, for example, they are less likely to follow the typical hierarchy of visually inspecting before mouthing objects (Ruff, 1986q). Additionally, preterm infants (in particular those at greater risk) take longer to approach objects and show less manipulative exploration and reduced focused attention (Landry & Chapieski, 1988; Ruff, 1986p; Ruff, 1988; Ruff et al., 1990; Ruff et al., 1984).

Sigman (1976) used an exploratory play paradigm to compare preterm and term-born infants at 8 month of age in their preference for novelty and found different patterns of exploration between the two groups. Preterm infants explored familiar objects for longer periods than term-born infants, despite having equal exposure to objects during a familiarization period. Findings were interpreted as evidence of preterm infants needing additional experience with objects for familiarization to occur.

In comparing preterm and term-born infants, Kopp and colleagues (1982a) defined sustained attention as the combined durations of four exploratory behaviours (looking, holding and looking, manipulating and examining, and mouthing). They found that sustained attention during exploratory play at 8 months of age predicted developmental status (as measured by the Bayley Mental Developmental Index) at 2 years of age. They also examined sustained attention in a hierarchical regression model. After adjusting for birth status variables (SES, ethnicity, birthweight, and gestational age) and developmental status, attention accounted for a significant proportion of the variance in outcomes at 2 years of age for preterm boys but not girls, suggesting that their findings could be due to a higher incidence of attention problems associated with later learning problems in preterm boys.

In very low birthweight infants, the duration of concentrated examining of objects during exploratory play at 7 months of age has been related to concurrent development and cognitive abilities at 2, 3, and 4/5 years of age (Lawson & Ruff, 2004e). Further relationships were also established between the 7-month-olds' focused attention measures and later ratings of hyperactivity/inattention through to the preschool years.

Risk of Prematurity in Relation to Later Outcome Problems

In general, increased risk for outcome problems associated with prematurity has been linked to earlier gestation and lower birthweight, as these infants more frequently experience common clinical conditions of prematurity such as respiratory distress syndrome, chronic lung disease, and infection, as well as the variety of treatments associated with these conditions (Stevenson et al., 1998). Contributing factors to outcome problems, particularly for the earlier-born infants, may also include intermittent apnea and bradycardia, and the relative vulnerability of the preterm infant's brain and related central nervous system complications such as intra-ventricular hemorrhage (Greene, 2002; Landry, Fletcher, Denson, & Chapieski, 1993). Recent structural magnetic resonance imaging (MRI) studies have reported brain abnormalities in very preterm infants assessed before discharge from the Neonatal Intensive Care Unity (NICU), (e.g., Inder, Warfield, Wang, Huppi, & Volpe, 2005; Miller et al., 2005; Peterson et al., 2003a) as well as later in childhood (Thompson et al., 2007), adolescence, and young adulthood (Allin et al., 2004; Peterson et al., 2003b; Stewart et al., 1999a). Thus, outcome differences may be due in part to differences in brain structure and functioning. Central nervous system insults due to prenatal or neonatal vulnerabilities or other complications are associated with later behavioural problems, including attention deficits (Dammann & Leviton, 1999; Stewart et al., 1999b).

The cause of premature birth should also be considered among the reasons for outcome problems in very preterm infants, since common abnormalities of the uterus, placenta, diabetes, high blood pressure, significant stress, and the presence of twins or triplets can potentially interfere with the growing fetus. Additional risk factors for premature birth, such as infection, metabolic disorders, and maternal stress have also been implicated, however up to half of preterm infants are born without a known cause (Berkowitz & Papiernik, 1993; Copper et al., 1996; Main, 1988). Thus, potential disruptions of development that occur in utero related to the underlying reasons for premature delivery, may in themselves alter the neurobehavioral trajectories of infants, potentially affecting regulatory processes including attention and autonomic flexibility and control.

In addition to prenatal insults, disruptions during the neonatal period also need to be considered. The preterm infant is born physiologically immature at a time of rapid brain development and is thereby developmentally vulnerable. ELGA infants born at or below 28 weeks gestation may spend 12 weeks or more in the extra-uterine environment of the NICU. The ELGA infants generally have the most complications in the neonatal period, requiring mechanical ventilation and extended NICU stay, which necessarily involves ongoing stressors including multiple painful procedures (e.g. intravenous insertion, repeated heel sticks for blood collection). Among VLGA infants born at 29 to 32 weeks gestation, some initially require oxygen, however, unlike the ELGA infants, it is usually not as prolonged, and there are fewer risks associated with these later born preterm infants in general, as their physiologic systems are more mature than ELGA infants.

The routine postnatal NICU care that is necessary for preterm infants has long been suggested as potentially having a detrimental effect on the development of infant regulatory systems, possibly explaining some of the later outcome differences seen between full-term and preterm infants, particularly for higher-risk preterms (Als, Lester, Tronick, & Brazelton, 1982; Graven et al., 1992; Grunau, 2002). Disruptions of regulatory processes associated with CNS immaturity can be manifested functionally in a lack of adaptive regulation, or physiologically in arousal or the organization of infant state. Although NICU practices have changed considerably over the last decades, Lawson, Daum, and Turkewitz (1977) suggested that a high degree of stimulation may disrupt the preterm infant's sensory integration. In particular, they suggested that because sound sources were not always visible in the NICU, that infants would orient either visually or by heart rate and would experience a dissociation of auditory and visual or tactile referents. Duffy, Als, and McAnulty (1990) proposed that the high degree of stimulation in the NICU for ELBW infants with immature brain development may lead to cortical disturbances related to later outcome difficulties. In response to concerns about the highly stimulating NICU environment, a widely implemented program of neonatal assessment and care was developed with the aim of minimizing the potential disruptions and adverse effects of the NICU (Als, 1998b; Als, Butler, Kosta, & McAnulty, 2005).

Regulation of Arousal

Differences in early attention, arousal, and orientation to stimulation may provide clues to understanding the etiology and developmental processes associated with later cognitive, learning, and attention problems in the very preterm population. The importance of developing the ability to regulate an alert state and arousal for infant functioning, in particular attention regulation, has long been emphasized (e.g., Field, 1981b; Mayes, 2000b; Rothbart, 1989). In Rothbart's (1989) theory, infant attention is intricately linked to reactivity and regulation and is considered to be part of the infant's self-regulation process. In this view, individual differences in nervous system organization are related to the infant's ability to modulate reaction to stimulation (Fox & Stifter, 1989). Thus, underlying difficulties in regulating response or maintaining an optimal arousal state, which involve the coordination of multiple neurobiological response systems, likely contribute to outcome differences between preterm and term-born infants in behaviour and cognition.

Both selective and sustained components of attention are directly related to state of arousal as well as changes in the autonomic nervous system, with very low or very high arousal levels associated with inability to regulate attention or less focused attention (Mayes & Bornstein, 1997; Ruff, 1988). Hyper- or hypo-arousal are seen as interfering with the infant's capacity to encode and process novel information (e.g., Field, 1981a; Mayes, 2000a). In this model, low arousal would be related to attention deficits characterized by low behavioural reactivity and low arousal in the spatial orienting system, or in brain systems closely tied to orienting responses (Ruff et al., 1996b). When arousal is low, attention is also easily disengaged, leading to higher distractibility (Posner et al., 1994). When the demands of tasks increase, arousal would also be expected to increase, leading to increased attention; however, for those individuals who become over-aroused, performance would decrease.

There is other evidence that preterm infants show differences in the range and threshold for arousal states, as well as the frequency of achieving the arousal states that are optimal for selective and sustained attention (Gardner & Karmel, 1983). In the neonatal period, studies by Judith Gardner and colleagues in the early 1980s (as cited in Gardner, Karmel, & Magnano, 1992) showed that infants adapt their attentional responses according to contextual differences in arousal states. For example, neonates showed visual preference toward less stimulating events when endogenously more aroused (unswaddled before feeding) and visual preferences towards more stimulating events when in the less aroused condition (swaddled after feeding). These studies suggested that arousal to stimulation and visual preferences in neonates are inseparable and interdependent processes (Gardner et al., 1992). This interaction was also found in high-risk very preterm infants, although somewhat dampened. Neonates with brain injury showed visual preference towards less stimulation when less aroused. These researchers suggest that this early organization of arousal and attention forms the basis by which infants organize and respond to information, and that it is out of this early organization that CNS insults exert their influence on later cognitive and perceptual development.

Tiffany Field has used an integrated approach to studying attention and arousal within the context of the infant's early interactions and relationships. In her work that found that heart rate was elevated prior to the infant's "looking away," gaze aversion was considered an adaptive response to over-stimulation, during which information processing and arousal regulation occur (Field, 1981b). Additionally, her findings suggested that there is a curvilinear relationship between looking away and the amount of stimulation presented, in that infants gaze away and show elevated heart rate both when stimulation is too low or too high. Importantly, high-risk preterm infants have been found to have higher thresholds and a more narrow range of response. In turn, this is thought to contribute to the excessive gaze aversion and elevated heart rate seen in preterm infants, which has been proposed to affect arousal modulation and information processing.

In summary, for preterm infants overall, the specific causes for outcome problems are varied, often include multiple risk factors, and are not always clear. However, both prenatal and postnatal factors have been implicated, including stress associated with neonatal intensive care, particularly for those infants who are hospitalized for prolonged periods. The adaptive challenges placed on the extremely preterm infant, at a time when their systems are immature for extra-uterine life, may result in subtle or marked changes in neurobehavioral response and altered development in systems of arousal and regulation. Importantly, disruption of arousal regulation can underlie problems in attention regulation as focused attention depends on the ability of the infant to regulate or modulate arousal so that it is neither too high nor too low. Infants who are over or under-aroused when faced with novelty are less able to regulate their attention, both in terms of selectivity and sustained attention, and there is evidence that these systems are altered in very preterm infants.

Attention and Heart Rate Response

Background and Theory

Cardiac measures have revealed important information about the regulation of infant attention, beyond that which is generally obtained through behavioural measures of looking (e.g., Lansink & Richards, 1997k; Richards et al., 1992). Behavioural changes in visual attention and information processing have been related to specific patterns of heart rate response and heart rate variability. Heart rate typically decreases when an infant orients to an external stimulus or an object of interest in the environment (Graham et al., 1983; Porges & Raskin, 1969). If this initial orientation is followed by a more intense and continued interest, whereby the infant examines the object or event with deliberate intent (as described in the previous section) the infant's visual focusing is accompanied by reduced motor activity, sustained decreases in heart rate, reduced respiration, and decreased heart rate variability, as detailed below.

There is a long history of interest in heart rate as it relates to behaviour and attention (e.g., Darrow, 1929; Lacey & Lacey, 1974c; Porges et al., 1969; Richards, 1988b). Multiple phases of heart rate response have been associated with different types of attention and various aspects of information processing (Casey & Richards, 1991a; Graham et al., 1983; Graham & Clifton, 1966; Lacey, 1967). Distinct phases of attention involve mechanisms of control at various levels of neurophysiological organization and activity; thus patterns of heart rate response and heart rate variability can be seen as indirect measures of neural integrity and can reflect central nervous system maturity (e.g., DiPietro et al., 1992).

When a stimulus is first detected, there is a pre-attentive processing phase of heart rate, referred to as "transient-change" (Graham, 1979). This is followed by an orienting response, first detailed by Pavlov (1927) and elaborated by Sokolov (1963), who proposed that subcortical mechanisms amplified or dampened the individual's response depending on signals fed back from the cortex. Variations in the direction of heart rate response (acceleration or deceleration), as related to the intensity or type of stimulus and the subject's attention, were noted before the turn of the 20th century by Mentz (as cited in van der Molen, Bashore, Halliday, & Callway, 1991). However, Lacey (1974b) established and found evidence for a theory in which cardiac slowing was seen to facilitate the detection of simple stimuli ("stimulus intake") and acceleration of heart rate was associated with "stimulus rejection" (Lacey, Kagan, Lacey, & Moss, 1963). Thus, for external stimuli, the orienting response, marked by predictable decreases in heart rate, was generally understood to be a period during which preliminary information regarding the novel object was processed (Graham et al., 1983; Porges et al., 1969).

In infancy, these predictable decreases of heart rate described behaviourally as "attentional capture" (Cohen, 1972b) or "reactive attention" (Richards, 1985b) were seen to allow the infant to evaluate stimulus novelty and to assess the need for further processing or allocation of resources (Kahneman, 1973). Further to the orienting response, the infant's continued interest in the object or event, as evidenced by the physical alterations in facial expression and motor activity, described in the previous section (e.g., Ruff, 1986o), is accompanied by a sustained deceleration of heart rate. Depending on the level of engagement, heart rate remains at levels below baseline, and heart rate variability decreases (Porges, 1976). Finally, an attention termination phase describes the return of heart rate to the pre-stimulus level (Richards, 1988a; Richards, 1988b).

Cardiac Autonomic Measures

Basal Heart Rate

Heart rate, as measured in beats-per-minute (bpm), or inter-beat intervals, also referred to as heart period, has been used extensively to study infant attention. Heart rate is derived from calculating the average distance between R waves using the electro-cardiac signal (heart period). Large heart periods or inter-beat intervals reflect a greater distance between the R-waves and a slowing of heart rate, whereas short heart periods or inter-beat-intervals indicate a faster heart rate. In this dissertation research study, heart period was converted to beats-per-minute to facilitate the interpretation of results.

Resting or basal heart rate is a relatively stable, heritable trait from infancy to early childhood (Van Hulle, Corley, Zahn-Waxler, Kagan, & Hewitt, 2000). A recent study found individual stability in basal heart rate prenatally, from 20 to 38 weeks gestational age, which, in turn, was related to childhood heart rate at 2 years of age (DiPietro, Bornstein, Hahn, Costigan, & Achy-Brou, 2007c). At birth, mean heart rate in healthy infants has been reported to be 130 bpm, with a standard deviation of 8.2 (Mehta et al., 2002). Typically, mean heart rate increases from birth with highest mean heart rates occurring between 1 and 3 months (mean of about 150/bpm), followed by decreases from about 3 months of age across infancy and early childhood (Bar-Haim, Marshall, & Fox, 2000d; Davignon et al., 1980; Rijnbeek, Witsenburg, Schrama, Hess, & Kors, 2001). Developmentally, basal heart rate decrease is greatest between 4 and 9 months of age, with further decreases across age to 4 years (Bar-Haim, Marshall, & Fox, 2000c). The decrease in heart rate typically seen across infancy is seen as reflecting the neural maturation of parasympathetic restraint (Bar-Haim, Marshall, & Fox, 2000b; Hofer, 1984). In term newborns, greater reactivity and low regulation of state has been related to elevated basal heart rate (Porter, 2003a; Spangler & Scheubeck, 1993), and lower neonatal basal heart rate has been found to be related to higher Mental Developmental Index (MDI) on the Bayley Scales of Infant Development at 8 months of age (Fox & Porges, 1985). A relationship between basal heart rate and development persists through later infancy. In term-born infants, lower basal heart rate at 6 months of age has been found to be associated with higher performance for concurrent as well as later development (MDI) at 12 months (Richards & Cameron, 1989).

Heart Rate Variability

Heart rate variability, defined as beat-to-beat fluctuations in heart rate or inter-beat interval times, has been assessed in various ways. A very common measure of short-term heart rate variability that has been used extensively in infant research (and is used in this dissertation research) consists of the standard deviation of heart periods (heart rate variance), calculated as the standard deviation or the mean absolute difference between sequential heart periods (Porges & Byrne, 1992). Heart rate variability can be used as an index of vagal activity. A notable example is parasympathetic or vagal activity, which is the rhythmic change in heart rate variability associated with frequency of spontaneous breathing (respiratory sinus arrhythmia [RSA]). In particular, the transient decreases or increases in heart rate or period (inter-beat-intervals [IBI's]) associated with inspiration and expiration, respectively. The RSA, as an indication of vagal influence, has been widely used to quantify parasympathetic activity using a method described by Porges (1985b; 1988) to extract the variability associated with breathing. This measure derived from this approach of modelling the heart rate pattern to extract so called physiologically valid components such as amplitude of RSA, is termed "vagal tone," and is viewed as the tonic level of parasympathetic input to the heart (Porges et al., 1992). Studies determining both heart rate variability using descriptive statistics (e.g., standard deviation of heart rate) and vagal tone have found high correlations between the two measures comprising Pearson *r's* between .6 and .8 (Fox et al., 1989). High vagal tone (and high RSA), which reflects tight coupling between cardiac and respiratory activity, is thought to suggest more mature central nervous system function (Porges, 1983). Spectral analyses of fluctuations in heart rate, which reflect various components of heart rate variability within different frequency bands, have also been used to infer the relative contributions of parasympathetic versus sympathetic central nervous system activity. For example, fluctuations of the high frequency (HF) band are seen as being affected predominantly by parasympathetic (vagal) activity and correspond to respiration rate; thus decreases in HF power are associated with withdrawal of vagal activity (e.g., Grossman, 1992a; Porges et al., 1992).

Heart rate variability has been studied extensively in obstetrics, and there is a long history of the use of heart rate patterns in the assessment and care of the fetus and in the care of neonates as indicators of risk or well-being (Porges, 1988; Porges, 1992b). Similar to heart rate, heart rate variability shows significant within-individual stability as measured from about 28 to 30 weeks gestation to the neonatal period and to 1 and 2 years of age (DiPietro, Bornstein, Hahn, Costigan, & Achy-Brou, 2007b; DiPietro, Costigan, Pressman, & Doussard-Roosevelt, 2000). Greater stability of basal heart rate variability early in the first year of life (from 3½ to 5 and 6 months of age) has been related to more positive developmental outcome at 12 months of age (Richards et al., 1989).

When infants are born preterm, heart rate variability measures of parasympathetic control increase in relation to post-conceptual age (e.g., Gournay, Drouin, & Roze, 2002a; Sahni et al., 2000). In the weeks following a normal term birth, decreases in heart rate variability have been reported (Harper et al., 1978; Schechtman, Harper, & Kluge, 1989a), with subsequent increases in heart rate variability and parasympathetic control from 1 month onwards through the first and second years of life (e.g., Richards, 1989c; Richards & Casey, 1991b; Schechtman, Harper, & Kluge, 1989b; Stifter & Jain, 1996). In a longitudinal studies, decreases in heart rate and increases heart rate variability have been reported from 3 to 4 months through 9 months (Izard et al., 1991) and continuing up through ages 14, 24, and 48 months (Bar-Haim, Marshall, & Fox, 2000a).

Differentiating Basal versus "Baseline-to-Task" Measures of Heart Rate Variability

Important distinctions have been made between baseline or "basal" heart rate variability and infant reactivity to stimuli, each of which provide important information (Alkon et al., 2006a; Bornstein & Suess, 2000a; DiPietro et al., 1992). Studies of baseline or "resting" measures of parasympathetic tone are thought to reflect the physiologic state of the infant when not responding to challenge (Alkon et al., 2006b) or have been conceptualized as providing "tonic" measures of autonomic functioning and the potential responsiveness of the individual (e.g., Porges, Doussard-Roosevelt, Portales, & Greenspan, 1996h).

The association between fetal, neonatal, and infant heart rate variability and development is based on the idea that increases in parasympathetic activation facilitate the regulation of numerous interrelated bio-behavioural systems. In healthy near-term fetuses between 36 and 40 weeks' gestation, there is evidence that high parasympathetic tone is associated with more optimal physiological state (increased control of heart rate and efficiency of homeostasis) (Groome, Loizou, Holland, Smith, & Hoff, 1999).

As basal measures, vagal tone and RSA have frequently been studied in the neonatal period. Generally, greater heart rate variability has been positively related to developmental outcome, whereas relatively lower "basal" heart rate variability (lower parasympathetic tone) has been found to occur more often in at-risk populations (e.g., Fox et al., 1985; Porges, 1988). Over the first year of life, baseline or "basal" measures of heart rate variability have also been linked to concurrent competencies. For example, in 3- to 6-month-old infants, higher baseline variability has been linked to less distractibility from attention to visual patterns (Richards, 1987c), higher concurrent development (MDI) on the Bayley Scales (Richards et al., 1989), and better recognition memory (e.g., Frick et al., 2001). At 3-, 5-, and 6-months, higher resting RSA was linked to greater sustained attention and to greater heart rate deceleration when the infants were presented with novel visual stimuli (Richards, 1987b; Richards, 1989b).

Rate of maturational change as indicated by basal measures of heart rate variability has also been studied in relation to developmental outcomes. In term-born infants, greater maturation of prenatal heart rate variability, as monitored from 28 or 32 weeks' gestation, predicted better mental, motor, and language outcomes at 2 and 3 years of age, suggesting that fetal heart rate variability can serve as an indication of developing neural control during gestation (DiPietro, Bornstein, Hahn, Costigan, & Achy-Brou, 2007a). In preterm infants born 1000–1500 g, greater RSA maturation and lower basal heart rate following birth, as measured from 33 to 35 weeks' gestation, was associated with better mental, gross motor, and social functioning at 3 years, as well as social competencies longitudinally at school age (Doussard-Roosevelt, McClenny, & Porges, 2001; Doussard-Roosevelt, Porges, Scanlon, Alemi, & Scanlon, 1997). Results of these studies suggest that baseline heart rate variability and rate of maturation in heart rate variability have prognostic value for early functioning.

In contrast to studies that have used "resting" or "maturational" measures of heart rate variability, "baseline-to-task change" studies of infant responsivity, which have been explored less frequently, are thought to provide data on the infant's capacity to regulate responses (Alkon et al., 2006c). Importantly, researchers who have conducted electrophysiologic studies of infant regulation have argued that baseline-to-task studies index the capacity for engagement and disengagement, which, depending on the challenge faced, may reflect higher-level cortical involvement. As a result, these studies are seen as having the potential to measure the regulation and organization of a variety of systems including emotions and cognition, as well as to reflect the regulation and integration of internal regulatory systems (Alkon et al., 2006d; Bornstein & Suess, 2000b). Prior to a review of baseline-to-task studies that are relevant to this dissertation research, theoretical frameworks supporting the study of attention and heart rate are outlined.

Theoretical Frameworks

Relating Heart Rate and Heart Rate Variability to Attention

As described earlier, various attentional behaviours have been linked to specific patterns or phases of the cardiac response. However, views of the role of heart rate change in relation to attention have differed. For example, some researchers have related heart rate deceleration to greater receptivity and responsiveness (Lacey & Lacey, 1980) and the enhancement of input of stimuli (Graham, 1979), whereas others have emphasized the indirect effect of reductions in motor activity (Obrist, 1981). Importantly, early cardiac autonomic research identified a relationship between gradual suppression of heart rate variability (i.e. beat-to-beat fluctuations in heart rate) and the increasing difficulty of a task or "perceptual load" (Kalsbeek & Ettema, 1963). Since that time, research findings provided evidence of a stabilizing of heart rate associated with sustained attentive observation of the external environment in both adults (e.g., Lacey, 1967; Porges et al., 1969) and newborn infants (e.g., Porges, Arnold, & Forbes, 1973; Porges, Stamps, & Walter, 1974). Studies of this nature led Porges (1976) to hypothesize that attention has two components: a reactive component consisting of directional heart rate response determined by the infant's perception of the stimulus, and a sustained component consisting of a reduction in heart rate variability during attention. The reduction in heart rate variability was viewed as a physiological strategy that facilitated sustained attention, mediated by the parasympathetic nervous system. To measure these changes in heart rate variability, Porges (1985a) developed an index of cardiac vagal tone, a basal measure of the homeostatic function of the vagal system and of regulation and responsiveness. Porges (1995d) also further developed the "polyvagal theory," a "neurogenic" model of vagal regulation, to explain how vagal pathways regulate heart rate and metabolic output in response to novelty, challenge, or less demanding situations. Vagal influences are seen as providing a restorative function during states of low environmental demand, such as sleep; vagal or parasympathetic influences affect heart rate at the sinoatrial node; thus heart rate is kept low. However, in situations of environmental challenge, vagal inhibition on the cardiac pacemaker is withdrawn, and heart rate increases. In this model, efferent pathways from the vagus to the heart provide a homeostatic function by way of negative feedback following the neural interpretation of the cardiac state from afferent vagal pathways. This negative feedback system, or "vagal brake," regulates changes in metabolic output, enabling the individual to engage and disengage from the environment, depending on the challenges of the situation (Porges, Doussard-Roosevelt, Portales, & Greenspan, 1996g). This system has been proposed to play a critical role in the regulation of active processes such as attention, information processing, and emotion (Porges, 1995c; Porges, Doussard-Roosevelt, Portales, & Greenspan, 1996f).

The Attention-Arousal System

John Richards has presented a model in which infant heart rate change during the presentation of stimuli is used to determine various phases of attention (e.g., Richards et al., 1992). He has recently extended his model by outlining the relationship between the development of a general arousal/attention system in the brain and the development of brain systems involved in attention and cognition (Richards, 2001; Richards, 2003b). When activated by sensory information, this general arousal system "energizes" or "invigorates" primary sensory areas in the cortex and influences other attention systems such as the posterior attention system described by Posner and his colleagues (e.g., Posner et al., 1990). In this arousal/attention model, changes in heart rate response that occur during periods of behavioural attention in infants can be seen as indirect measures of the brain areas that are recruited and activated during those periods (Richards, 2003b). Specifically, the phase of sustained deceleration of heart rate is seen as a marker of the non-specific arousal of the brain (Richards, 2001; Richards, 2004). As indicated earlier, neural control of the heart rate changes associated with changes in attention originate from cardioinhibitory centres in the orbitofrontal cortex via the vagus (10^{th} cranial nerve), which act through the parasympathetic nervous system when heart rate slows along with the engagement of the arousal system (Panneton & Richards, in preparation). Richards (2001) suggests that the arousal system that is activated in the brain during sustained attention not only energizes specific brain systems involved in cognitive activities, but also acts to select behaviour that is adaptive to the specific demands of the task and the goals of the infant.

In contrast to disorganized or less-coordinated brain states, focused attention is seen as a state of brain activation in which neurotransmitters and neural networks are functionally organized and coordinated. This increases the general proficiency of responses involving attention and cognition such as the efficient encoding, storing, and retrieval of information. In this view, results of studies that associate relevant psychological with physiological processes allow inferences to be made about brain development and inform a developmental cognitive neuroscience approach to attention (Richards, 2001).

Across the first year of life, infants have shown increased recognition memory (Frick, Colombo, & Saxon, 1999; Frick et al., 2001; Richards, 1997c) and less distractibility (Lansink & Richards, 1997j) when the acquisition of information occurred during heightened arousal, as indicated by sustained decelerations in heart rate. Richards maintains that attention has a facilitative effect on infant recognition memory because the brain systems responsible for information acquisition and recognition are enhanced during attention (Richards, 2003b). Supported by studies showing developmental change in heart rate and brain responses using event-related potentials (ERPs) that are associated with attention (Richards, 1989a; Richards, 2003a). Richards (2003b) emphasizes the dramatic development in this general attention/arousal system over the first year of life.

Baseline-to-Task Studies

As described earlier, there is an extensive history of research on heart rate change in response to various conditions or stimuli. Studies that have examined heart rate response and changes in heart rate variability in relation to infant focused attention will be reviewed. Relevant "baseline-to-task" studies of heart rate and heart rate variability that have informed the rationale and hypotheses in this dissertation research are also discussed.

Developmentally, a number of studies have found that infants who display greater regulation of heart rate and heart rate variability in response to a variety of stimuli or conditions also show relatively more positive behaviours and development. In keeping with other studies that linked "basal" heart rate variability to infant competencies, Huffman et al. (1998) found that 3-month-old infants who had high baseline vagal tone showed fewer negative behaviours during an experimental procedure involving a series of visual, auditory, and tactile stimuli. However, with regards to baseline-to-task responses, it was the infants who decreased vagal tone during the experimental procedure, who were rated by their mothers as having longer attention spans and more easily soothed. In another study, 9-month-old infants who suppressed their cardiac vagal tone while undergoing a developmental assessment demonstrated fewer social problems at 3 years of age, as compared to infants who had difficulty decreasing vagal tone from the baseline to test situation (Porges, Doussard-Roosevelt, Portales, & Greenspan, 1996e). Interestingly, infant suppression of vagal tone or reduction in beat-to-beat variability during cognitive engagement appears to be a fairly consistent pattern, elicited both in normal term-born and at- risk populations. Suppression of RSA was reported for both term-born and preterm infants during a contingency learning task, provided infants learned the task (Haley, Grunau, Oberlander, & Weinberg, in press). Suppression of vagal tone has also been reported during a developmental assessment in both healthy term-born infants between 8 and 11 months of age and regulatory-disordered infants of the same age (DeGangi, DiPietro, Greenspan, & Porges, 1991).

Porges et al. (1996d) distinguished between resting and dynamic measures of vagal tone. Greater parasympathetic activity at rest supports restorative processes. However, during states of challenge, the vagus acts to regulate cardiac and consequently metabolic output, that when regulated allows the infant to recruit behaviours and psychological processes to engage and disengage with environmental demands. In the polyvagal theory these responses are mediated by the "vagal brake", which represents the graded inhibition of the cardiac pacemaker. Thus, in the view of Porges and his colleagues, the vagal brake is seen as the mechanism through which infants contingently interact with objects. Decreases in vagal tone are seen as the appropriate regulation of the vagal brake during attention demanding tasks. Importantly, Porges et al. make the point that heart rate is not always highly correlated with changes in vagal tone because heart rate is not completely determined by this "graded" inhibition of the vagal brake.

In summary, a number of studies provide evidence for a relationship between increased infant cardiac autonomic regulation and better ability to respond and adapt to the environment. In infancy, suppression of heart rate variability has been documented during tasks involving attention and cognition. Distinguishing between measures of high vagal tone or "basal" measures of heart rate variability versus baseline-to-task (dynamic) changes in heart rate variability is important, as each represents different systems of response strategy (Porges, Doussard-Roosevelt, Portales, & Greenspan, 1996c).

Magnitude of Heart Rate Change

As described earlier, studies that have examined patterns of infant heart rate response, such as the characteristic deceleration in heart rate associated with initial orienting and sustained interest, have spanned the last 50 years. Further to establishing the direction of heart rate change during orienting and the sustained continued decrease in heart rate that accompanies the infant's focused interest, the nature and significance of these heart rate changes have also been examined. At age 6-months, only those infants who showed heart rate deceleration during the presentation of the stimulus successfully demonstrated visual recognition memory (i.e., looked longer at the novel stimulus), supporting the view that greater decreases in heart rate in response to visual stimuli represent greater developmental competence or neural integrity (Linnemeyer & Porges, 1986). Similarly, Richards (1994) found that 3- to 6-month-old infants successfully showed novelty preference when they were exposed to visual patterns during a period of prolonged deceleration of heart rate. By contrast, novelty preference was not seen when infants were exposed to the stimuli during the period when their heart rates were beginning to accelerate back to baseline (attention termination).

Richards (1985a) found that 5-month-old infants showed a decelerative heart rate response during exposure to visual stimuli in a habituation study, whereas younger infants aged 3½ months showed an accelerative response. Richards and Casey (1991c) found that heart rate response during sustained attention increased with age (at 3, 5, and 6 months). Ruff and Rothbart (1996b) point out that the magnitude of heart rate deceleration in response to various stimuli increases from 2 to 9 months of age, coinciding with an intense interest in novelty and the "operation of the orienting/investigative system."

Magnitude of deceleration in heart rate response has also been linked to duration of looking. Based on an early study that linked duration of visual fixation to magnitude degree of heart rate deceleration, Lewis, Kagan, Campbell, and Kalafat (1966) proposed that an intensity measure of attention could be determined. Recent findings suggest that over the ages of 3, 5, 6, 9, and 12 months, there is greater magnitude of sustained heart rate deceleration particularly in response to more complex and dynamic stimuli (Courage, Reynolds, & Richards, 2006c). When infants were presented with a variety of visual stimuli (presented on a screen) that varied according to static/dynamic and simple/complex properties, greater decreases in heart rate from 6 through 12 months of age also paralleled increases in duration of looking, particularly for complex stimuli.

In summary, magnitude of heart rate deceleration has been associated with increased duration of looking and improved recognition memory. Numerous studies support the view that greater decreases in heart rate in response to visual stimuli represent greater maturity, developmental competence, and neural integrity.

Focused Attention and Heart Rate Response

In several studies, the integrity of behavioural and physiological systems as they relate to attention has been examined. There is evidence to directly support the hypothesis that there is an overlap between focused attention to visual stimuli, and the heart-rate defined phases of sustained attention (Richards et al., 1992). Richards and his colleagues have found that active encoding of information coincides with prolonged deceleration of heart rate, as demonstrated by a relative lack of behavioural distraction (Casey & Richards, 1988; Richards, 1987a). Additionally, findings support the idea that information processing can occur in response to a brief exposure to stimuli, provided that the engagement occurs during an attentive state. For example, when infants between 3 and 6 months of age were exposed to stimuli during the phase of heart rate that was characterized by sustained deceleration following orienting, as compared to other phases, they performed better on visual recognition-memory tasks (Frick et al., 2001; Richards, 1997b).

In another study of infant attention and heart rate, photographs of faces were shown to infants 3 to 9 months of age (Colombo, Shaddy, Richman, Maikranz, & Blaga, 2004). In this study, older infants showed greater heart rate deceleration following the presentation of the stimuli, maintained deceleration for a greater proportion of each look, and terminated their looking more efficiently.

In summary, these findings have suggested that the organization and integrity of heart rate together with attention increase over the first year of life. Further studies of term-born infants also support the view that concordance of behaviour and physiology reflects integrity of behaviour or increased efficiency of functioning. Because these studies have examined infant attention during the exploration of 3-dimensional objects, they are discussed in greater detail below.

Studies of Attention and Heart Rate during Infant Exploratory Play

Few studies have examined infant attention and heart rate response during exploratory play in infants. Important distinctions are to be made between these studies and infant studies that use static or screen displays of visual stimuli. One obvious difference is that infants manipulate the objects or toys that they are engaged with in the former but not in the latter studies. For studies of this nature, concerns have been raised about the influence of infant's activity in manipulating objects on heart rate and direction of heart rate response, particularly in infants of at least 6 months of age, who presumably have a greater intent to grasp an object (e.g., Pomerleau & Malcuit, 1980b). However, in a recent study of infant looking and reaching in 7½-month-old infants, actual reaching did not alter the autonomic and behavioural changes that are typically associated with attention to simple displays (O'Sullivan & Berthier, 2003b). Furthermore, attention was maintained throughout reaching, providing behavioural and physiological evidence of more intense engagement during manual exploration than during simple looking.

In a baseline-to-task study of exploratory play in two-year-old children, Hughes and Hutt (1979b) examined changes in heart rate and heart rate variability from baseline to periods of free play, exploration, and puzzle solving. They found that distinctions could be made between these specific behaviours, based on their findings that suppression of heart rate variability was greater during exploration and during puzzle solving as compared to during periods of unstructured free play. Based on their findings, they suggested that the task demands of exploration and puzzle solving are greater than those of unstructured free play. Further to this study, two studies of term-born infants conducted by Lansink and colleagues are of particular relevance to this current dissertation research. In one of the studies, Lansink et al. (1997i) examined propensity for distraction in term-born infants aged 6, 9, and 12 months while they explored 3-

dimensional objects. While infants interacted with novel objects, distracting stimuli were presented either during behavioural focused attention (examining) or casual attention, as defined by Holly Ruff and her colleagues (e.g., Ruff, 1986n). Additionally, using on-line judgements of heart rate while infants explored the novel objects, distracting stimuli were presented to the infants either during sustained heart rate deceleration or during the time when heart rate had returned to the pre-stimulus level (attention termination). Infants showed less propensity for distraction when distracting stimuli were presented either during behavioural focused attention or during phases characterized by sustained deceleration of heart-rate that follows orienting (compared to casual attention or the phase of heart rate as it returns to the pre-stimulus level). Furthermore, Lansink et al. found latency (time) to distraction was longest when heart rate and behaviour were congruent with attention measures, suggesting that higher levels of information processing occur when both heart rate and behavioural ratings indicate attentional engagement. Following the data acquisition, periods during which the infant was judged to be in focused attention (using off-line video-recordings), and periods during which heart rate was judged as showing sustained deceleration (using off-line computer analyses of heart rate data files) were used to examine the congruence between these two measures. When heart rate was used as an anchor, the two measures overlapped by 61%; however, when focused behaviours were judged according to coherence of heart rate deceleration, overlap was only 40%. The authors think this may have occurred in part because they included focused attention periods that were very short, during which acceleration occurred. Nevertheless, these results revealed a temporal overlap between behavioural measures of focused attention and heart rate measures during infant exploration of objects. This study also suggested that greater coherence of behavioural focused attention and heart rate response reflects more efficient neural recruitment and coordination and greater neural integrity.

In a second study, also conducted with term-born infants ages 6, 9, and 12 months, Lansink, Mintz, and Richards (2000) collected heart rate and behavioural measures of attention during infant exploration of objects, again as operationally defined for this dissertation research (e.g., Ruff, 1986m). They reported large decelerations of heart rate at the beginning of behaviourally defined focused attention, but little heart-rate change for more casual looking (i.e. engaged but not in a focused way). Importantly, they found that focused attention (as defined using either behaviour or heart rate) was usually preceded and followed by casual attention. However, only casual looks toward the object that engaged attention sufficiently to hold the look were accompanied by immediate heart rate deceleration and eventual focused attention. If casual looks did not become focused, infants were more inclined to look away, and this occurred most often when heart rate had returned to pre-stimulus level. This indicated coherence between the cycling of casual attention and focused attention; however, this cycling was loosely rather than tightly coupled to the cycling of heart-rate phases of sustained deceleration and return to pre-stimulus levels. There were developmental increases in the sequencing and organization of attention during a look, as older infants were more likely to engage in multiple attention cycles.

Finally, some recent studies assessed changes in heart rate coincident with periods of behavioural focused attention as defined by Ruff (1986l). In these studies, 6- and 12-month-old term-born infants were exposed to background television (with different types of programs) during either the first or second half of toy play sessions (Setliff, Earl, Murphy, & Courage, 2007; Setliff, Murphy, & Courage, 2008). Infants at both ages engaged in toy play despite the presence of the background television; however, they glanced frequently at the television, increasing their looks as they became more familiar with the toys. The older infants showed more focused attention and were less distracted by the television than the 6 month infants. At 12-months of age, infants showed the greatest magnitude of heart rate deceleration during educational shows. However, at 6-months, infants showed greater heart rate deceleration while the television was on regardless of the type of programming, suggesting a greater depth of processing, and, as Ruff et al. (1986k) suggest, possibly reflecting "peripheral narrowing" in the face of a distracting stimulus.

In summary, these studies provide evidence for a more intense focus on the part of the infant when both heart rate and behaviour indicate focused attention. Furthermore, these studies suggest that behavioural and heart-rate measures of attention are loosely coupled temporally. The studies not only confirm the distinction between casual and focused attention formerly used in behavioural studies (Ruff et al., 1991), but also shed important light on the nature of, and relationship between, focused attention and heart rate patterns in full-term infants during toy exploration in the second half of the first year of life.

Heart Rate Response and Heart Rate Variability in the Preterm Infant

There is ample evidence that heart-rate responses may be altered as a result of premature birth. As noted earlier in the review, the extra-uterine environmental experience of the very preterm infant occurs at a time of very rapid brain development, often includes pain, and can impose significant stress on the immature central nervous system (CNS). The preterm infant's adaptation to the extra-uterine environment may be one factor affecting the development of physiological response systems (Eiselt et al., 1993a; Grunau et al., 2001). Following their premature birth, the infant's successful transition to the extrauterine environment and subsequent adaptation over the neonatal period is dependent on both the stability/instability of the neonate and it's interactions with the environment (Verklan & Sparks, 2001). In vulnerable preterms, stability can be disrupted as a result of seemingly innocuous stimuli such as regular caregiving procedures (e.g., Holsti, Grunau, Oberlander, & Whitfield, 2005b; Perry et al., 1990), or events such as social interaction (Gorski, Hole, Leonard, & Martin, 1983).

In recognition of the vulnerabilities of the preterm infant and the potential adverse effects of necessary routine NICU care, regulation of the preterm infant's behavioural and physiological processes is the predominant goal of developmental care (Als, 1998a). However, while significant progress in recent years in the developmental care of premature infants has yielded positive results (e.g., Als et al., 2004), the treatment necessary for the high-risk premature infant's survival in the NICU, which can include painful and stressful experiences, may lead to dysregulation and inhibit development of integrative self-regulatory processes (Grunau, 2003). One can view the very preterm infant's adaptation to extra-uterine life as more or less successful, with those infants who experience less adaptation predisposed to later outcome difficulties. However, the pathways according to which adaptation challenges during early development may lead to specific childhood outcomes such as behaviour problems are not well understood (Olson, 2002). Stress response to pain involves a complex interaction of CNS-initiated physiologic processes (Franck, 1998) and if these processes are immature, may interfere with the neonate's regulatory capacities (Lynam, 1995). This can have immediate impact, as evidenced by the disorganization of behavioural and physiologic states (Craig, Whitfield, Grunau, Linton, & Hadjistavropoulos, 1993; Johnston, Stevens, Yang, & Horton, 1996) or adverse physiological consequences such as fluctuations in blood pressure that increase the risk of intraventricular hemorrhage and periventricular leukomalacia (Volpe, 1995).

Prematurity is associated with severe respiratory difficulties due to Respiratory Distress Syndrome (RDS) related to immature lung development. Apnea of prematurity, is related to the immaturity of brain stem respiratory control centers; thus its prevalence and severity increases with earlier prematurity, with rates of greater than 85% reported in infants born <28 weeks gestation (Hunt, 2006). ELGA infants are also at greater risk of acquired infection and late-onset sepsis may be a significant risk factor for chronic respiratory difficulties (bronchopulmonary dysplasia; BPD), which involves injury, inflammation and residual scarring in the lungs. Infants with multiple perinatal risk factors including postnatal infections spend significantly more days on mechanical ventilation (Stoll & Hansen, 2003).

There is evidence for longer-term direct and indirect effects on regulation and development of the infant's extra-uterine experience in the neonatal intensive care (NICU) environment. Studies on the impact of early NICU pain show altered physiological and behavioural reactivity in very preterm infants subsequent to procedural pain while still in the NICU at 32 weeks post-conception (Grunau et al., 2005a; Grunau, Oberlander, Whitfield, Fitzgerald, & Lee, 2001; Holsti, Grunau, Oberlander, & Whitfield, 2005a; Johnston & Stevens, 1996), as well as later in infancy (Grunau et al., 2001; Oberlander et al., 2000a). Moreover, basal stress hormone regulation is shifted in infants born extremely preterm (Grunau et al., 2007b; Grunau, Weinberg, & Whitfield, 2004b). Thus, disruptions of regulatory processes associated with CNS immaturity and the impact of adverse experience can be manifested physiologically or functionally in a lack of adaptive function, arousal, or state organization. For preterm and full-term infants, the importance of regulating state and arousal has been emphasized and underlies the development of control processes such as attention regulation (Rothbart, 1989).

Basal Heart Rate and Heart Rate Variability

There is evidence that heart rate response may be altered in very preterm infants. Elevated heart rate has been reported in preterm infants; however, many studies comparing preterm to term infants have been conducted in the neonatal period prior to preterm infant discharge from the neonatal intensive care unit albeit close to or at term equivalent (36 to 38 weeks gestational age). However, heart rate is dependent on post-natal age as well as chronological age, therefore these differences are somewhat difficult to interpret. For example, in neonatal studies of infants at 36 to 38 weeks conceptional age, high-risk preterm infants have been shown to have elevated baseline heart rate of approximately 30 bpm higher than infants born at term (Field, 1979; Krafchuk et al., 1983; Rose, Schmidt, & Bridger, 1976). This difference may be due to the increase in HR seen in the first 2 months of life reflecting "acceleration" of the maturational course in preterm infants (Eiselt et al., 1993b). Alternatively, it has been hypothesized that extra-uterine life may delay maturation or alter autonomic regulation (Eiselt et al., 1993c). In a study of preterm infants at term equivalent, Eiselt et al. found that compared to term-born infants, preterm infants had higher heart rate and lower amplitude of heart rate variability in the high-, mid-, and low-frequency bands; however, they determined that differences were largely due to diminished parasympathetic component of heart rate variability. Similarly, Henslee, Schechtman, Lee, and Harper (1997d) found that compared to term-born infants, preterm infants with apnea of prematurity exhibited higher heart rate and reduced heart rate variability at 40 weeks post-conception. Eiselt et al. noted that the differences seen between groups may reflect either acceleration or delay of maturational processes, and that the underlying reasons for premature delivery that may also affect autonomic regulation should be considered.

While it can be argued that differences between preterm infants at term equivalent, compared to infants born at term may be attributable to differences in postnatal age, there is also evidence that differences in resting heart rate between preterm and term-born infants may persist beyond the newborn period. Henslee et al. (1997c) also found that for infants who were born at earlier gestation ages (<30 weeks) and in infants with respiratory distress syndrome (RDS) who were born between 30 and 35 weeks gestation, differences persisted over the following 6 months. They proposed that premature birth and complications associated with prematurity might have long-term effects on central and peripheral mechanisms that control cardiovascular activity. In another high-risk sample of extremely low birthweight infants (ELBW; ≤ 800g) seen at 8 months of age, basal heart rate was found to be on average 11 bpm higher than term-born controls, possibly reflecting a "resetting" of autonomic regulation (Grunau et al., 2001).

In summary, differences in heart rate and heart rate variability between preterm (particularly higher-risk preterms) and term-born infants persist beyond the neonatal period into the first year of life. Based on these findings, it has been proposed that premature birth, and complications associated with prematurity, as well as stress of adapting to repeated procedures, might have long term effects on central and peripheral mechanisms that control cardiovascular activity (e.g., Eiselt et al., 1993d; Grunau et al., 2001; Henslee, Schechtman, Lee, & Harper, 1997b).

Baseline-To-Task Studies: Heart Rate Response in Preterm Infants

There are few studies of "baseline-to-task" changes in heart rate or heart-rate variability in preterm infants, particularly as related to perinatal risk factors. Early studies showed that full-term infants showed both behavioural response and heart rate change in response to a variety of stimuli, while preterm infants showed less coupling of response (Field, Dempsey, Hatch, & Ting, 1979; Rose et al., 1976). Rose et al. (1976) reported behavioural and heart rate response to tactile stimuli in full-term infants, but weaker behavioural and no significant cardiac response in the preterm infants. These studies suggested that autonomic and behavioural systems were less integrated in the preterm neonate.

With regards to attention, some studies have shown that infants with likely CNS damage have unusual heart rate responses during attention. In one study, which compared preterm to full-term infants at 3 months of age, heart rate was 15 to 20 beats-per-minute faster for preterms in response to visual stimuli (Fox & Lewis, 1983a). Other differences in heart rate response have been noted in preterms, including longer latency to response (Schulman, 1970), less habituation of heart rate response (slower recovery) following a novel stimulus (Fox & Lewis, 1983b). Furthermore, heart rate response to video stimuli (patterns and Sesame Street) that reflected decreased orienting and less sustained attention at 3 and 6 months of age, were reported, particularly in higher risk preterm infants, defined by respiratory problems in the neonatal period (Fox & Lewis, 1983c; Richards, 1994b). In a recent study of 5-month-old preterm and term-born infants, Stroganova et al. (2006b) evaluated two types of attention (exogenous and endogenous), during which infants' regulation of heart rate variability (RSA) was measured. They used two tasks that would elicit either a reflexive interest (soap bubbles) or a sustained more internally driven interest (visual expectation paradigm using a disappearing and re-appearing doll). Preterm infants displayed less RSA response to endogenous attention compared to full-term infants, which the authors interpreted as consistent with diminished parasympathetic control. In a study that examined the relationship between contingency learning and heart rate, in 5- to 10-months-olds, the highest risk preterm infants (defined by the need for mechanical ventilation) showed delayed cardiac reactivity accompanied by a smaller increase in response to the contingency (Millar & Weir, 2007). In another study of contingency learning in term-born compared to preterm infants at 3 months corrected age, infants who learned the task showed greater suppression of heart rate variability (RSA) than non-learners (Haley et al., in press). This suggested that the capacity to regulate parasympathetic activity during a challenge enhances learning. Overall, preterm infants showed less learning and shorter duration of looking. Furthermore, with regards to heart rate, preterm infants had higher basal rate, demonstrated greater increases in heart rate to contingency, and dampened heart rate response to non-reinforcement. The findings support the view that preterm infants have impaired regulation of arousal in early infancy.

Another study compared relationships between infant regulation of heart rate and competence as defined by development, and sophistication in exploratory play, in term-born versus preterm infants at 8 months corrected age (DiPietro et al., 1992). Infants were classified according to whether they increased or decreased their vagal tone (an index of parasympathetic cardiac response) to a surprise stimulus (jack-in-the-box). Infants who showed increased vagal tone were found to have higher developmental scores at 8-months CCA, and showed more sophisticated exploratory play. Furthermore, preterm infants showed less time examining objects, and tended to decrease vagal tone in response to the surprise stimulus. Perinatal risk factors such as more respiratory support, and higher number of days hospitalized were related to poorer exploratory play and decreased range of examining behaviours (DiPietro et al., 1992).

In summary, in baseline-to-task studies, there is evidence that in response to a variety of stimuli, preterm infants show patterns of heart rate and heart rate variability that indicate poorer orienting, less sustained attention, and less integration of behavioural and heart rate response, compared to infants born full-term. Furthermore, there is evidence that those infants who are less efficient in modulating their heart rate responses are those with more perinatal risk factors, greater illness severity, or born at the earliest gestational ages.

Overview of Research Plan

In summary, children born very preterm have a significantly higher incidence of attention, cognitive and learning problems, particularly in areas of selective and sustained attention, visual memory, and visually based problem solving. The ability to focus and sustain attention is central to cognitive development. Findings from numerous studies emphasize the importance of focused attention as reflecting underlying processes related to individual differences in cognitive potential, thus it constitutes a vital construct in the study of infant development. Considering the extent of attention-related problems in infants born very preterm (≤32 weeks gestation), there is a comparatively scant literature on the early development of attention regulation in the first year of life. There is a particular lack of studies of behaviours that are ecologically appropriate in a naturalistic context (such as independent infant exploratory play), and few studies address both behavioural and physiological indices of attention.

Focused attention, which refers to the selective aspects and intensive aspects of attention, can be indexed by observing a variety of distinct behaviours such as facial expressions of interest and concentration during the exploration of objects. Using an established paradigm of exploratory play with 3-dimensional objects, global ratings of behavioural focused attention have been developed for the identification of relative developmental risk in infants born very low birthweight (VLBW; ≤1500 g), (Lawson et al., 2001). However, (to my knowledge) in these 5-point global ratings of preterm infants have not been compared to healthy term-born infants. Thus the present study is the first to examine the 5-point ratings of global attention during naturalistic exploratory play in very preterm infants compared to healthy term-born controls.

In this study, infants born preterm at very low gestational age (VLGA; ≤ 32 weeks) were observed during independent exploratory play, during which heart rate measures were recorded continuously. Thus, focused attention was examined behaviourally and physiologically, as well as the relationship between behavioural and heart rate responses. Examining the quality and organization of attention, as well as the integrity of related physiological responses in early infancy, is essential for understanding the nature and etiology of these processes and their link to problems in the very preterm population later in childhood.

Studies of term-born infants that have examined developmental changes in both attention and heart rate across infancy provide a basis for determining what differences might be expected in preterm infants. This dissertation study builds on an established body of research conducted with term-born infants that has related specific phases of attention to patterns of heart rate response. Heart rate measures have been related to maturity and developmental outcome, and appear to reflect regulatory patterns that may underlie the ease or difficulty with which infants acquire specific abilities. Behaviour and cardiac autonomic responses reflect the function of the developing nervous system, moreover they can be viewed as indirect measures of the generalized state of brain arousal-activation during infant attention (Richards, 2001; Richards, 2003b). Thus, integration of behaviour and physiology can provide a window to integrity or maturity of regulatory systems that may not be evident using single measures. For studies of biologically vulnerable infants, such as those born very preterm, this is particularly important as a potential way to identify alterations in systems that reflect varying degrees of neurodevelopmental integrity.

Focused attention has been studied using behavioural and cardiac autonomic measures together in various paradigms of infant information processing, including object exploration in term-born infants (e.g., Lansink & Richards, 1997h). Specifically, this research builds on studies of term-born infants that show decreased heart rate variability during cognitive challenge and exploratory play, and decreased heart rate during periods of sustained behavioural focused attention. In the literature on preterm infants, there is ample evidence that difficulties in attention and physiologic regulation occur, particularly in relation to greater perinatal risk associated with extremely low gestational age, or greater illness severity in the newborn period. Numerous studies suggest that the ability to modulate heart rate and heart rate variability is more compromised in preterm infants. While research on preterms has been conducted in each of these areas separately, to my knowledge there are no studies that have combined behavioural and physiological components to study early attention processes in this vulnerable population.

In addition to providing information for the first time on global ratings of focused attention in very preterm compared to term-born infants, there are additional novel contributions in this dissertation research. In this research study, the cohort of infants is recently born, which has significance in terms of current neonatal intensive care practices. Furthermore, previous studies included heterogeneous samples of preterm infants with a wide range of gestational age, whereas in the current study, infants born extremely low gestational ages (ELGA; ≤ 28 weeks gestation) were compared with infants born at very low gestational ages (VLGA; 29-32 weeks gestation).

The limit of viability of extremely preterm infants has been lowered substantially during the 1990s, and medical treatment has changed over time. Therefore studies from different periods are not directly comparable. For example, for several years, steroids were administered postnatally to infants with severe BPD, to ameliorate severe respiratory compromise, however, due to concerns regarding adverse effects on brain development the use of steroids postnatally has been reduced significantly in current practice. Moreover, the definition of "high-risk" has changed since infants of far lower gestational age at birth now survive (Wilson-Costello, Friedman, Minich, Fanaroff, & Hack, 2005). Thus studies carried out during the 1970s to 1990s may not be directly applicable to current NICU survivors. Furthermore, studies of VLBW infants typically included both those born at very low gestational age, as well as infants born small for gestational age with intrauterine growth retardation. This dissertation study defined risk according to gestational age, selecting only those infants who were born with birthweight appropriate for gestational age, and comparing ELGA with VLGA infants. Using this careful sample selection will provide greater clarity for identifying the degree of prematurity associated with altered attention regulation. Furthermore, few studies have had sufficient sample size to examine potential differences based on sex, despite the fact that there is evidence that preterm boys, particularly those born at lower gestation, show greater illness severity in the newborn period than their female counterparts and are at greater risk for later developmental problems. Thus, in addition to examining differences according to gestational age at birth, this dissertation study extends knowledge in this area by specifically examining focused attention in relation to sex. These gaps in the literature are addressed in the present study, which tested hypotheses concerning infant focused attention during exploratory play with novel objects, using behavioural and heart rate indices of response. Infants were compared according to gestational age status (ELGA, VLGA, Term-born) and by sex, at 8-months of age CCA. The main goals of this study were to examine the effects of prematurity and sex on infant focused attention and regulation of heart rate during independent exploration of novel objects.

Hypotheses

1. Preterm ELGA infants, compared to preterm VLGA and Term-born infants will show:
    a. Poorer attention behaviours, including lower global focused attention and shorter peak focus;

b. Patterns of heart rate that reflect higher arousal (higher mean HR), less suppression of heart rate variability during exploratory play, and less heart rate change (deceleration) during behaviourally identified periods of focused attention;

2. Preterm boys (both ELGA and VLGA) will show greater negative effects compared to preterm girls.

3. For the ELGA and VLGA preterm infants, after adjusting for perinatal risk factors, better focused attention and greater heart rate change will be associated with higher cognitive functioning.

CHAPTER 3: RESEARCH DESIGN AND METHODS

Overview

This cross-sectional study used quantitative methods of analyses to compare focused attention and heart rate response during independent exploratory play in ELGA (≤28 weeks GA), VLGA (29 to 32 weeks) and term-born infants (37 to 41 weeks GA), and by sex. Infants were seen at 8-months of age (+/- 2-weeks), using corrected age (CA) for the preterm infants.

Ethics

Ethics approval was obtained through the University of British Columbia's Clinical Research Ethics Board (CREB), and the Research Review Committee of the Children's and Women's Health Centre of British Columbia (Appendix D). According to the standards of research practice guidelines, data was collected and coded using unique study identification numbers to protect the identity of patients. The use of study identification numbers enabled coders to rate videotapes while remaining blinded to gestational age group status of the infants.

Participants

The 129 infants that were included in this dissertation research study were from a larger cohort of 207 preterm and term-born infants who were seen at 8-months CA as part of an ongoing longitudinal program of research funded by National Institutes for Health, with additional funding from the Canadian Institutes of Health Research, the Human Early

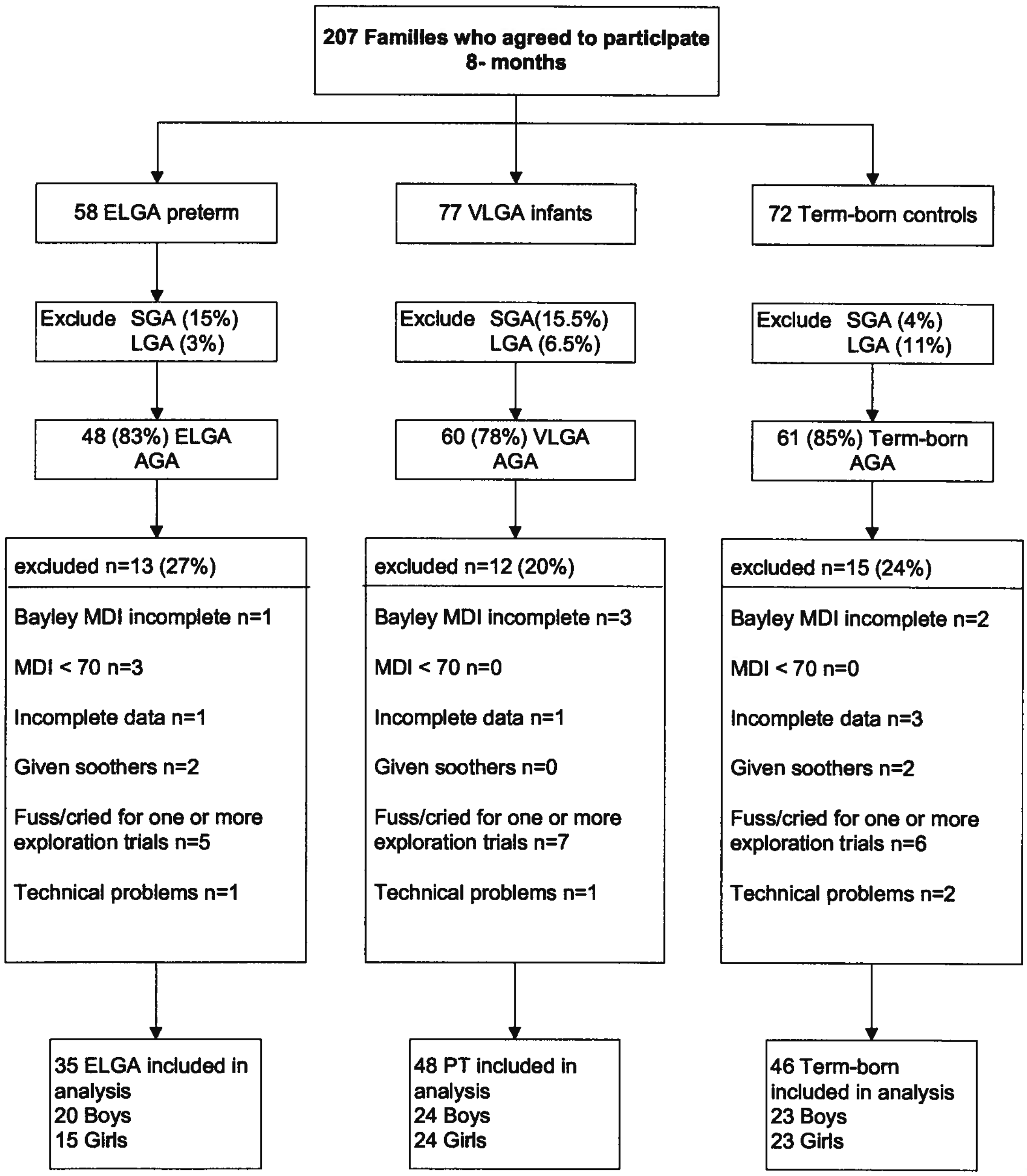
Learning Partnership (through the B.C. Ministry of Children and Family Development) and the Michael Smith Foundation for Health Research. This larger program of research was funded to study the effects of premature birth and early pain exposure on regulatory processes and development (e.g., Grunau et al., 2005b; Grunau et al., 2007c; Grunau, Weinberg, & Whitfield, 2004a; Haley et al., in press; Haley, Weinberg, & Grunau, 2006; Tu et al., 2007b).

The preterm infants were recruited from the regional level III neonatal intensive care unit (NICU) at Children's and Women's Health Centre of British Columbia, Vancouver (C&W), affiliated with the University of British Columbia. Healthy term-born infants were recruited through their pediatricians in the community. Written parent informed consent for all study patients were signed at the time of recruitment, and consent was obtained again at the time of the 8-month visit.

From the original sample, infants were excluded if they had significant intraventricular hemorrhage (IVH grade III or grade IV) and/or periventricular leukomalacia (PVL) on neonatal head ultrasound, as these are risk factors for major neuromotor and neurosensory impairment. Infants with a major congenital anomaly, major neurosensory or severe motor impairment, or maternal report of illicit drug use (e.g. cocaine, heroin) during pregnancy were also excluded from the study. Intra-uterine exposure to maternal use of illicit drugs poses a separate risk to those risks associated with very preterm birth. For the present study, only infants born at birthweight appropriate for gestational age (AGA) were included, since outcomes have been found to differ for infants born small for gestational age (SGA) (Arnold, Kramer, Hobbs, McLean,

& Usher, 1991). Infants born at birthweights that were large for gestational age (LGA) were also excluded due to links with gestational diabetes and adverse perinatal outcomes (e.g., Lao & Wong, 2002). From the sample of 207 infants who returned at 8-months CA, 169 (81.6%) met AGA criteria. Of the ELGA infants excluded due to birth size, 15% were SGA and 3% were large for gestational age (LGA). Percentages of SGA and LGA infants that were excluded for birth size in the VLGA groups were 15.5% and 6.5% respectively, and 4% SGA and 11% LGA for the Term-born infants. Of the 169 AGA infants selected for this study, from the 48 ELGA infants, 60 VLGA, and 61 Term-born AGA infants, a total of n=13 (27%) ELGA, n=12 (20%) VLGA, and n=15 (24%) of the Term-born infants were excluded from the larger AGA sample of 169 infants due to a variety of reasons. Infants were excluded if they did not complete the Bayley Scales of Infant Development, Mental Development Index (MDI) (ELGA=1; VLGA=3; Term-born=2), or obtained an MDI <70 (ELGA=3). Infants with Developmental Quotients of less than 70 are classified as having Significantly Delayed Performance (Bayley, 1993). Infants were also excluded if they were clearly fussy or cried for any of the toy exploration sequences (ELGA=5; VLGA=7; Term-born=6). Infants were also excluded if given soothers (ELGA=2; Term-born=2) due to possible confounding effects of sucking on arousal(e.g., Cranston Anderson, Burroughs, & Measel, 1983). Furthermore, infants were excluded due to incomplete data or technical problems with heart rate acquisition (ELGA=1; VLGA=1; Term-born=3). The final sample consisted of 35 ELGA, 48 VLGA and 46 Term-born infants, with a total of 67 boys and 62 girls. Figure 1 consists of a flow chart that describes sample selection and the reasons for exclusion in each of the three gestational age groups.

Figure 1: Sample Selection and Reasons for Exclusion



SGA: small for gestational age; AGA: appropriate for gestational age; LGA: large for gestational age

Procedures

Participating infants were tracked across time and families were contacted and scheduled prior to the infant turning 8-months of age. Prior to coming to the laboratory, the parent was asked not to reveal the birth status of their infant (preterm versus healthy term-born) to the Research Assistants and professional staff, who were blinded to all infant information and group status during the research testing. Infants were healthy on the test day by parent report. Research testing was carried out in the Early Human Experience Unit at Community Child Health Research (CCHR), Child and Family Research Institute, affiliated with the Children's and Women's Health Centre of B.C. and the University of British Columbia. Standardized assessment on the Bayley Scales of Infant Development (BSID-II) were administered primarily in the Early Human Experience Unit at Community Child Health Research; however, infants who were part of the Neonatal Follow-up Programme at C&W received their Bayley assessment in a clinical setting.

For the research protocol, the parent and infant were brought into a quiet testing room, where they remained for the entire data collection. The testing room was equipped with two inobtrusive ceiling-cameras, one positioned to view the infant, who was seated in a strategically placed infant high-chair next to a testing table, and the other camera positioned to view the mother. The purpose-built testing room had a one-way viewing window from which a Research Technician in an adjacent room monitored the continuous acquisition of heart-rate data. Cardiac signal acquistion was computer-synchronized with the video recordings of behaviour, and an inaudible tone generator foot pedal was used to mark events. To verify heart rate data acquisition and minimize data loss while adhering to a standard protocol, the Research Technician and Research Assistant were equipped with two-way communication devices, which were not audible to others in the room.

The Research Assistant attached three disposable Ag-AgCl electrodes in a triangular pattern on the infant's chest. The electrodes were connected via sheilded cables to an ECG computer in an adjacent observation room, through a port drilled into the wall connecting the testing and observation rooms. Once the ECG signal was verified, a baseline of at least 3 minutes was acquired. As with other infant studies, parents held the infant and were instructed to refrain from engaging the infant or from purposely distracting the infant with objects. The infant was seated in a high-chair equipped with a tray upon which they could independently examine toy stimuli. The parent was seated next to the infant but out of direct view (to the side and rear of the infant) and asked to refrain from engaging with the infant during the toy exploration task. Each toy was placed on the tray in front of the infant according to methods described in previous studies (e.g., Ruff, 1986j). Single objects were used as infants of this age have been found to sustain focused attention for longer periods of time with single rather than several objects presented simultaneously (Ruff et al., 1990). The four individual novel toys were presented sequentially, each for 90-seconds, throughout which heart rate and video recordings were acquired continuously. If the toy was dropped or thrown, the Research Assistant retrieved the toy and placed it back on the infant's tray. According to methods described (e.g., Ruff, 1986i; Ruff et al., 1991), toys were presented in a standard order, not counterbalanced for order. Prior to the administration of the developmental assessment the electrodes were removed from the infant's chest. The infant was moved to the parent's lap at small testing table where a Physiotherapist or Occupational Therapist, trained in infant developmental assessment and blinded to group status, administered the Mental and Psychomotor scales of the Bayley Scales of Infant Development-2nd Edition (BSID-II).

Measures

Neonatal and Infant Characteristics

Prospective medical and nursing chart review was carried out by a Neonatal Research Nurse, to collect information on infant characteristics including birthweight, gestational age at birth, Apgar score at 5 minutes, illness severity using the Score for Neonatal Acute Physiology (SNAP-II), (Richardson, Corcoran, Escobar, & Lee, 2001b), Neonatal Medical Index (NMI), (Korner et al., 1993b), head ultrasound scan results, days of mechanical ventilation, and other relevant medical and nursing data. Demographic family information was obtained by questionnaire.

Focused Attention

Global Ratings of Focused Attention

Global ratings of focused attention were derived according to the methods by Lawson and Ruff (2001), (see Appendix A). These 5-point ratings of global attention were developed for clinical use and validated on 71 very low gestational age (VLGA) infants at 7 months, and 62 VLBW infants at 12 months during exploratory play using concurrent quantitative measures of focused attention: duration (r = .83) and number of focused episodes (r= .79) at 7 months. Coders rated each of the infant's four toy exploration sequences with a global attention score from 1 to 5, according to the level of infant focused attention. The coder's judgements were based on descriptions of an integration of different behaviours that reflected the duration, intensity and quality of the infant's focused engagement and exploration. Thus single global ratings were assigned for each of the infant's four toy exploration sequences. Lawson and Ruff's working guidelines for rating infant focused attention include 5 descriptions ranked on the basis of varying degrees of in-attentive/ attentive behaviours. To ensure reliability, two trained coders independently coded all toy exploration sequences. Inter-rater reliability, as reported by Lawson and Ruff (2001), was established on 144 sequences for 7-month infants with perfect agreement on 65%, disagreement by 1 point on 34%, and disagreement by 2 points on 1% of the sequences. For the current study, ratings were done in accordance with Lawson and Ruff's procedures where initial ratings were accepted if exact and re-rated by both coders if they differed. If re-rated scores differed by 1 point, a mid-point score was derived. If re-ratings were off by more than one point, a third trained coder was used to settle the difference. For the current study, coders had perfect agreement on 68% of the ratings, and disagreed by 1 point on 31% of the ratings, and by 2 points on less than 1% of the ratings. Using the 5-point scale, all infants had individual ratings for each of the four toy exploration sequences. For the purposes of relating level of attention to heart rate, the average of the four individual global ratings was divided into three levels of Global Attentiveness (Inattentive = rating 1 to 2.5 [n=47];

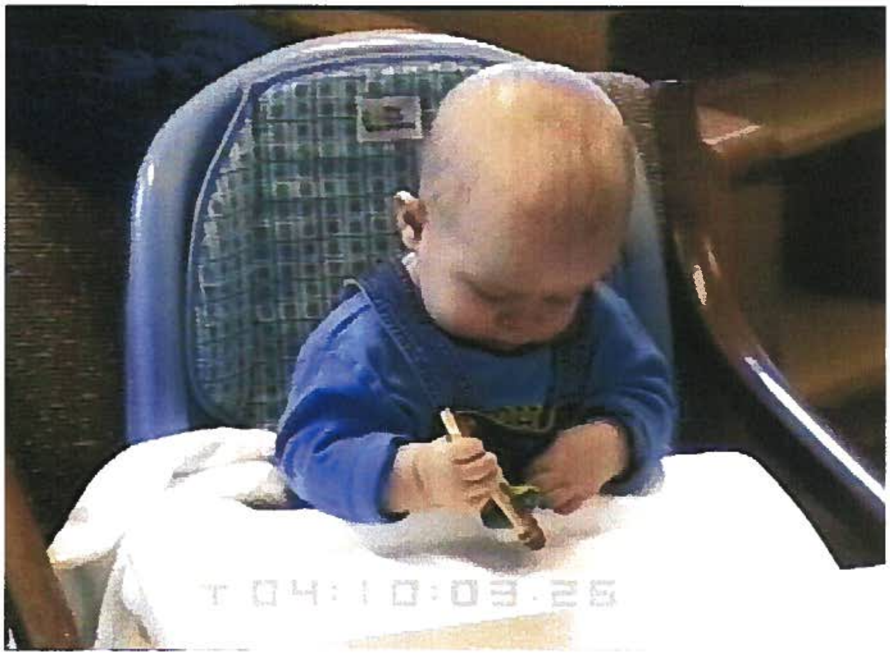
Moderately Attentive = 2.63 to 3 [n=49]; Very Attentive >3 [n=33]). Additionally, to compare results of the current study to those of Lawson and Ruff (see Appendix A), infants were classified according to the distributions of their global focused attention ratings for each of toys (all toy ratings, 1 or 1.5; at least one rating of 2 and none >2.5; at least one rating of 3 and none >3.5; at least one rating of 4 and none >4.5; at least one rating of 5).

Figure 2a: Infant Focused Attention during Novel Toy Exploration

Duration of Focused Attention

Focused attention was coded second-by-second from video recordings of infants throughout each of the four 90-second sequences of object exploration, according to the methods and definitions of focused attention provided by Holly Ruff and colleagues (Ruff, 1984; Ruff, 1986h; Ruff et al., 1990). The Noldus Corporation Observer software (version 5.0) was used to code focused attention periods and to provide accuracy in timing of onset and offset of the exploratory play and duration of focused attention, for later comparison to heart rate data. Significant and moderate to high internal consistency has been shown for measures of focused attention as established by Holly Ruff with high correlations among toy sequences in a single test session (as cited in Lawson et al., 2001), and an interval of 2 weeks (Ruff, 1988; Ruff & Dubiner, 1987). Inter-observer reliability has been reported to be high, with correlations for the duration of focused attention (seconds) and the number of focused looking episodes (i.e. greater than .90 according to (Lawson et al., 2001). In the current study, two independent raters, who were blind to the infant's group status and all other information about the infants, coded periods of focused attention (Ruff, 1986g; Ruff et al., 1991; Ruff et al., 1984) and established reliability for duration and number of focused attention episodes on a random sample for 20% of the larger sample. Calculations were based on overall duration of focused attention for individual toy stimuli, as well as on a second-by-second basis throughout each 90-second sequence, where a second was defined as having or not having focused attention. Inter-rater reliability, using Kappa coefficients for the intraclass correlation, was 0.784 for the number of episodes of focused attention, and 0.829 for overall duration of focused attention. Inter-rater reliability on a second-by- second basis for the four toy stimuli was 0.718. For the current study, two timed measures were derived from the second-by-second coding, one that reflected the total time (seconds) that the infant showed focused attention (total duration of focused attention) and the other that reflected the infant's longest focused episode (peak focus) for each of the toys. Only periods of focused attention greater than 2 seconds in duration were analysed due to problems of using focused episodes of less than 2 seconds (Lansink & Richards, 1997). Together with ratings of global attention, peak focus was used in the main analyses. Additional measures were derived including time to the first focused attention episode for each of the toys (latency), number of seond-by-second focused attention episodes, and the number of times toys were thrown from the table.

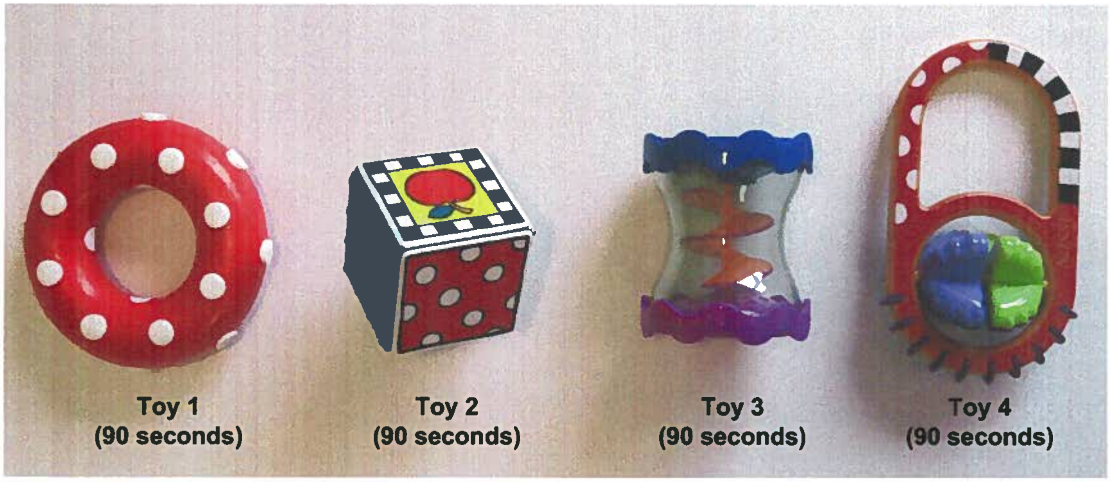
Figure 2b: Infant Focused Attention during Novel Toy Exploration



Novel Toy Stimuli

The toy stimuli were unique to this study and available commercially through Sassy Division of Amram's, Brampton, Canada. The toys were carefully selected to be complex enough to elicit the infant's interest but not so interesting that they failed to differentiate more attentive from less attentive infants (H. A. Ruff, personal communication, March 2001). The four novel toys included Toy 1: Ring with raised spots, Toy 2: Textured cube with patterns/images, Toy 3: Transparent cylinder with spiral inlay, Toy 4: Gripper with rotating parts. All toy stimuli were washable rather than cloth or plush for infection control purposes. The four novel toys used in the current study are shown in Figure 3.

Figure 3: Four Novel Toy Stimuli used in Exploration Paradigm



Infant State and Activity

Infant state and level of activity during exploration were rated, for each toy stimulus presentation using 3-point ratings (not fussy to very fussy/crying and calm to very active). Infants were excluded only if they were very fussy or cried during any of the exploratory sequences, since a certain degree of activity normally accompanies manipulative exploration of novel objects such as banging or waving.

Infant Development

Development was assessed using the Bayley Scales of Infant Development (BSID II), Mental Development Index (MDI), which is the most widely used standardized developmental test in infants and very young children (Bendersky & Lewis, 2001). MDI ≥ 70 was used to select infants who were free of significant cognitive impairment.

Additionally, MDI was examined as outcome measures for preterm infants in relation to perinatal risk factors, global ratings of focused attention and heart rate response.

Infant Heart Rate Response

Electrocardiographic (ECG) activity was recorded online, and monitored during the testing protocol to ensure accurate recording. Signals were digitally sampled at 360 Hz using a computer based data acquisition system (Boston Medical Technologies, 1996). This custom physiologic signal processing software was also used to process and analyse heart rate data. R waves were detected from the sampled ECG and were used to form a smoothed instantaneous 4-Hz time series using transfer function (Berger, Saul, & Cohen, 1989). Interbeat interval (IBI) data, derived using time domain signals as the beat-to-beat change measured in milleseconds or the distance between the R-waves, was collected for a resting baseline of at least 3 minutes prior to the presentation of the toy stimuli, and during infant exploration of the four toy stimuli presented successively for 90-seconds each.

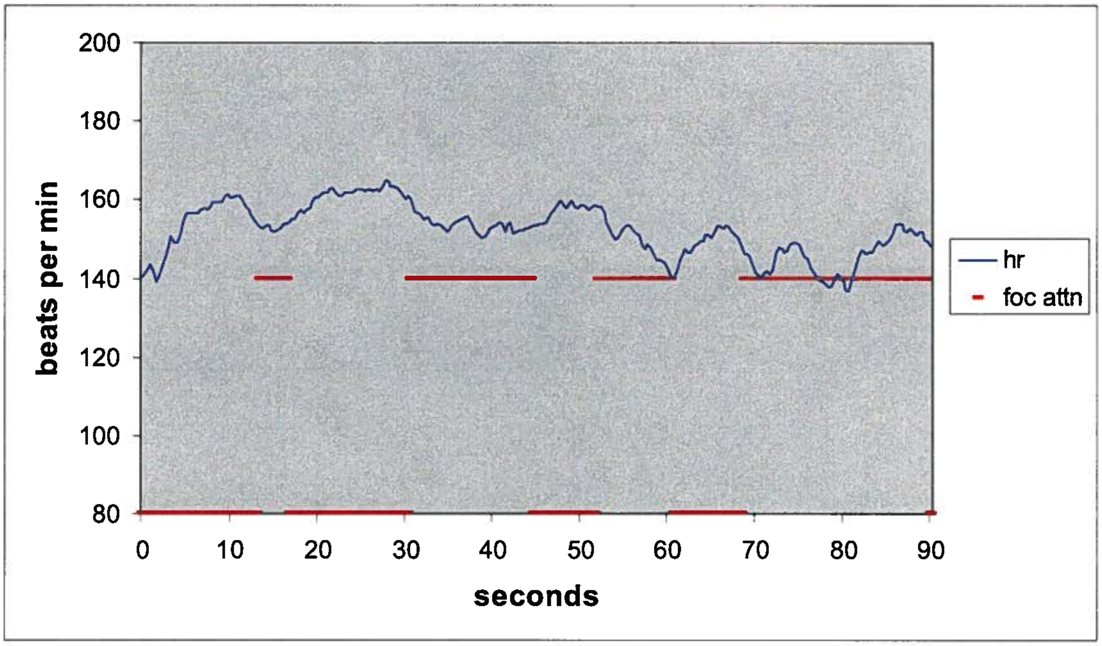
Mean Heart Rate and Heart Rate Variability

Mean HR and standard deviation of HR (HRSD) were derived for each of these five periods (Baseline, Toys 1-4) using the weighted average heart periods. The epoch selection criteria were based on quantitative signal stationarity, and the ECG signal data were individually checked and where necessary, hand-edited for obvious signal detection errors. ECG data with gross artifact were not used in the analyses and infants without complete data were excluded from the study.

Heart Rate Change during Focused Attention

The relationship between focused attention and heart rate was also examined at a detailed level by relating the IBI (HR) data to second-by-second focused attention data using a custom software program designed and programmed by G. Giles and R. Thomas (2007) that enabled analyses at the level of each of the infant's focused episodes. The software program was designed to calculate HR change for all periods of focused attention (Average HR Change), for the infant's longest focused look (HR Change Peak Focus) and the greatest heart rate change during the peak focus (Magnitude HR Change Peak Focus), commonly used in other studies of infant focused attention and heart rate (Lansink et al., 2000; Setliff et al., 2007). The software program analysed focused episodes that were 2.5 seconds apart from adjacent focused episodes, in order to avoid overlap and a potential refractory period during which heart rate could possibly be attenuated (Casey & Richards, 1991b). As shown below in Figure 4, periods of focused attention (represented by the red lines) were examined in relation to changes in heart rate during exploratory play.

Figure 4: Heart Rate Change as related to Episodes of Focused Attention



HR change scores for all focused episodes were calculated from a mean HR over a 2.5 second reference point starting 5 seconds before the beginning of each focused episode to the mean HR during the focused episode. For the infant's single longest (peak) focus, from this same reference point, the mean HR change, and the lowest heart rate during the peak focus (magnitude of HR deceleration) were calculated. Timing heart rate change from this reference point effectively removes stimulus orientation time from the measure. Orienting often begins during the more casual forms of attention that precede focused attention; since it does not vary significantly from one kind of event to another, removing orienting allows for ascertaining HR change as a function of the dependent variables (Lansink et al., 2000). These HR change scores were expected to provide representative information about the direction and magnitude of heart rate change during focused attention. Each of the three HR change scores were examined in relation to 3 levels of

Global Attentiveness (Inattentive, Moderately Attentive, Very Attentive) for all of the infants, the 3 gestational age groups (ELGA, VLGA, Term) and for the girls and boys.

Organizational Plan

Prior to the main results section, demographic data is presented according to gestational age status and sex. This is followed by a comprehensive summary of analyses on four preliminary behavioural indices of focused attention including latency, number and total duration of focused episodes, and number of times toys were thrown. Together with the summary, data for the four preliminary measures by group and sex are provided in Table 4. These preliminary analyses address hypothesis 1a and hypothesis 3, as detailed below. Detailed results for the preliminary measures can be found in the Appendices B. The main results are then organized into three main sections, which address hypotheses 1, 2 and 3, as shown below. Tables and figures are inserted into the text to present and illustrate findings. Because of the large number of comparisons among the three gestational age groups, and between the two sexes, Table 8 in Appendix C provides a summary of results by group and sex, which shows the statistically significant findings. Group by sex interaction effects were not included in Table 8, due to the lack of statistically significant group by sex differences.

Hypotheses

1. Preterm ELGA infants, compared to preterm VLGA and Term-born infants will show:

a. Poorer attention behaviours, including lower global focused attention and shorter peak focus;

b. Patterns of heart rate that reflect: higher arousal (higher mean HR), less suppression of heart rate variability during exploratory play, and less heart rate change (deceleration) during behaviourally identified periods of focused attention;

2. Preterm boys (both ELGA and VLGA) will show greater negative effects compared to preterm girls.

3. For the ELGA and VLGA preterm infants, after adjusting for perinatal risk factors, better focused attention and greater heart rate change will be associated with higher cognitive functioning.

Primary Analyses

In the primary analyses, the first section examines the main focused attention behaviours, which include ratings of global attention and peak focus. Second, changes in heart rate and standard deviation of heart rate from baseline and across the infant exploration of each of the four toy stimuli are examined. This section also examines the relationship of focused attention and heart rate change specifically during the infant's episodes of focused attention. Finally, for the preterm infants only, relationships between perinatal risk factors, focused attention, heart rate change and development are examined. In this section the potential contribution of focused attention and heart rate response as related to cognitive developmental outcome at 8-months of age is assessed.

Statistical Analyses

Overviews are provided in each section, which outline the variables for data analyses and the statistical methods used. With regards to any of the repeated measures analyses, all data were examined for sphericity, and when present, Greenhouse-Geisser values were used to determine significance. All of the significance levels for the ANOVA's were set at $P < 0.05$. Post hoc comparisons were conducted using Fisher's Least Significant Difference (LSD).

The heart rate data (mean HR, and HR change scores) were examined for outliers, defined as any value more than 3 standard deviations above or below the mean. Outlier values were winsorized following the method of Tukey (1977) and retained for data analysis.

CHAPTER 4: RESULTS

Demographic Data

Infant Characteristics

Infant characteristics and demographics by gestational group (ELGA, VLGA and Term-born) are presented in Table 1. Comparing the groups, there were no significant differences in distribution of sex of the infant ($p=.771$). By definition, there were significant group differences in birthweight and gestational age at birth ($p<.0001$). As expected, neonatal health status as measured by the total Apgar score at 5 minutes was significantly lower for ELGA versus both VLGA ($p=.001$) and the Term-born infants ($p<.0001$), and between the VLGA and the Term-born infants ($p= .024$). The Neonatal Medical Index (NMI) is intended to stratify preterm infants into risk groups for serious complications and summarizes the infant's condition during hospitalization (Korner et al., 1993a). As would be expected, on the NMI the ELGA infants were rated significantly higher (more at risk) than either VLGA or Term-born groups ($p<.0001$) and VLGA more at risk than the Term-born infants ($p=.0001$). For data collected in the Neonatal Intensive Care Unit (NICU) only for the preterm infants, ELGA infants had higher illness severity on the first day of life than VLGA infants, according to the Score for Neonatal Acute Physiology (SNAP II, Day 1),(Richardson, Corcoran, Escobar, & Lee, 2001a), ($p<.0001$), and higher number of days on mechanical ventilation (Days on Ventilation), ($p<.0001$). Amongst the three groups, there were no differences in the percentage of first-born infants, however there were significantly more twins in the VLGA as compared to the

Term-born group (p=.009). The mean chronological age for the Term-born infants and the mean corrected chronological age (CCA) for the preterm infants did not differ. There were no significant group differences on the mean Mental Development Index from the Bayley Scales of Infant Development (MDI, BSID II), (p=.29).

Table 1: Infant Characteristics by Gestational Age Group

Characteristic	**ELGA** GA≤ 28 weeks N=35	**VLGA** GA29-32 weeks N=48	**Term-Born** GA37-41 weeks N= 46	**P**
Gestational Age (weeks) Mean (SD)	26.5 (1.6)	31.2 (1.2)	39.9 (1.1)	<.0001
Sex Boys Girls	20 15	24 24	23 23	.771
Birthweight (grams) Mean (SD)	903.6 (223.2)	1627.3 (329.9)	3493.4 (367.4)	<.0001
Apgar Score at 5 min Mean (SD)	7.5 (1.9)	8.5 (1.3)	9.1 (.33)	<.0001
Neonatal Medical Index (NMI) Mean (SD)	4.5 (.8)	2.5 (1.1)	1 (0.0)	<.0001
SNAP II (Day 1) Mean (SD)	20.5 (12.2)	7.6 (9.1)	N/A	<.0001
Ventilation (days) Mean (SD)	29.8 (28.2)	1.3 (2.6)	N/A	<.0001
First Born (percentage)	51.4 n=1 missing	54.2 n=1 missing	47.8	.555
Twins (percentage)	14.3	22.9	4.3	.034
Chronological Age at Visit (months) (Corrected for Prematurity) Mean (SD)	8.0 (.29)	8.1 (.28)	8.0 (.32)	.249
MDI Bayley *(Mean:100, SD:15)* Mean (SD)	94.7 (10.2)	96.3 (7.2)	97.4 (5.9)	.29

N/A indicates not applicable.

Family and Parent Characteristics

For the family characteristics, which are presented below in Table 2, there were no significant differences among the three groups in terms of marital status, number of children in the home, or whether English was the main language used at home.

Table 2: Family Characteristics

	ELGA N=35	VLGA N=48	Term-Born N=46	P
Family				
Marital Status (percentage) Married/Common Law Single	 97.2 2.8	 91.7 6.3	 91.3 2.2 n=3 missing	 .760
Number of Children in Home Mean (SD)	 1.8 (.9)	 1.8 (1.1)	 1.7 (.7)	 .738
Main Language in Home (percentage) English Other	 88.6 11.4	 81.3 16.6 n=1 missing	 89.0 11.0	 .635

For parents of infants in the study, as presented below in Table 3, there were no significant differences in the percentage of parents born in Canada (versus another country of birth), or in the percentage of parents whose first language was English. For all infants, maternal ethnicity was predominantly Caucasian (74%), followed by Asian (19%), the proportions of which did not differ among the three groups. For the entire sample, father's ethnicity was also predominantly Caucasian (75 %) followed by Asian (16%), and did not differ among the three groups. The mother's age at the time of delivery was 2.5 years younger in the ELGA than the VLGA and Term-born groups (p=.029). The fathers of ELGA infants were, on average, 2 to 3 years younger at the time of their infant's birth, compared to the fathers of both the VLGA (p=.04) and Term-born infants (p=.003). Parental education differed significantly in that the mothers of ELGA and VLGA infants had fewer years of education than the mothers of the Term-born infants (p=.0001 and p=.009 respectively). Fathers of ELGA infants had significantly fewer years of education than the fathers of both VLGA and Term-born infants (p=.034 and p=.001 respectively).

Table 3: Parental Characteristics

	ELGA N=35	VLGA N=48	Term-Born N=46	P
Mother				
Mother's Age (years) Mean (SD) Range (years)	 31.2 (5.5) 19 to 39	 33.7 (5.3) 18 to 47	 33.8 (4.70) 25 to 43	 .05
Mother's Country of Birth (percentage) Canada Other	 68.6 31.4	 72.9 25.0 n=1 missing	 78.3 21.7	 .613
Mother's Ethnicity (percentage) First Nations Caucasian Asian Other	 14.3 62.9 20.0 2.9	 0 75.0 20.8 4.2	 0 15.2 80.4 4.3	 .654
Mother's First Language (percentage) English Other	 77.1 22.9	 75.0 23.0 n=1 missing	 80.4 17.4 n=1 missing	 .776
Mother's Education (years) Mean (SD)	 14.4 (2.9)	 15.4 (2.4)	 16.9 (3.02)	 <.0001

Table 3 continued

Father				
Father's Age (years) Mean (SD) Range (years)	 33.2 (6.0) 19 to 44	 35.4 (4.5) 25 to 47	 36.5 (4.3) 27 to 46	 .011
Father's Country of Birth (percentage) Canada Other	 74.3 25.7	 62.5 33.3 n=2 missing	 71.7 28.3	 .646
Father's Ethnicity (percentage) First Nations Caucasian Asian Other	 14.3 65.7 17.1 2.9	 0 76.1 19.6 4.3 n=2 missing	 0 80.0 11.1 8.9 n=1 missing	 .531
Father's First Language (percentage) English Other	 80.0 20.0	 77.1 18.7 n=2 missing	 87.0 13.0	 .630
Father's Education (years) Mean (SD)	 14.1 (3.9)	 15.8 (3.5)	 16.8 (3.1)	. 005

Preliminary Analyses

Preliminary Focused Attention Measures

Overview

In addition to the focused attention measures used in the main analyses, which included the infant's global ratings of focused attention (Global Focused Attention) and the infant's ability to sustain focused attention, as measured by the longest focus (Peak Focus), separate ANOVAs were conducted to assess preliminary measures related to infant focused attention. Number of Focused Episodes was analysed as it represents a different construct than duration measures such as peak focus. Total duration of focused attention (Duration Focused Attention) was analysed as it represents one of the most commonly used measure in infant studies. The total number of times that toys were thrown (Toys Thrown) and the average time or latency to organize a focused response (Latency) were also analysed as behaviours that are inversely related to infant focused attention. Following analyses of these preliminary measures by Group (ELGA, VLGA, Term-born) and Sex, bivariate correlations, separately by Group and Sex, were carried out between the preliminary measures (Number of Focused Episodes, Total Duration, Latency, Toys Thrown) and two primary measures (Global Focused Attention, Peak Focus). Bivariate correlations were also run between Global Focused Attention and Peak Focus. These preliminary analyses provided information about the nature of focused attention in 8-month infants according to gestational status and sex, and to examine the overlap of data for data reduction.

So as not to detract from the main focus of the study, a summary of preliminary results is provided, together with data in Table 4, as shown below. A more detailed report of preliminary analyses can be found in Appendix B.

Table 4: Preliminary Focused Attention Measures (Mean [SD])

Group	Sex	Average Latency (sec)	Focused Episodes (total number)	Toys Thrown (total number)	Average Duration (sec)
ELGA	Boys	12.2 (9.8)	7.1 (4.5)	3.3 (5.0)	11.5 (10.7)
	Girls	11.5 (9.1)	10.7 (5.9)	.73 (1.2)	16.8 (12.0)
	Totals	11.9 (9.4)	8.7 (5.4)	2.17 (4.0)	13.7 (11.4)
VLGA	Boys	14.1 (8.8)	7.4 (3.8)	4.3 (6.5)	10.6 (6.9)
	Girls	10.7 (6.5)	10.3 (5.0)	1.9 (3.0)	18.0 (13.8)
	Totals	12.4 (7.8)	8.9 (4.6)	3.1 (5.2)	14.3 (9.6)
Term-Born	Boys	15.6 (12.1)	10.3 (5.4)	4.0 (4.2)	15.7 (10.6)
	Girls	12.4 (10.1)	10.0 (5.2)	3.2 (5.7)	16.5 (11.7)
	Totals	14.0 (11.1)	10.2 (5.3)	3.6 (5.0)	16.0 (11.1)

Summary of Preliminary Analyses

There were no statistically significant differences between the ELGA, VLGA and Term-born groups in the number of focused episodes, or the total duration of focused attention, across the four toys. However, compared to boys, girls showed more focused episodes, and significantly longer total duration of focused attention. As expected, the number of focused episodes and total duration of focused attention were highly correlated with average peak focus and global focused attention for all groups and each sex.

Comparing the gestational age groups, infants did not differ in the average time (latency) it took to organize a focused response, or in the amount of toy throwing. However overall, boys threw toys significantly more often than girls. Generally there were negative associations between latency/toys thrown and both duration of average peak focus and ratings of global focused attention. However, the ELGA infants did not show the typical inverse pattern between latency and global focused attention (i.e. shorter latency and higher global focused attention) suggesting that, at least for this group, the time taken to organize a focused response does not necessarily impact global focused attention. Similarly, unlike the term-born infants and girls, neither ELGA, nor VLGA infants or the boys showed the typical relationship between more toys thrown and shorter sustained focus (Average Peak Focus). However, a generally consistent pattern was seen amongst all groups of the more toys thrown, the lower the global attention.

The preliminary measures (Latency, Number Focused Episodes, Toys Thrown, Duration Focused Attention) and the primary measures (Global Focused Attention, Average Peak Focus), were highly correlated across groups and sex. Because of this overlap, beyond providing preliminary data to elucidate the nature of focused attention according to gestational age and sex, as summarized above, Number of Focused Episodes and Total Duration were not used in the main analyses.

The primary measures (Global Focused Attention, Average Peak Focus) were significantly correlated suggesting that the longer the infants were able to sustain their focus, the higher they were rated on global focused attention. This pattern was consistent for all infant groups and for both boys and girls. As the two primary behavioural measures in this study, Global Focused Attention and Average Peak Focus represent different constructs, one based on ratings of global focused attention and the other on duration of sustained attention, thus both were used in the main analyses. For a thorough report of preliminary results please refer to Appendix B.

Primary Analyses

Overview

The main dependent variables were the global rating of focused attention (Global Focused Attention) and the longest time that the infant sustained focus for each of the toys (Peak Focus). The two main dependent variables were examined in a 3 Group (ELGA, VLGA, Term-born) by 2 Sex (Boys, Girls) by 4 Toy Sequence (Toys 1-4), with the Toy Sequence as repeated measures, using separate mixed model ANOVAs. Results are presented in Table 5 and presented graphically in Figures 5, 6 and 7.

Global Focused Attention

Main Effects

Exploratory Toy Sequences

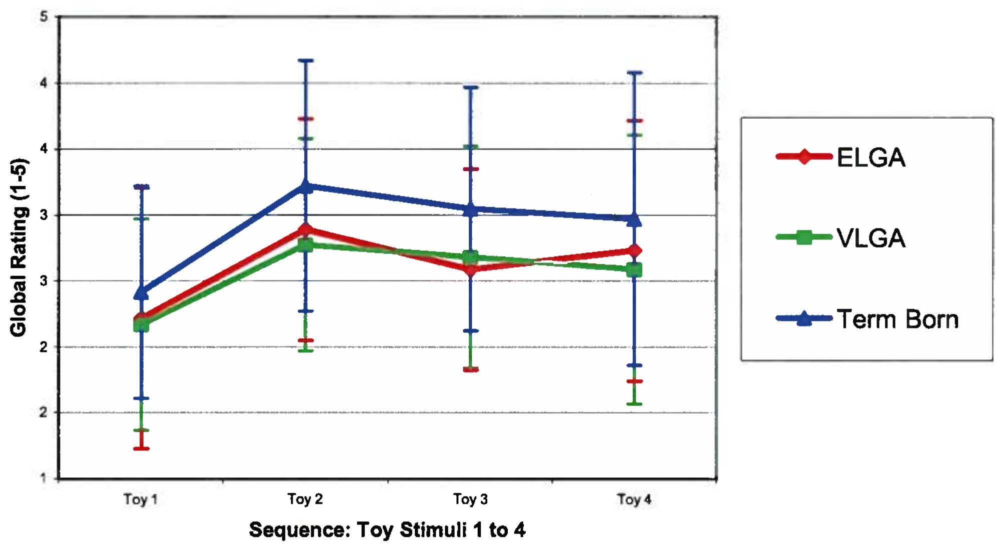
There was a significant main effect of the repeated measures factor, Toy Sequence (F [3,369] = 29.644] $p < .0001$) with significantly lower Global Focused Attention for Toy 1, as compared to the subsequent Toys 1-3 ($p < .0001$). Furthermore, as seen in Figure 5, Toy 2 was rated higher on Global Focused Attention than Toy 3 ($p = .04$), but not Toy 4.

Group

With regards to Global Focused Attention, there was also significant main effect of Group (F [2,123] = 3.06, $p = .05$). Post hoc comparisons showed that the Term-born infants were significantly higher on Global Focused Attention than the VLGA infants (p

= .018), as shown in Figure 5. Term-born infants were marginally higher than ELGA infants however this did not reach statistical significance (p = .063).

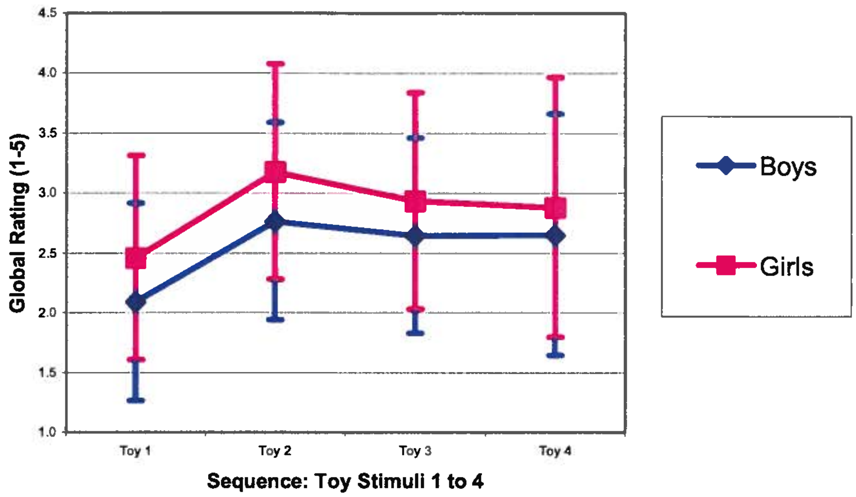
Figure 5: Global Ratings of Focused Attention by Gestational Age Group



Sex

There was also a significant main effect of Sex, with girls higher on Global Focused Attention than boys (F[1,123] = 6.553, p = .012), as shown in Figure 6.

Figure 6: Global Ratings of Focused Attention by Sex



Interaction Effects

There were no statistically significant 2-way interactions (Toys by Group, Toys by Sex, Group by Sex), or 3-way interaction (Group by Sex by Toy Sequence), each with $p > .25$.

In summary, global ratings of focused attention were significantly lower in the VLGA compared to the Term-born infants. However global ratings of focused attention were only marginally lower (not significantly) in the ELGA compared to Term-born infants. Overall, global ratings of focused attention were significantly higher in girls as compared to boys.

Table 5: Primary Focused Attention Measures (Mean [SD])

Group	Sex	Average Global Focused Attention (Global rating 1-5)	Average Peak Focus (sec)
ELGA	Boys	2.4 (.61)	8.5 (5.9)
	Girls	2.9 (.80)	8.6 (5.4)
	Totals	2.6 (.73)	8.5 (5.6)
VLGA	Boys	2.3 (.61)	7.1 (3.1)
	Girls	2.8 (.73)	9.9 (6.9)
	Totals	2.5 (.70)	8.5 (5.5)
Term-Born	Boys	2.9 (.78)	8.4 (4.1)
	Girls	3.0 (.83)	10.1 (5.5)
	Totals	2.9 (.80)	9.2 (4.9)

Additional Analyses for Global Focused Attention

Proportion of Inattentive, Moderately Attentive, Very Attentive Infants

The above analyses on Global Focused Attention were based on an average of the four global ratings of focused attention across the 4 toys. Based on this average score, the proportion of infants rated at three levels of attentiveness (1 to 2.5 [n=47], Inattentive; 2.6 to 3 [n=49], Moderately Attentive; >3 [n=33], Very Attentive), in each of the three gestational age groups was also assessed. This data was used in later analyses to relate infant's average global attentiveness to heart rate data.

For the lowest level of attentiveness, 40% of ELGA, 42% of VLGA and 28% of Term-born infants were inattentive. Moderately Attentive ratings were 34% of ELGA, 40% of VLGA and 40% of Term-born infants. Very Attentive ratings were 26% of ELGA, 19% of VLGA and 33% of Term-born infants. Chi square analyses did not show statistically significant differences (F [1,4] = 1.368] p = .242).

The proportions of boys rated from Inattentive, Moderately Attentive to Very Attentive were 43%, 37% and 19% respectively, compared to girls 29%, 39% and 32%. Chi Square analyses of the three levels of Global Attentiveness was significant for Sex, with girls performing better than boys (F [1,4] = 3.859] p = .049).

Distributions of Categorical Groupings from 5-point Ratings

For the purposes of comparing data to previous reports, distributions of infants in 5 levels of ratings were also analysed (Lawson et al., 2001). While these ratings were not used in further analyses, they did allow for direct comparison to previous ratings of 7-month very low birthweight infants in the earlier study (Lawson et al., 2001). These ratings for the ELGA, VLGA and Term-born infants at 8-months, considering scores for each toy, were: all ratings 1 or 1.5: 0%, 4.2% and 0% for ELGA, VLGA, Term-born respectively; at least one rating of 2 and no rating >2.5: 20% 19%, 11%; at least one rating of 3 and no rating > 3.5: 26%, 41%, 33%; at least one rating of 4 and no rating > 4.5):, 31%, 19%, 28%; at least one rating of 5: 8.3%, 25% and 67%. Chi Square analysis of the 5 levels for the 3 gestational age groups approached significance (F[1,8] = 3.653] p = .056).

Peak Focus

Main Effects

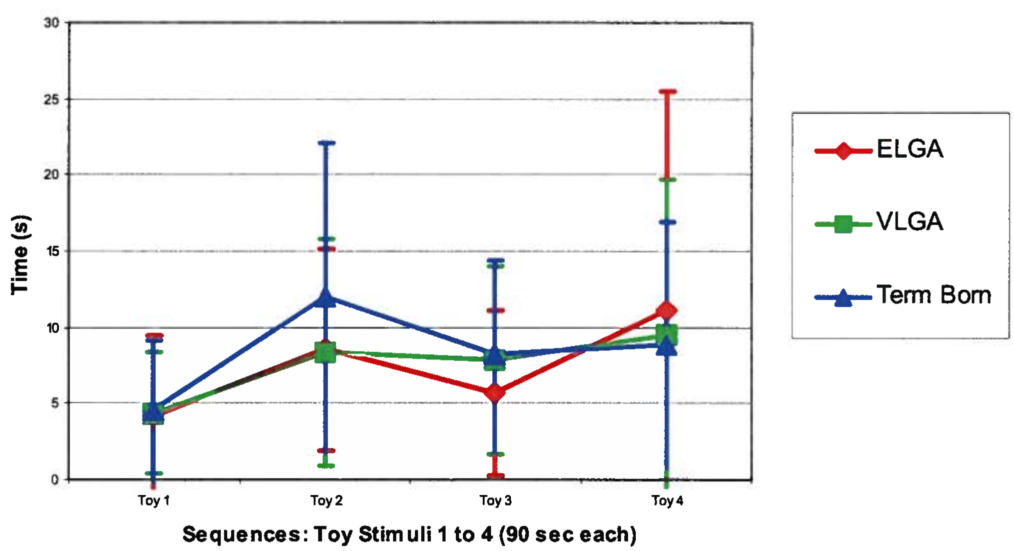
Exploratory Toy Sequences

There was a significant main effect of Toy Sequence on Peak Focus ($F [3,369] = 19.224]$ $p < .0001$). Specifically, there was a significantly shorter Peak Focus for Toy 1, compared to the subsequent three Toys ($p < .0001$). Furthermore, as shown in Figure 7, there was a longer Peak Focus for Toy 2 than Toy 3 ($p = .001$), but not Toy 4. Peak Focus was shorter for Toy 3 than Toy 4 ($p = .005$).

Group

There was no main effect of Group on Peak Focus ($F [2,123] = .408$, $p = .666$).

Figure 7: Peak Focus by Gestational Age Group



Sex

The pattern of Peak Focus across the four toys was strikingly similar for both sexes. Girls had a marginally longer average Peak Focus (9.7 seconds, SD 6.0) as compared to boys (8.0 seconds, SD 4.4), however these differences did not reach statistical significance ($F[1,123] = 3.386$, $p = .068$).

Interaction Effects

For Peak Focus, there were no statistically significant 2-way interactions (Toy Sequence by Group, $p = .081$, Toy Sequence by Sex, $p > .5$, Group by Sex, $p > .5$). The 3-way interaction (Group by Sex by Toy Sequence) was also non-significant ($p > .25$).

Additional Analyses for Peak Focus

Single Peak Focus

Further to examining Peak Focus across the four toys, an ANOVA was conducted on the single longest focus of the infant (Single Peak Focus), comparing Group and Sex. Single Peak Focus was used to examine changes in heart rate concurrent with focused attention. For the Single Peak Focus, there were no significant effects for Group ($F[2,123] = .138$, $p = .871$), Sex ($F[2,123] = 2.412$, $p = .123$) or Group by Sex ($F[2,123] = .222$, $p = .801$).

In summary, infants did not differ in the average duration of their Peak Focus or their single longest focus (Single Peak Focus), according to gestational group status. There was a trend for girls to show a slightly longer average peak focus however, this was marginal and did not reach statistical significance.

Heart Rate and Heart Rate Variability Response during Toy Exploration

Overview

In order to examine heart rate (HR) data, separate 5 (Sequences = Baseline followed by four exploratory Toy Sequences; repeated measures) by 3 (Group) by 2 (Sex) mixed model ANOVAs were carried out on mean HR and heart rate variability (standard deviation of heart rate; HRSD). Mean Heart rate and Standard deviation of heart rate were determined for the 90-second Baseline and each of the four 90-second exploratory Toy Sequences as presented below in Table 6.

Table 6: Heart Rate Response during Baseline and Toy Exploration (Mean [SD])

Group	Sex	Heart Rate (Beats-per-minute)					Heart Rate Variability (Standard Deviation of Heart Rate)				
		Baseline	Toy Exploration				Baseline	Toy Exploration			
			Toy 1	Toy 2	Toy 3	Toy 4		Toy 1	Toy 2	Toy 3	Toy 4
ELGA	Boys	144.8 (12.3)	137.4 (11.6)	138.9 (10.9)	139.2 (10.9)	140.4 (10.2)	6.8 (1.6)	5.9 (1.9)	5.7 (1.9)	5.1 (1.4)	5.8 (1.9)
	Girls	141.6 (8.6)	134.1 (10.8)	136.7 (10.2)	135.9 (9.7)	136.8 (10.0)	7.4 (2.4)	5.9 (2.3)	5.9 (2.1)	5.1 (1.0)	5.4 (1.7)
	Totals	143.5 (10.9)	136.0 (11.2)	138.0 (10.5)	137.8 (10.4)	138.9 (10.1)	7.1 (2.0)	5.9 (2.0)	5.8 (2.0)	5.1 (1.2)	5.6 (1.8)
VLGA	Boys	138.0 (11.7)	133.7 (9.3)	135.2 (10.5)	134.2 (9.6)	135.0 (9.1)	6.1 (1.8)	5.6 (1.6)	5.4 (1.2)	5.2 (1.4)	5.3 (1.3)
	Girls	139.4 (12.6)	134.8 (9.9)	136.8 (9.2)	136.6 (8.8)	137.3 (9.2)	7.3 (2.8)	6.4 (1.3)	5.7 (1.9)	5.4 (1.3)	5.8 (1.1)
	Totals	138.7 (12.1)	134.2 (9.5)	136.0 (9.8)	135.4 (9.2)	136.1 (9.1)	6.7 (2.4)	6.0 (1.5)	5.6 (1.6)	5.3 (1.3)	5.5 (1.2)
Term-Born	Boys	137.8 (8.9)	131.2 (7.8)	131.8 (7.7)	132.3 (6.4)	132.8 (7.0)	7.4 (2.1)	6.7 (2.3)	5.4 (1.4)	5.8 (2.4)	5.7 (1.5)
	Girls	140.1 (9.6)	134.7 (7.3)	137.2 (6.5)	137.4 (7.1)	138.5 (7.5)	7.2 (2.3)	5.6 (1.4)	5.7 (1.5)	4.9 (1.4)	5.0 (1.4)
	Totals	138.9 (9.2)	133.0 (7.7)	134.5 (7.6)	134.8 (7.2)	135.6 (7.8)	7.3 (2.2)	6.1 (2.0)	5.5 (1.4)	5.3 (2.0)	5.4 (1.5)

Mean Heart Rate Response during Toy Exploration

Main Effects

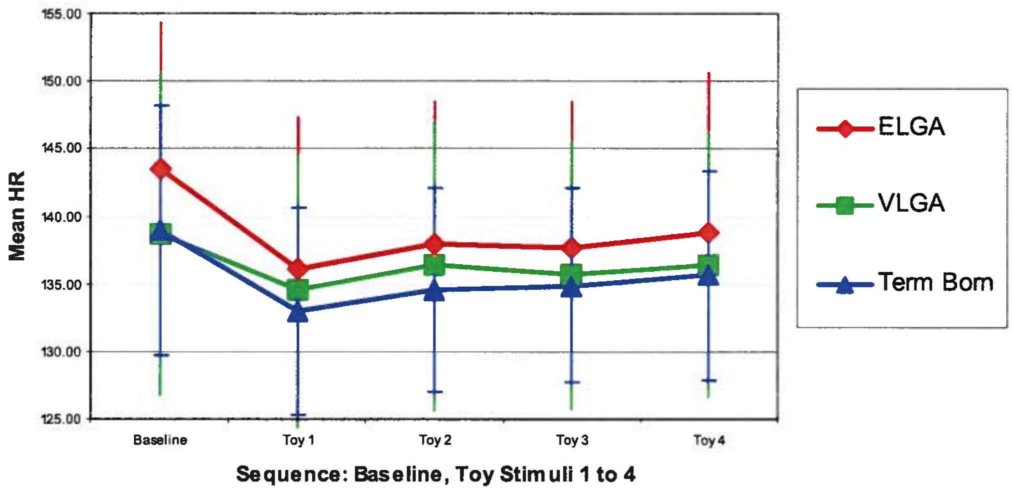
Baseline and Toy Exploration Sequences

There was a significant effect of Toy Sequence ($F [4, 492] = 42.930$, $p < .0001$), with post hoc comparisons showing a significant decrease in mean HR from Baseline, as a reference point, to Toy 1 ($p < .0001$). Specifically, HR decreased from the Baseline HR of 140.1 bpm (SD 10.9) to 134.3 (SD 9.4) for the first Toy (average decrease of 6 bpm). Using the first Toy as a reference point, HR increased slightly thereafter to each of the three subsequent Toys ($p < .0001$). Changes in mean HR from Baseline across the four Toys are shown in Figure 8.

Group

There was no significant main effect of Group on HR ($F[2, 123] = 1.397$, $p = .251$). Change in mean HR from Baseline across the four Toys for each gestational age Group is shown below in Figure 8.

Figure 8: Mean Heart Rate: Baseline to Toy Exploration by Gestational Age Group



Sex

There was no significant main effect of Sex on HR (F[1,123] = .408, p = .524).

Interaction Effects

There were no statistically significant 2-way interactions involving mean HR (all p's >.150). The 3-way interaction was also not significant (Group by Sex by Sequence, p > .250).

To summarize, the most striking change in mean HR was from Baseline to the first Toy exploration, reflecting a significant drop during the initial presentation of the first toy stimulus. This initial decrease in mean HR to the first toy sequence was a pattern seen across all groups and both sexes and likely reflected a general orienting response.

The initial drop from baseline to the first toy was followed by slight but significant increases in mean HR from the first toy to the subsequent three toy explorations.

Heart Rate Variability (HRSD)

Main Effects

Baseline and Toy Exploration Sequences

There was a significant effect of Sequence on heart rate variability, as indexed by heart rate standard deviation (HRSD); ($F[4, 492] = 29.766$, $p < .0001$). Similar to mean HR, post hoc comparisons showed that HRSD decreased significantly from Baseline to the Toy Sequence ($p < .0001$). However, while mean HR showed a subsequent increase, heart rate variability showed a pattern of continued decrease from the first Toy across the entire Toy Sequence of exploration. The mean standard deviation of heart rate (HRSD) was sampled every 90 seconds. As can be seen below in Figure 9, decreases in mean heart rate variability were significant from Baseline to Toy 1, and from Toy 1 as a reference point to Toy 3 ($p <.0001$), and Toy 4 ($p = .02$).

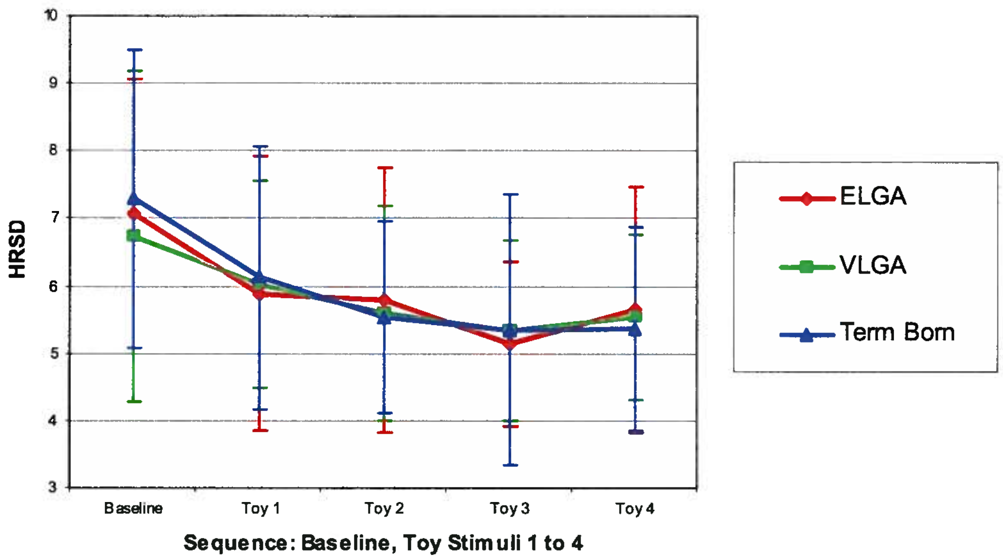
Group

There was no main effect of Group on HRSD ($F[2,123] = .068$, $p = .935$)

Sex

There was no main effect of Sex on HRSD ($F[1,123] = .045$, $p = .832$).

Figure 9: Heart Rate Variability: Baseline to Toy Exploration by Gestational Age Group (Standard Deviation of Heart Rate; mean HRSD sampled for each of the four 90-second exploration sequences)



Interaction Effects

For HRSD, there were no statistically significant interactions between Group and Sequence ($p < .250$), or Sequence by Sex ($p < .15$); Group by Sex did not reach statistical significance ($F[2,123] = 2.627$, $p = .076$). The 3-way interaction was also not significant (Group by Sex by Sequence, $p > .250$).

In summary, heart rate variability decreased significantly from baseline to the first toy and continued to decrease across the entire exploration period. This pattern was consistent for all of the infant groups, and for both girls and boys.

Relating Heart Rate and Heart Rate Variability to Global Attentiveness

Overview

One of the aims of this study was to assess heart rate change in relation to behavioural focused attention during exploratory play. Therefore, analyses were conducted to determine whether HR change during focused attention was related to level of Global Attentiveness, with three categorical levels of Attentiveness (Inattentive, Moderately Attentive, Very Attentive) as a between groups factor. The attentiveness levels were based on Lawson and Ruff's (2001) 5-point ratings, averaged for the four toys and separated into three groups, Inattentive: ≤ 2.5 (n=47), Moderately Attentive: 2.6 to 3 (n=49) and Very Attentive >3 (n=33). Additionally, a mixed model ANOVA was conducted examining change in mean heart rate variability (HRSD) across the four Toys, with level of Global Attentiveness (Inattentive, 1 to 2.5; Moderately Attentive, >3; Very Attentive, >3) as a between groups factor. For these analyses involving heart rate variability (HRSD), the Baseline Sequence of HRSD was not included, as differences in variability have different meaning during rest versus engagement. Mean HR from baseline across the four toys was not analysed in relation to Global Attentiveness as previous studies have emphasized changes in heart rate variability rather than changes in mean heart rate, as correlated with attention (Porges, 1995b).

Heart Rate Change as related to Level of Global Attentiveness

Overview

Analyses were conducted to determine whether HR change during focused attention was related to level of Global Attentiveness. Separate ANOVAs were conducted to examine three HR change scores with three groupings of Global Attentiveness (Inattentive, 1 to 2.5; Moderately Attentive, >3; Very Attentive, >3) as a between groups factor.

As detailed in the methods section, HR change scores were calculated for each of the infant's focused episodes and then averaged (Average HR Change). Additionally, HR change scores were calculated for the infant's longest focus (HR Change Peak Focus) and the greatest magnitude of HR change (deceleration) for the peak focus (Magnitude HR Change Peak Focus). Relationships between magnitude of HR change during the peak focus and level of global attentiveness are illustrated in Figure 10.

Average HR Change

There were no significant differences among the levels of Global Attentiveness on Average HR Change across all focused attention episodes ($F[2,122] = 1.647$, $p = .197$).

HR Change during Peak Focus

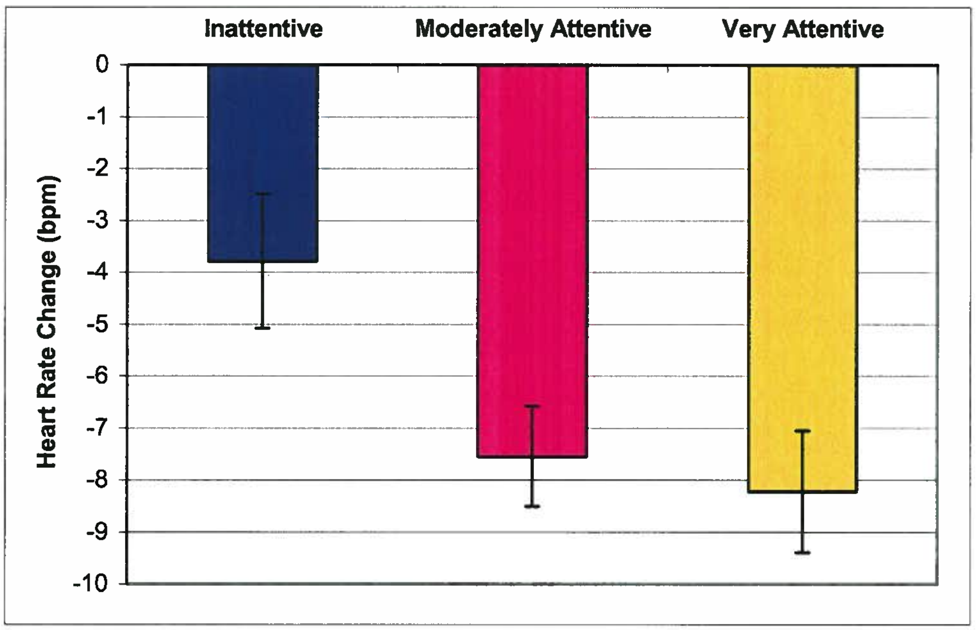
There was no significant difference of the level of Global Attentiveness on HR Change for the Peak Focus ($F[2,122] = 2.746$, $p = .068$).

Magnitude of HR Change during Peak Focus

There were significant effects of level of Global Attentiveness on Magnitude HR Change during the Peak Focus ($F[2,122] = 3.748$, $p = .026$). Infants who were rated the lowest (Inattentive) showed significantly less magnitude of HR deceleration during their single

Peak Focus (-3.8 bpm, SD 7.6), compared to Moderately Attentive (-7.5 bpm, SD 7.0, p=.021) or Very Attentive infants (-8.2 bpm SD 7.2, p=.012). These data, which are displayed in Figure 10, indicate a relationship between greater magnitude of HR deceleration concurrent with focused episodes and attentiveness, regardless of birth status or sex.

Figure 10: Magnitude of HR Change (Peak Focus) in relation to Global Attentiveness



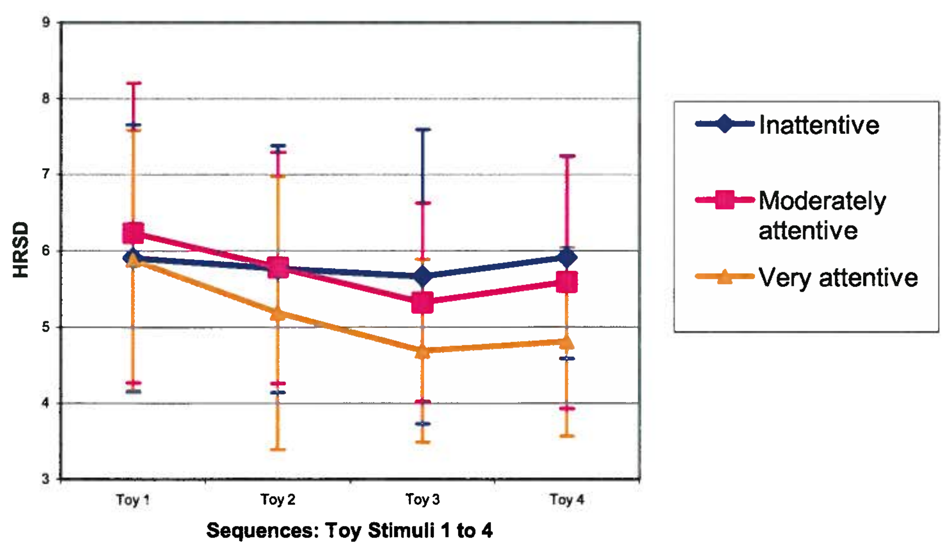
Change in Heart Rate Variability (HRSD) as related to Level of Global Attentiveness

Main Effects

Global Attentiveness

There was a significant main effect of Global Attentiveness on heart rate variability (HRSD), (F[2,126] =3.478, p = .034). As shown below in Figure 11, infants who were rated as Very Attentive on Global Ratings of Focused Attention (i.e. average rating across 4 toys of greater than 3) showed significantly greater decreases in heart rate variability across the four 90-second toy exploratory Sequences compared to either the Moderately Attentive (p = .029) or Inattentive infants (p=.015).

Figure 11: Heart Rate Variability (HRSD) by Three Levels of Global Attentiveness (Mean HRSD sampled for each of the four 90-second exploration sequences)



Toy Sequence

There was a significant main effect of Toy Sequence ($F[3,378] = 8.546$, $p < .0001$). Specifically, decreases in heart rate variability were evident from Toy 1 to Toy 2 ($p = .016$), and from Toy 2 to Toy 3 ($p < .029$).

Interaction Effect

There was no significant level of Global Attentiveness by Toy Sequence interaction effect ($F[3,378] = 1.574$, $p = .157$).

In summary, there were significant differences in heart rate variability (HRSD) according to level of Global Attentiveness. These analyses, conducted on the entire sample, suggest that the very attentive infants show greater suppression of heart rate variability across the toy exploration sequence than moderately attentive or the least attentive infants.

Heart Rate Change during Focused Episodes by Group and Sex

Overview

Further to results showing that magnitude of HR deceleration during focused episodes was related to level of global attentiveness for the entire sample, separate Group by Sex ANOVAs were conducted for the three HR change scores. HR change by Group and Sex are provided below in Table 7.

Table 7: HR Change during Focused Attention (Beats-per-minute) (Mean [SD])

Group	Sex	Average HR Change	HR Change Peak Focus	Magnitude HR Change Peak Focus
ELGA	Boys	.68 (4.0)	-2.7 (3.8)	-8.3 (4.7)
	Girls	-3.4 (2.6)	-6.1 (6.1)	-12.2 (8.7)
	Totals	-1.8 (3.7)	-4.1 (5.1)	-9.8 (6.4)
VLGA	Boys	.26 (3.4)	-.65 (5.4)	-6.0 (6.0)
	Girls	-.38 (3.4)	.66 (8.5)	-5.7 (10.3)
	Totals	-.06 (3.4)	.00 (7.1)	-5.7 (7.7)
Term-Born	Boys	-.37 (3.5)	.67(6.8)	-4.6 (7.4)
	Girl	-1.3 (3.3)	-1.3 (6.0)	-7.1 (7.1)
	Totals	-.85 (3.4)	-.34 (6.4)	-5.8 (7.3)

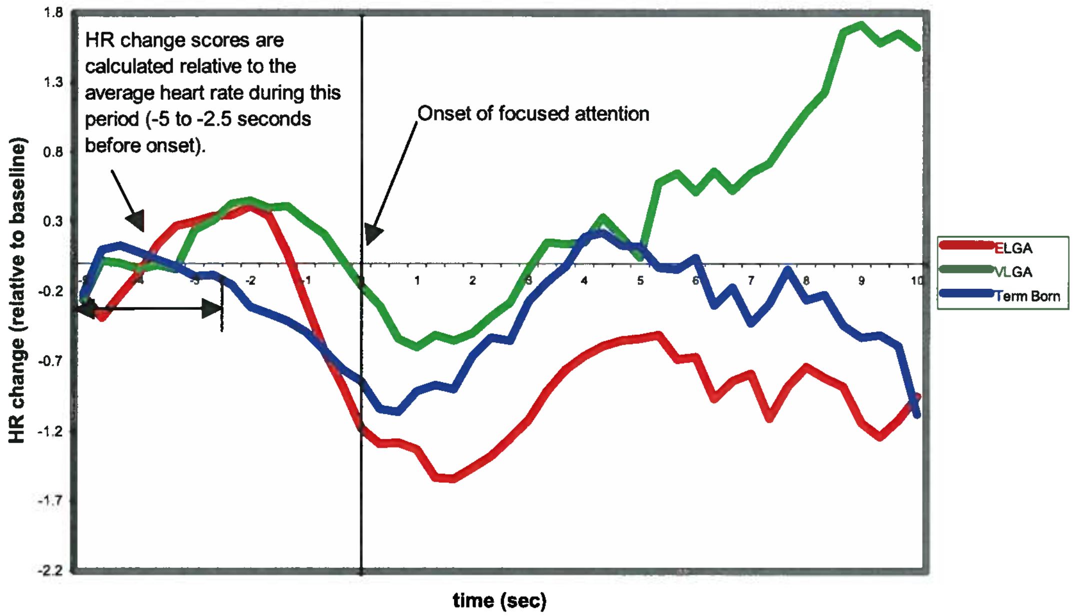
Average HR Change during Focused Attention Episodes

Main Effects

Group

For the Average HR Change across all focused episodes, there was a significant main effect of Group (F[2,119] = 3.24, p = .043). Post hoc comparisons showed a significant difference between the ELGA and VLGA infants (p = .012), however no differences between ELGA and Term-born infants (p = .269). Differences between VLGA and Term-born infants were not significant (p=.127). As shown below, mean HR change, as averaged across all focused episodes, is displayed graphically in Figure 12.according to gestational age group.

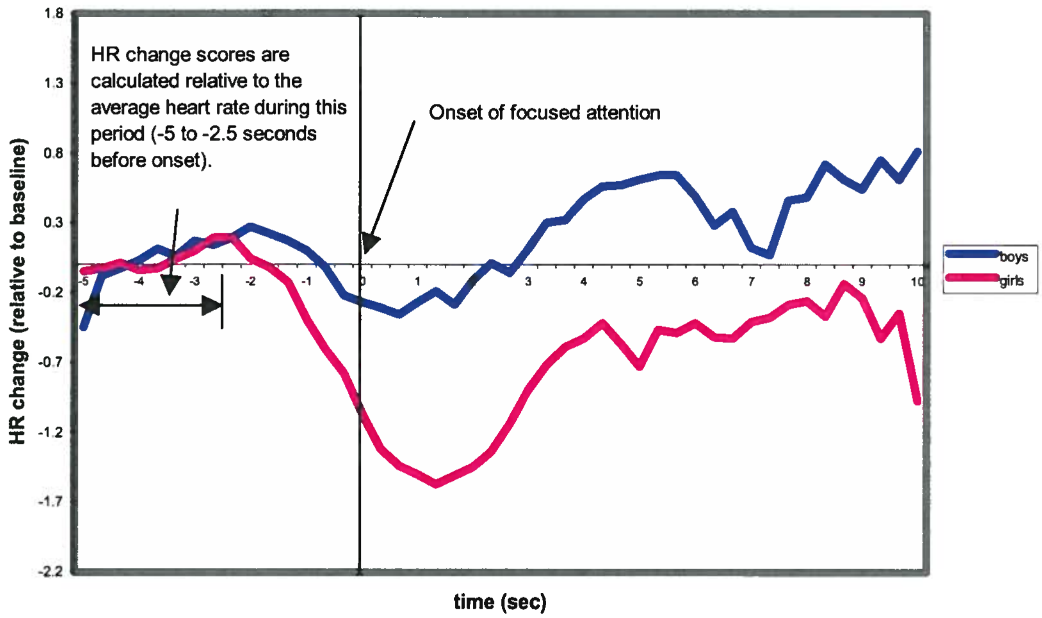
Figure 12: Mean HR Change during All Focused Episodes by Gestational Age Group



Sex

There was also a significant main effect of Sex on the Average HR Change during focused episodes with girls showing significantly more heart rate change (deceleration) than boys (F[1,119] =5.393, p = .022). Mean HR change, as averaged across all focused episodes is displayed graphically according to sex in Figure 13 below.

Figure 13: Mean HR Change during All Focused Episodes by Gestational Age Group



Interaction Effects

There was no significant Group by Sex effect of Average HR Change during focused attention episodes (F[1,119] =.989, p=.375).

HR Change during Peak Focus

Main Effects

Group

There was a significant main effect of Group on the mean HR Change during the infant's Peak Focus (F[2,119] =5.262, p = .006). Post hoc comparisons showed that ELGA infants decreased mean HR by 4.1 bpm (SD 5.1), which was significantly more than the VLGA infants (0.0 bpm, SD 7.1, p = .003), and Term-born infants (0.3 bpm, SD 6.4, p = .007).

Sex

For the mean HR Change during Peak Focus, there was no significant effect of Sex (F[1,119] =1.434, p = .237).

Interaction Effects

There was no significant Group by Sex interaction on the mean HR change during Peak Focus (F[1,119] =1.488, p = .230).

Magnitude of HR Change (Deceleration) during Peak Focus

Overview

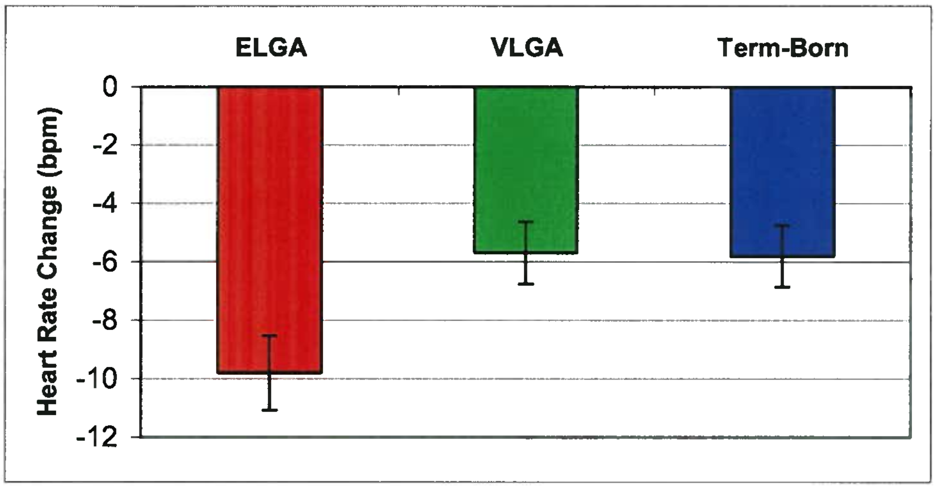
The lowest HR during the Peak Focus (Magnitude HR Change Peak Focus) was assessed to provide an indication of the magnitude or depth of heart rate deceleration, comparing the three gestational age Groups by Sex.

Main Effects

Group

There was a significant main effect of Group on Magnitude HR Change Peak Focus (F[2,119] =4.287, p = .016). Post hoc comparisons indicated that ELGA infants showed significantly greater magnitude of deceleration than either the VLGA (p=.009) or Term-born infants (p=.011). As shown in Table 7 and illustrated in Figure 14, for the ELGA infants the average magnitude of HR change (deceleration) during the Peak Focus was 9.8 bpm (SD 6.4), whereas the average magnitude of HR change concurrent with the Peak Focus for the VLGA and Term-born consisted of HR decreases of 5.7 bpm (*SD* 7.7) and 5.8 bpm (*SD* 7.3) respectively.

Figure 14: Magnitude of HR Change (Peak Focus) in Relation to Gestational Age Group



Sex

There were no significant main effect for Sex on Magnitude HR Change Peak Focus (F[1,119] =1.897, p = .171). The magnitude of heart rate change (deceleration) concurrent with the peak focus according to sex of the infant is provided in Table 7.

Interaction Effect

There was no interaction between Group and Sex for Magnitude HR Change Peak Focus (F[2,119] =.880, p = .417).

In summary, contrary to our hypothesis, on average the higher risk ELGA infants showed more rather than less heart rate change (deceleration) across focused attention episodes in comparison to the VLGA infants. For the peak focus, the ELGA infants also showed significantly greater mean, and magnitude of, heart rate change (deceleration) in comparison to either the VLGA or the Term-born infants. Overall, girls showed deceleration more consistently than boys across all groups and all episodes of focused attention.

Perinatal Risk

Overview

For the preterm infants only, perinatal risk factors were examined in relation to average Global Focused Attention and Peak Focus, and to HR change scores concurrent with episodes of focused attention (Average HR Change, HR Change Peak Focus, and Magnitude HR Change Peak Focus). In addition, perinatal risk factors were explored in relation to the Mental Development Index on the Bayley Scales (BSID II, MDI). Even though latency was a preliminary measure, it has been found differentiate higher versus lower-risk preterm infants (Ruff, 1988; Ruff, 1986e), therefore latency was examined in relation to perinatal risk factors.

Perinatal risk factors, including gestational age, Apgar at 5 min, days on mechanical ventilation, and early illness severity (SNAP II) and global risk (NMI) are inter-correlated, however they were analyzed separately to illustrate the relative effects of different perinatal attributes. For this sample of preterm infants born at birth weights appropriate for gestational age (AGA), results for birthweight would be consistent with gestational age and therefore birthweight was not included as a risk factor. Correlations were carried out separately for ELGA and VLGA groups, based on the differences between the two groups in the relationships between latency and global attentiveness, and between focused attention and cardiac response.

Perinatal Risk as related to Global Focused Attention and Peak Focus

For the ELGA infants, none of the perinatal risk factors were related to average Global Focused Attention or average Peak Focus ($p > .25$). For the VLGA infants, perinatal risk factors were not related to either Global Focused Attention ($p > .05$) or average Peak Focus ($p > .05$).

Perinatal Risk as related to MDI and Latency

None of the perinatal risk factors were significantly related to Bayley MDI for either the ELGA ($p > .05$) or VLGA ($p > .25$) infants. As previously shown in Table 1, it should be pointed out that there were no significant group differences on the mean Mental Development Index from the Bayley Scales of Infant Development (MDI, Bayley II), ($p = .290$). In relating further perinatal risk factors, for ELGA infants, there was a significant positive association between higher total Days on Ventilation required by the preterm infant and longer Latency to the first focused episode ($r = .37$, $p = .036$). This relationship was not seen in VLGA infants ($r = .11$, $p = .457$).

Perinatal Risk Factors as related to Heart Rate Change

For the ELGA infants, the longer the infant was ventilated the greater the Average HR Change across all focused episodes ($r = -.557$, $p = .001$). For the VLGA infants, there were significant correlations between greater early illness severity (higher SNAP II Day 1 Scores) and both the mean ($r = -.342$, $p = .020$), and Magnitude HR Change for the Peak Focus ($r = -.324$, $p < .028$), indicating greater illness severity was associated with more change in HR.

Correlations between Focused Attention, HR Change and MDI

Term-born Controls

The relationship between perinatal risk factors and focused attention, heart rate change and MDI were explored only for the preterm infants. However, as a basis for comparison, relationships of focused attention, heart rate and MDI for the Term-born infants were also examined. For term-born infants, neither average Peak Focus, or average Global Focused Attention, nor HR change were significantly associated with MDI ($p > .1$).

Perinatal Risk, HR Change and Focused Attention in Relation to Concurrent Cognitive Development

Overview

Hierarchical linear regressions were conducted to determine whether Average HR Change during focused attention, and either Global Focused Attention or Peak Focus, added to illness severity and adverse NICU experience in predicting concurrent cognitive development (Bayely MDI). In order to reduce multicollinearity, only one measure representing early neonatal illness severity (SNAP II, Day 1), and one measure representing level of illness across the NICU stay (Days of Ventilation), were used. In the first regression model, these two perinatal risk factors were entered first, followed by Average HR Change in the second block, average Global Focused Attention in the third block, and sex in the fourth block. A second set of regression analyses were run with the same factors in the first, second and fourth blocks, and adding Peak Focus to the third block (rather than Global Focused Attention, which was removed from the third block). Since the relationships between focused attention and cardiac response differed for ELGA and VLGA infants, regression analyses predicting MDI were run separately for the two subgroups of preterm infants.

Predicting Mental Development (Bayley MDI)

For the ELGA infants, SNAP II and Days of Ventilation did not predict MDI. However, the addition of Average HR Change (averaged across all focused episodes) significantly predicted MDI ($F[1,29] = 15.492$, $p < .0001$), with the overall model accounting for 30% of the variance (Adjusted R Square = .303). Further, when Global Focused Attention was added to the model, the change was not statistically significant. However, the overall model remained significant ($F[4,28] = 5.376$, $p = .002$) and the variance in predicting MDI increased marginally by about 5% (Total Adjusted R Square = .354). Sex did not add significantly to the model.

When regressions were re-run, using the same factors in the first, second and fourth blocks and adding Peak Focus (rather than Global Focused Attention) in the third block, this resulted in significant change in the F statistic ($F[1,28] = 11.628$, $p = .002$). Peak

Focus accounted for an additional 19% of the variance (after Average HR Change; $F_{change}[1,28] = 11.628$, $p=.002$) resulting in a significant overall model in predicting concurrent MDI ($F[4, 28] = 8.674$, $p < .0001$; Total Adjusted R Square = .49). The addition of sex produced no significant change in the model (Total Adjusted Square = .50). For the VLGA infants, none of the models were significant ($p > .50$).

The hierarchical regressions were run only on the preterm infant groups, however, as noted above for Term-born infants, average Peak Focus, Global Focused Attention and average HR change (across all focused episodes) were not significantly associated with MDI ($p > .10$).

In summary, given the limited number of infants in the ELGA group (n= 33), and the number of predictor variables, results must be viewed cautiously. Nevertheless, the amount of variance in predicting MDI as explained by average heart rate change and peak focus for the ELGA infants is striking.

CHAPTER 5: DISCUSSION

Overview

This study was conducted to compare focused attention and heart rate response in ELGA, VLGA and term-born infants during their exploratory play with novel objects. Recent studies of very low birthweight infants have linked focused attention during infant exploratory play to preschool cognition (Lawson et al., 2004c; Lawson & Ruff, 2004f). Additionally, research with term-born infants has shown that focused attention and information processing are associated with sustained decreases in heart rate, which show developmental changes in infancy (Lansink et al., 2000; Lansink & Richards, 1997g). However, to my knowledge, there are no studies that have examined the relationship between focused attention and heart rate response in preterm infants during exploratory play. Moreover, for very preterm infants, who are vulnerable to problems in attention and cognition, the relative contributions of perinatal risk and both focused attention and heart rate change in relation to cognitive development have not previously been examined. This study extends knowledge from previous research on behavioural focused attention during exploratory play, by comparing well-defined groups of very preterm infants (ELGA, VLGA) to healthy term-born infants. The clinical relevance of these findings together with the significance of focused attention for future research is discussed.

Summary of findings in relation to the hypotheses

To summarize, the first hypothesis (a) that ELGA and VLGA infants would show behaviours that reflect poorer attention compared to term-born infants, while exploring 3-

dimensional toys, was partially confirmed. Surprisingly, the highest risk ELGA infants did not show the greatest effects in behavioural attention, rather the VLGA infants were rated significantly lower than term on global attention and the ELGA only marginally so. There were no group differences in peak focus. The first hypotheses (b) that ELGA and VLGA preterm infants would show higher arousal (higher mean heart rate) and less suppression of heart rate variability from baseline to toy exploration compared to term-born infants, were not supported. Furthermore, the second hypothesis that the effects would be greater in ELGA or VLGA boys compared to girls in respective gestational age groups was not supported for either the behavioural or cardiac autonomic measures, since no significant interactions were found. Rather there were main effects of sex for a number of the focused attention behaviours, and girls showed greater heart rate deceleration during their peak focus. The third hypothesis was that better focused attention and greater heart rate change would be associated with higher cognitive functioning in preterm ELGA and VLGA infants, after adjusting for perinatal risk factors. This hypothesis was strongly supported in ELGA, but not VLGA infants.

Focused Attention Behaviours: Preliminary Analyses

The hypothesis that ELGA and VLGA infants would show behaviours that reflect poorer attention compared to term-born infants, while exploring 3-dimensional toys, was partially confirmed. In the preliminary analyses, surprisingly, ELGA, VLGA and term-born infants did not differ when compared on several behaviours that either indicated, or were related to infant focused attention. These included the average time (latency) it took to organize a focused response following the presentation of a novel toy, the infant's total number of focused episodes and the amount of toy throwing. Nor were there any group differences in the total duration of focused attention over the four 90-second toy sequences. The primary behaviours of interest in this study were infant global focused attention for each of the four toys and sustained focus (peak focus). However, as latency, number and total duration of focused attention are behaviours commonly reported in the literature, these preliminary behaviours were also compared across gestational age groups.

In contrast to the present findings, previous studies of preterm and term-born infants have found differences in total duration of focused attention or examining (Landry et al., 1988; Ruff, 1988; Ruff, 1986d). On the other hand, the problems of using total duration of attention, particularly as infants can have similar total fixation times based on very different variations in number and duration of looks have been previously discussed (Cohen, 1972c; Colombo, 2001). Furthermore, the duration of focused attention is largely dependent on complexity of the stimuli (Courage, Reynolds, & Richards, 2006b). Most studies of term-born infant exploratory play during the first year of life report age-differences based only on the intensity of the infant's engagement and very specific examining behaviours (McCall, 1974; Ruff, 1984; Ruff et al., 1990), or the sequencing and organization of attention (Lansink et al., 2000). In other studies comparing preterm to term-born infants, differences have been found only by separating lower from higher risk infants based on early illness severity, medical and neurobehavioural history (Ruff et al., 1984; Sigman, 1976). However, in separating preterm infants according to risk, differences have not always been found. For example, in a study of 12-month-old preterm infants separated according to risk, there were no differences in duration of focused attention, however risk groups were differentiated based on latency of response (Ruff, 1988). Differences in latency between preterm and term-born infants have also been reported elsewhere (Ruff, 1986c). Thus, in the current study, the lack of gestational age differences in latency of response was inconsistent with previous findings. All groups were equally fast to organize and activate a focused response, which consisted of about 12 seconds per toy. Ruff (1986b) found that 7-month term-born infants took about 11 seconds, while preterm infants took an average of 10 seconds longer. In the current study, VLGA and term-born infants showed a fairly consistent pattern, whereby the longer it took to organize a focused response (latency), the shorter the sustained (peak) focus and the lower their ratings of global attention. However, it was interesting that for ELGA infants, this pattern was not apparent. In contrast with the other groups, this suggests that the time that ELGA infants take to organize and activate a response may not necessarily impact overall levels of focused attention. The term-born infants also showed a pattern whereby, the more they threw toys, the shorter was the length of their sustained (peak) focus. Interestingly, this pattern was not seen in the ELGA and VLGA preterm infants, whereby the number of toys thrown was not associated with the length of sustained focus.

Focused Attention: Primary Analyses

The hypothesis that ELGA, VLGA and term-born infants would show poorer attention, with greater effects for the ELGA and male sex for ELGA and VLGA infants was tested by comparing the infant's sustained (peak) focus, and their global ratings of focused attention. Shorter sustained focus was expected in these infants who were expected to show relatively less persistence and motivation in processing specific features of the novel toy. These hypotheses were based on the relative risks associated with ELGA or male preterm status. Consistent with findings for the preliminary behaviours, the ELGA, VLGA and term-born infants did not differ in their length of sustained focus (average peak focus), nor did the ELGA or VLGA boys differ from their gestational age female counterparts.

Although in the current study, no differences were found on overall duration spent in focused attention, term-born infants were significantly higher on global focused attention than VLGA preterm infants (p=.018), and marginally higher, than ELGA (p=.063), using an established global rating scale for infant exploratory play (Lawson et al., 2001). Thus, the hypothesis that preterm infants would show poorer attention than term-born infants was only partially confirmed, and surprisingly, the highest risk ELGA infants did not show the greatest effects in behavioural attention. Furthermore, the hypothesis that the effects would be greater in ELGA or VLGA boys compared to girls in respective gestational age groups was not supported, since no significant interactions were found.

Using the global ratings of focused attention, the data in the present study of 8-month infants were compared to ratings of 71 VLBW (24 to 36 weeks gestation, 525 to 1470 grams) provided by Lawson and Ruff (2001) as seen in Appendix A. The distributions of ratings of focused attention for the 8-month preterm infants in the current study varied considerably in relation to the distributions of 7-month preterm infants by

Lawson and Ruff (2001). For example, 30% and 42% of the 7-month preterm infants fell in the two lowest of the five distributions, whereas the proportions of 8-month infants in these same two lowest distributions, whether they were preterm or not, were markedly lower (0% and 20% of ELGA; 4.2% and 19% of VLGA; 0% and 11% of term-born infant). The raters used the same training tapes and two coders rated each exploratory sequence and re-rated sequences when not exact, according to Lawson and Ruff's (2001) specific guidelines. Furthermore, levels of exact ratings were similar to those reported by Lawson and Ruff, and further to agreement on the global ratings, inter-rater reliability was established on timed-coding of focused attention which was highly correlated with the global ratings. Thus the differences between the two studies were not likely due to coding differences, rather, the preterm samples differed, as well as infant age. The transition period between 7 and 8 months marks a developmental period characterized by significant increases in endogenous attention (Colombo, 2001). Thus, 8-month-old infants would be expected to show more focused attention than 7-month-old infants. Perhaps less obvious, but of critical importance in explaining the differing proportions of infants in the two studies, particularly in the lowest distributions, was that the two samples of preterm infants would have differed significantly in terms of the risk factors associated with premature birth. Lawson and Ruff (2001) defined prematurity based on birthweight (<1500g), and included a heterogeneous sample of infants of birthweights to 1470g, born up to 36 weeks GA seen for clinical follow-up. According to population-based statistics, birthweights of 1500g for boys and 1400g for girls fall at the 50th percentile for 30 weeks of completed gestation (Kramer, 2001), thus by definition, their sample included a significant proportion of infants that were growth-retarded in utero, born small-for-gestational age (SGA), who are at greater risk for childhood attention difficulties (e.g., Robson et al., 1998). Additionally, the Lawson and Ruff sample of preterm infants were recruited from clinical follow-up, without exclusions. Thus, in their study, it appears that they included infants with developmental delay, significant intraventricular hemorrhage (IVH grade III or IV) and/or periventricular leukomalacia (PVL), all of which are associated with significantly adverse outcomes. The current sample of infants, born between 500g and 2390g, at 23 to 32 weeks GA, included only infants born appropriate for gestational age (AGA), and infants who had higher risk for adverse effects were excluded (i.e. IVH grade III or IV and/or PVL). Moreover, infants with cognitive delay (Bayley MDI <70), and/or significant sensory and/or motor impairment were excluded. Additionally, in the current study, infants were excluded who were clearly fussy at the onset or during toy exploration. Thus, from the larger group at initial recruitment, the present sample represents the highest functioning preterm infants, who thereby would likely adapt more easily to novel situations. Use of the strict exclusion criteria may have excluded infants who by virtue of their fussiness may also have been those infants who would show poorer attention in toy exploration. Negative emotionality at 1 and 2 years of age in combination with low attentiveness has been linked to poorer cognitive outcome at preschool age (Lawson et al., 2004c). If criteria for inclusion in the present study had been less restrictive, there would most likely have been a greater proportion of inattentive or marginally attentive ELGA and VLGA infants.

Sex Differences in Focused Attention

The hypothesis that ELGA and VLGA preterm boys would show less behavioural focused attention than their female gestational age counterparts was not supported, as there were no group by sex interactions in any of the analyses for focused attention behaviours. On the other hand, unexpectedly, the findings pointed to an overall sex difference. Not only were girls more attentive than boys on the global ratings, but they also focused attention longer and returned to examine toys more often, as seen in their greater number of focused episodes. Conversely, boys showed more toy throwing. There were also interesting differences in the association of toy throwing and length of sustained (peak) focus. Regardless of gestational group status, for girls, the more they threw the toys the shorter the length of their peak focus, however for the boys, toy throwing was not associated with the length of sustained focus.

The patterns of behaviours seen in boys and girls suggests sex differences in focused attention style during toy exploration, that remarkably, can be observed as early as the second half of the first year of life. On the whole, in studies of infant focused attention, sex differences have either not been reported or not examined, most likely due to sample size restrictions. However, differences in style of focused attention have been previously alluded to based on the idea that female infants attend to different features in the environment (Cohen, 1972d). In a newborn study of both preterm and term-born infants, Rose et al. (1976) reported that the lower behavioural responsiveness to tactile stimuli in preterm infants compared to term-born infants was due mainly to males, and suggested that findings from studies conducted from birth more likely reflect a biological rather than social basis of differentiation.

In one of the few studies of preterm and term-born infants that did examine sex effects, girls were more involved in exploring novel objects than boys (Sigman, 1976). Also during exploratory play, for full-term infants, sex was found to moderate the effects of early attentiveness on later cognition (Lawson et al., 2004c). In their study, Lawson and Ruff, separated infants as having either high or low negativity and high and low attentiveness and found that from a sample of 44 boys and 30 girls, there were more than three times the number of boys in the more negative/ less attentive group (7 girls and 24 boys). Other studies of exploratory play in full term infants and toddlers have reported no sex differences in duration of focused attention, for example using single or multiple toys at 10 and 26 months (Ruff & Capozzoli, 2003), or in 6-month infants while they explored objects with conditions of background television on or off (Setliff et al., 2007).

To summarize, there were three key findings related to infant focused attention behaviours. First, there were few, if any effects of ELGA and VLGA preterm status on the various focused attention behaviours including latency, number and duration of focused attention episodes. Contrary to the expected pattern, there were no greater effects of risk status (ELGA) or male infants within the ELGA and VLGA groups on focused attention behaviours. The second key finding was that it was the VLGA infants who differed significantly from the term-born infants in global attentiveness, rather than the ELGA group. Possible reasons for this are discussed in light of the ELGA findings of greater heart rate deceleration during focused attention episodes, which may reflect greater attentional effort and enhance the capacity to attend to the toys, however at greater "cost". The third key finding was that girls displayed greater attentiveness, longer focused attention, a greater number of focused episodes, and less toy throwing. Sex effects need to be considered more routinely in infant attention research of both term-born and preterm infants.

Change in Mean Heart Rate and Heart Rate Variability

The hypotheses that ELGA and VLGA preterm infants would show higher arousal (higher mean heart rate) and less suppression of heart rate variability from baseline to toy exploration compared to term-born infants, were not supported. Differences, particularly for ELGA infants, were expected based on theory and research that has documented differences in preterm infant arousal regulation that impacts their capacity to respond to novel stimuli (e.g., Field, 1981a; Mayes, 2000c) and evidence of differences in heart rate and heart rate variability that persist into the first year of life (e.g., Eiselt et al., 1993e; Grunau et al., 2001; Henslee, Schechtman, Lee, & Harper, 1997a). Furthermore, there were no differences between the ELGA and VLGA boys and girls in suppression of heart rate variability. Therefore the hypothesis that preterm boys would show greater negative effects with regards to cardiac autonomic measures was not supported.

The strikingly similar patterns of mean heart rate and heart rate variability, as measured from baseline across the entire exploratory play period for all groups and both sexes, suggests that there were strong effects of the novel toys. In other words, for all 8-month infants, regardless of sex or preterm status, the paradigm of exploratory play appears to be very robust in consistently eliciting visual interest as well as predictable decreases in mean heart rate and heart rate variability. All groups and both sexes showed a pattern of dramatic change in heart rate and heart rate variability from baseline to the first toy stimulus. From the first toy, heart rate subsequently increased slightly to the end of the infant's toy exploration. While the usual method for this paradigm is to present toys in a uniform sequence, varying the order would potentially have determined whether the pattern of heart rate response was due to specific toy properties. However, because the first toy elicited the least interest of all toys, the significant drop in mean heart rate from baseline to the first toy presumably reflected initial orienting and alteration in engagement. By contrast, heart rate variability showed continuous decrease over the entire period of exploratory play, which suggests that there are task demands and cognitive effort associated with infant's independent exploratory play. This continued decrease likely reflected corresponding parasympathetic influence, activated with the presentation of novel toys, resulting in continued suppression of heart rate variability, as determined by the infant's level of engagement. It is possible that systems related to changes in heart rate variability (suppression) as compared to heart rate may have different temporal effects beyond their initial activation. On the other hand, mean heart rate is influenced by numerous physiologic and biochemical changes other than vagal input and compared to heart rate variability, may less likely correlate with sustained attention (Porges, 1995a).

Consistent with the current findings, Hughes and Hutt (1979c) found that in normal term-born toddlers, mean heart rate and heart rate variability decreased significantly from baseline to exploratory play. Suppression of heart rate variability has also been reported in normal term-born 9-month old infants during the administration of the Bayley Scales of Infant Development (Porges, Doussard-Roosevelt, Portales, & Greenspan, 1996b) and in 3 month-old preterm and full-term infants who showed learning on a contingency task (Haley et al., in press). The pattern of decreased heart rate and heart rate variability seen for all groups during toy exploration in the present study, as well as the greater decrease in heart rate variability seen for the very attentive infants, is consistent with findings that exploratory play with objects is accompanied by vagal outflow, increasing the period of heartbeat and decreasing heart rate and heart rate variability.

Importantly, the hypothesis in the current study that the ELGA and VLGA infants would show less suppression of heart rate variability was based on research using other attention paradigms, for example studies that showed decreased heart rate orienting and less sustained attention in higher risk preterm infants to 2-dimensional video stimuli (Fox & Lewis, 1983d; Richards, 1994a), and altered parasympathetic control in preterm infants as evidenced by a lack of decrease of vagal tone to a surprise jack-in-the-box (DiPietro et al., 1992), or lack of increase in RSA during anticipation to a visual expectation task (Stroganova, Posikera, Pisarevskii, & Tsetlin, 2006a). However, as can be seen in the latter two studies, it is difficult to compare findings across different paradigms.

By contrast, the relative lack of difference between the gestational age groups in the current study, suggests that exploratory play elicits consistent behavioural interest and predictable decreases in heart rate variability in most infants. Therefore, it is possible that, given this paradigm, infants of 8-months, who either lack focused attention, or fail to show decreases in heart rate variability, might comprise those infants who are most "at-risk" for problems in attention regulation.

Suppression of Heart Rate Variability and Global Attentiveness

Regardless of gestational age risk group, very attentive infants showed greater suppression of heart rate variability across toy exploration than their inattentive or moderately attentive peers. These results verify a relationship between attentiveness during exploratory play and suppression of heart rate variability, which validates the premise upon which the hypotheses were based. Less suppression was expected to be associated with greater biological risk (i.e. earlier birth), which, as detailed above, was not supported. Greater suppression of heart rate variability was associated with learning in a contingency learning study of 3-month preterm and term-born infants (Haley et al., in press), with the more evidence of discrepancy in suppression between the learners and non-learners in the preterm group. In line with the present results, research with term-born infants has demonstrated an association between suppression of heart rate variability and faster habituation (e.g., Bornstein & Suess, 2000c) or suppression of vagal tone from baseline to tasks on the Bayley Scales of Infant Development with fewer behavioural problems at preschool age (Porges, Doussard-Roosevelt, Portales, & Greenspan, 1996a).

The finding that greater attentiveness was associated with greater suppression of heart rate variability supports the general hypothesis that suppression in heart rate variability is an index of mental effort and attention (Porges, 1992a). Furthermore the finding suggests that suppression of heart rate variability plays an important role in the regulation of attention during exploratory play. Together with other baseline-to-task studies that have linked greater regulation of heart rate variability to a variety of infant competencies, suppression of heart rate variability during exploratory play appears to be a valuable index of focused attention and engagement.

Heart Rate Change as related to Global Attentiveness

At a more detailed level of analyses, changes in heart rate during the infant's focused episodes were also examined in relation to global attentiveness. Infants who were rated as globally less attentive during exploratory play showed less decrease in heart rate (-3.8 bpm) than moderately (-7.4 bpm), or very attentive infants (-8.8 bpm), during the longest period of focus (peak focus). It should be noted that there was large individual variation of response in all groups (standard deviations $\geq$ 7 bpm). Moreover, attentiveness only had effects on magnitude of heart rate change, which in turn only distinguished the inattentive from the more attentive infants, suggesting that deceleration occurs on average when attention is moderately or highly focused. Conversely, in terms of heart rate variability, it was the very attentive infants who were distinguished from their less attentive peers by showing greater suppression. One might speculate that heart rate deceleration during periods of focus may reflect a presence or absence of processing, while suppression of heart rate variability across a period of engagement may represent level or degree of interest and engagement.

Other studies have demonstrated enhanced learning during heart rate deceleration. In term-born infants age 5 to 6 months, recognition memory occurred only for those infants whose heart rates decelerated during the presentation of stimuli (Linnemeyer et al., 1986), or when stimuli were presented during prolonged deceleration of heart rate

(Richards, 1997a)which supports the view that cognitive processing is more likely to occur during a phase characterized by decrements in heart rate.

Heart Rate Change during Focused Attention by Group and Sex

When heart rate change during episodes of focused attention was compared across gestational age groups, surprisingly, and contrary to the hypothesis in this study, ELGA infants showed consistently greater, rather than less, heart rate deceleration during periods of focus compared to VLGA infants. Unexpectedly, ELGA infants also showed greater mean heart rate deceleration, and greater magnitude of heart rate deceleration (absolute minimum HR) for the peak focus, compared to the VLGA and term-born infants. With findings in the reverse direction of what was expected, the hypothesis that ELGA infants would show a lesser heart rate response was not confirmed. Furthermore, VLGA infants did not differ in heart rate change from the term-born infants. The fact that there were no group by sex effects of heart rate change rejects the hypothesis that ELGA and VLGA preterm boys would show less heart rate change during focused attention. In considering the entire sample, girls showed greater mean heart rate deceleration than boys, averaged across focused episodes ($p = .022$), which is consistent with the finding in this study that girls were globally more attentive and focused for longer periods.

While there are no previous studies of exploratory play in preterm infants with which to compare these results, Lansink and Richards (1997f) used criteria specific to their lab to define heart rate deceleration in 6, 9 and 12 month term infants, and reported an overall 51% overlap with focused attention, suggesting a loose association of the two indices during infant's exploratory play. However, they attributed some lack of concordance to the inclusion of very short periods of focus, during which acceleration generally occurred. During exploratory play, a similar pattern of loose association was also described by Lansink et al. (2000) again in term-born infants, with greater overlap of attention sequences occurring during sustained decreases in heart rate, and a greater number of attention sequences, as the infants matured.

To compare current findings to those of Lansink and Richard's (1997e), in the present study, girls were more likely to show multiple attention sequences and overlap, with 70% of the girls, compared to 52% of the boys demonstrating any degree of heart rate deceleration, as averaged across all focused attention episodes. With regards to the gestational age groups, 63% of the term-born, 67% of the ELGA, and 54% of the VLGA infants showed any degree of deceleration as averaged across all periods of focused attention, suggesting also a "loose association" of behaviour and heart rate. However, for the mean, and magnitude of deceleration for the peak focus, ELGA infants decreased heart rate more consistently (82% and 100% for mean and magnitude) in contrast to the VLGA (54% and 80%) and term-born infants (53% and 80% respectively). These findings suggest that heart rate deceleration and focused attention may be more tightly coupled in ELGA infants, particularly in relation to sustained periods of focus. This having been said, differences seen in the magnitude of heart rate change, or overlap of focused attention and heart rate response may vary according the effects of other systems. For example, there is an extensive literature in adults that compares acceleration and deceleration according to timing of the stimulus, mental anticipation of the stimulus, task completion, or whether a motor response is forthcoming (Jennings, 1986; Jennings &

Wood, 1977; Lacey & Lacey, 1974a). Thus, during exploratory play with novel objects, it is possible that some infants showed an accelerative rather than decelerative response during focused episodes in anticipation of manipulating the toy in a more vigorous manner. When Polmerau and Malcuit (1980a) placed objects within the reach of infants ages 1½ to 5½ months, heart rate decreased when objects were distal, however when moved closer, heart rate accelerated to baseline. They concluded that the acceleration reflected the infants anticipated reaching. However, other researchers have disputed this interpretation suggesting that Polmerau et al. found acceleration due to infant distraction (O'Sullivan & Berthier, 2003a). Along with other studies that have shown decelerative heart rate responses during 3-dimensional toy play (Lansink et al., 2000; Lansink & Richards, 1997d), O'Sullivan and Berthier have provided evidence that rejects the view that overt manual action interferes with vagal activation accompanying attention engagement.

During exploratory play, Lansink et al. (2000) described the loose association of focused attention and heart rate, whereby, depending on the infant's tendency to re-engage, there would be multiple cycles of the two indices that vary in terms of overlap. Thus, it is possible that the ELGA infants may differ in their style of engagement and re-engagement, showing temporal differences in the cycling or approach, and therefore differences in the coupling of the cardiac and attention systems.

Lansink et al. (1997c) speculated that intermediate levels of attention or information processing were possibly represented by the relative discordance of heart rate and attention. This raises the possibility that some infants in the current study may have processed specific features of the toys, using intermediate levels of focused attention. While most studies of exploratory play equate longer duration of examining with greater competence, it is also generally acknowledged that the complexity of the objects determine the extent to which this occurs (e.g., Courage, Reynolds, & Richards, 2006a; Oakes et al., 1994; Ruff, 1986f). In future studies, the hypothesis that infants process features of toys using various degrees of attention could be tested by comparing the proportion of concordant responses for more or less complex stimuli amongst various risk groups.

Given the finding that ELGA infants were rated marginally lower, but not statistically significantly different on global attentiveness than term-born infants ($p = .063$), it could be argued that their greater heart rate deceleration might reflect increased attentional effort in order to compensate for deficits in information processing. There are studies that report greater heart rate deceleration during attention tasks in children with attention deficit disorders (Dykman, Ackerman, & Oglesby, 1992; Jennings, vanderMolen, Pelham, Debski, & Hoza, 1997). Jennings and his colleagues also presented data that reflected attentional compensation among elders who performed as well as college students on memory tasks, however showed significantly larger heart rate decelerations during memorization of the material to be recalled (Jennings, Nebes, & Yovetich, 1990). They suggest that attentional compensation can be detected by greater heart rate deceleration, when performance is on par with the reference group. While it is difficult to compare results of studies from such disparate populations and ages, there are also infant studies of attention and heart rate during exploratory play in line with this explanation. In a study of exploratory play, Setliff et al. (2007) found that when normal term-born 6 month-old infants were engaged in focused attention to toys, they showed significantly more heart rate deceleration when background television was on versus off, and 12 month-old infants showed greater deceleration when background television consisted of child oriented programming (Setliff et al., 2008). Their findings suggested that in the presence of potentially distracting stimuli, infants show greater heart rate deceleration, which may reflect greater capacity in attending to the toys. With these findings in mind, the greater deceleration in ELGA infants may be due to differences in their propensity for distraction. Thus, further to suggesting that the ELGA infants in the present study may be showing attentional compensation, the greater heart rate deceleration may also reflect enhanced attentional effort and greater "peripheral narrowing", so as to avoid distraction. This view is consistent with Richard's (2001) attention/arousal model, whereby the arousal system that is activated during sustained attention energizes specific brain systems involved in cognitive activities, and acts to select behaviour that is adaptive to the specific demands of the task and the goals of the infant. Within this framework, it is possible that, compared to other infants ELGA infants may both require and recruit greater cognitive effort and more attentional resources. Consistent with this explanation, in a study of exploratory play in 7 and 12 month-old infants, when objects were simple, the younger infants examined objects longer than the older infants, which as the authors suggest, was a reflection of increased information-processing load (Oakes et al., 1994). The pattern seen in these 7-month infants supports the assumption that duration of attention decreases along with increasing efficiency of information processing (Cohen, 1991). In the current study it should be noted that there were no gestational-age differences in focused attention for any of the timed measures. Thus in the present study, greater heart rate deceleration (rather than duration of examining) in the ELGA infants may reflect increased information processing load. Therefore in some instances, change in heart rate may be a more reliable index of engagement than behaviour.

Based on an arousal model, preterm infants have been characterized as hypo- or hyper-responsive to a variety of stimuli (e.g., Gardner et al., 1983; Krafchuk et al., 1983; Rose et al., 1976). Thus, the ELGA infants may also have a lower threshold for the orienting response, which may account for greater heart rate deceleration compared to the other groups. This greater responsiveness of heart rate deceleration could be seen as adaptive if it improves the capacity to focus and compensates for deficits in information processing, however it is possible that this over-regulation may occur at some metabolic cost.

While speculative, over time, differences in cardiac physiology may have pathophysiological implications for a variety of systems including cardiovascular health over the course of development. There are studies conducted in the newborn period that have found evidence of altered short term reflex cardiovascular control associated with premature birth, and evidence of more serious circulatory dysfunction associated with chronic lung disease (e.g., Cohen, Lagercrantz, & Katz-Salamon, 2007). Gournay, Drouin and Roze (2002b) who studied preterm infants at birth and at term-equivalent, found evidence of lower baroreflex control, which regulates variations in blood pressure by responses of heart rate and arterial vascular tone. They suggest that sympathovagal imbalance in preterm infants can potentially identify a population more susceptible to stress. Infants who have a lower "threshold" of response may show dysregulation in other response systems. There is a recent body of literature showing dysregulation in preterm infants. For example, ELGA infants show differences in their regulation of cortisol from 3 through 18 months of age, suggesting a long term "resetting" of endocrine stress systems, which may have negative effects on neurodevelopment and health (Grunau et al., 2007d).

It is interesting that the VLGA infants in this study did not show a similar pattern of heart rate change during focused attention to the ELGA infants. Though tentative, the lowered responsiveness of VLGA compared to the ELGA infants may be related to the differences in timing of the transient effects of birth relative to the maturation of the cardiac autonomic system. DiPietro (2007d), in a longitudinal study of heart rate and heart rate variability, suggested that individual differences in autonomic control originate during the fetal period. Thus it is conceivable that altered regulation of heart rate occurred during the ELGA and VLGA infants' extended NICU hospitalization, which is during the 3rd trimester of "fetal life", in the extrauterine environment.

In summary, there are a number of possibilities regarding the apparent differences between the ELGA infants and both VLGA and term-born infants, and between girls and boys in relation to heart rate deceleration coincident with focused attention. The relation between gestational age or sex and heart rate deceleration during focused attention is not straightforward. This relationship may be a function of the relative complexity of the objects explored, the amount of cognitive or attentional effort expended, differences in peripheral narrowing, arousal or threshold of response, or whether a motor response is forthcoming. It is likely that the girls and ELGA infants may each have shown differences in pattern of heart rate deceleration for different reasons. One could argue that the sex difference may more likely be due to an anticipated motor response as in the current study the boys threw toys more often. On the other hand, the differences in the ELGA infants, largely in the magnitude of response could reflect hyper-reactive orienting, greater attentional effort and recruitment of arousal systems to compensate for vulnerabilities or lack of neural integrity. This explanation of enhanced heart rate deceleration for the ELGA infants is likely the most plausible, particularly based on the findings in the current study, where heart rate deceleration accounted for a significant proportion of the variance in predicting concurrent Bayley MDI.

Associating Perinatal Risk with 8-Month Focused Attention, Heart Rate Change and Development

For the preterm infants, specific perinatal risk factors were examined in relation to focused attention, heart rate change and concurrent cognitive development. The associations were examined separately for ELGA and VLGA groups, based on the differences between the two groups in the relationships between focused attention and cardiac response and between latency and attentiveness.

Importantly, the longer the ELGA infants were on mechanical ventilation, the greater the mean heart rate deceleration across all focused periods. This finding provides important new information about autonomic reactivity in relation to behavioural attention in infants born extremely preterm. Moreover, the longer that the ELGA infants were on mechanical ventilation, the longer the time (latency) it took to focus after the toy was presented. This was consistent with previous studies that found behavioural latency differentiated higher from lower-risk preterm infants (Ruff, 1986a; Ruff, 1988). For the VLGA infants, there were significant correlations between greater early illness severity (higher SNAP II, Day 1 Scores) and both the mean and magnitude of heart rate deceleration for the peak focus, indicating greater illness severity was associated with more change in heart rate. Interestingly, in the current study, none of the perinatal risk factors were related to behavioural indices of infant global attention or length of sustained focus for either the ELGA or VLGA infants. This is inconsistent with the study by DiPietro et al. (1992) that reported inverse relationships between length of respiratory support, number of days hospitalized and both duration and range of behaviours shown in infant examining and exploratory play. Based on findings in the current study, it appears that the integration of autonomic regulation with behavioural attention is altered in extremely preterm infants, rather than attention per se.

Predicting Developmental Competence (Mental Development Index; MDI)

The third hypothesis of this study was that better focused attention and greater heart rate change would be associated with higher cognitive functioning in preterm ELGA and VLGA infants, after adjusting for perinatal risk factors. This hypothesis was strongly supported in ELGA, but not VLGA infants.

Among the ELGA infants, after adjusting for perinatal risk factors (illness severity following preterm birth, and duration of mechanical ventilation to reflect illness over the course of the NICU stay) greater mean heart rate deceleration across all focused episodes accounted for 30% of the variance in concurrent cognition. When the average length of peak focus was added, an additional 19% of the variance was explained. In contrast, neither global attention nor sex, were significant predictors. With 49% of the variance accounted for, the extent to which ELGA infants decrease their heart rate during focused attention and sustain focus in response to novel objects is strongly linked to cognitive development. While these regulatory capacities were clearly associated with cognitive development in ELGA infants, there were no such associations between focused attention or heart rate and developmental competence for either the VLGA or term-born infants. In view of these differences, as can be seen in Table 1, it should be noted that there were no significant group differences on the mean Bayley II MDI, (p=.290), likely due to the strict exclusion criteria for the preterm sample.

Though considered as less at-risk than the ELGA infants, the VLGA infants represent a heterogeneous group of infants who vary markedly in terms of their illness severity and needs for medical intervention. This may underlie the lack of a clear relationship between focused attention, heart rate change and development for the VLGA infants. Interestingly, VLGA infants showed more variation in their HR change during focused attention compared to ELGA infants. For example, for the peak focus, 54% and 80% showed any degree of deceleration for the mean and magnitude of response, compared to 82% and 100% of the ELGA infants.

Given that all the infants were born AGA, the difference between the ELGA and VLGA groups was the timing of birth, which occurred at different time-points of physiological and brain development. The third trimester of fetal life not only marks a period of rapid brain development, but also maturation of cardiovascular systems, which may be disrupted differentially according to timing of birth. Though speculative, it is conceivable that ELGA and VLGA infants may differ due to these differences in timing of the disruptive effects of birth and transition to extra-uterine life. The ELGA infants' prolonged exposure to an extrauterine life, at a time when central nervous systems are immature may provide some explanation of alterations in arousal that affect neuronal substrates involved in the development of attention systems. While, the effects of a later transition are generally regarded as posing fewer risks, there is a need for careful studies of the differential effects of timing of preterm birth on attention and cardiac regulation. For example, Feldman and Eidelman (2003) showed that maturation of cardiac vagal tone between 32 and 37 weeks GA was shifted (positively) in preterm infants who received mother-infant skin-to-skin (kangaroo care).

The findings in the present study suggest that the nature of attention problems in children who were born very preterm needs to be more clearly specified, particularly according to varying gestational age groups. Moreover, the findings point to the importance of studying the possible mechanisms for outcome differences in clearly defined groups.

Clinical Relevance

The findings in the current study support Lawson and Ruff's (2001) proposal that as an adjunct to traditional developmental assessment, measures of focused attention may have potential use in the clinical setting. Given the relationship between measures of focused attention and cognitive development, further studies are warranted to explore the possibility of the usefulness of assessing focused attention in the follow-up of high-risk infants. This having been said, there are important distinctions to be made about the assessment of infant focused attention during exploratory play with novel objects, against the backdrop of continued use of standard developmental tests, which have limited use in predicting later cognitive functioning for most infants, except those who have or are at significant risk of delay (Crowe, Deitz, & Bennett, 1987; Harris & Langkamp, 1994; Lewis & McGurk, 1972). Traditional developmental tests are generally based on developmental milestones, whereby the acquisition of a particular sensori-motor, or language-related ability is determined. Given this approach, qualitative differences in demonstrated abilities or cognitive processing are generally not assessed. Because it is important to identify at-risk infants early in life, it would be potentially advantageous to determine the quality, intensity or persistence of information processing or attentional capacity, as it is likely these aspects that influence more complex functioning. Furthermore, with regards to standardized tests, the infant's successful completion depends in part on the skills or "scaffolding techniques" that are part of an experienced examiner's repertoire. Therefore, infants who are at-risk for problems may obtain scores that overestimate their abilities. On the other hand, the infant's independent exploration of novel toys may reflect a more accurate sampling of their natural tendency to engage cognitively with objects, and because of this, is more likely to predict later cognition than milestone-based assessment. Therefore observing the infant's regulation of attention during independent exploration of novel objects can provide important clinical information. Furthermore, incorporating routine assessment of early attention regulation will potentially increase understanding of the relationship between early attention and later cognition. This approach would also enable clinicians to identify infants most at risk and in need of potentially appropriate interventions and/or monitoring and follow-up cognitive and behavioural evaluation. Research shows that sensitive and responsive parental interventions are effective in promoting attentiveness, particularly for infants who showed poorer behavioural attention (Ruff et al., 1991).

The findings in the present study are consistent with other studies that have shown moderate prediction of focused attention during exploratory play to later cognitive development (Lawson et al., 2004c; e.g., Lawson & Ruff, 2004g). Thus observations of an infant's interaction with individually presented novel objects can provide clinicians and parents with valuable information. While reporting development in infancy and early childhood must be cautious, due to the wide variation of individual outcomes, as an adjunct to standard developmental assessment, positive feedback to parents regarding an infant's focused attention can encourage parents to support the development of this basic function.

Length of sustained (peak) focus also has important clinical relevance, and as a measure of persistence, can reveal whether the infant can maintain his or her interest, resist distraction and fully explore many features of a novel object. Furthermore, the results from the present study suggest that, amongst AGA infants who are not developmentally delayed, relatively lower attentiveness can be identified in 20% to 40% of 8-month very preterm infants, based on distributed or averaged ratings of global focused attention on Lawson and Ruff's 5-point global scale (Lawson et al., 2001). The paradigm of exploratory play appears to elicit predictable behavioural and cardiac autonomic responses, therefore the robustness of the paradigm should withstand the fact that toys have not been standardized, provided that novelty is ensured and that toys vary in complexity with age (M. L. Courage, personal communication, April, 2008).

Infant ability to focus attention has important links to multiple aspects of development. The high prevalence of developmental problems in children born very preterm, and the current economic realities in medicine and education, not only justify but also necessitate objective approaches that emphasize the very early identification of key factors that underlie developmental processes. Potentially, ability to focus attention and regulate heart rate can be used as early markers of risk, not for the specific diagnostic label of attention problems per se, but the early identification of precursors of developmental and behavioural risk, which can guide early prevention and intervention programming.

Future Directions

Infant attention can be inferred using a variety of paradigms. In this study I have explored the infant's global focused attention, sustained focus and heart rate response during exploratory play, as related to gestational age risk and sex. Furthermore, I have explored the contribution of focused attention and regulation of heart rate to infant cognitive development, while considering perinatal risk. Recent studies have linked focused attention to cognition in the preschool years (Lawson et al., 2004c; Lawson & Ruff, 2004h). Thus, an obvious future direction for research in this area is to examine the predictive value of heart rate regulation during exploratory play on later attention and cognition in the follow-up of extremely preterm infants.

Given the unexpected findings that the magnitude of heart rate deceleration was greatest in the ELGA infants, studies are needed to replicate these findings. Additionally, studies could potentially test the hypothesis that ELGA infants showed a compensatory pattern of greater attentional effort, using commonly used methodologies such as latency to distraction during infant's focused attention, or alternatively, time to distraction during heart rate deceleration (e.g., Lansink & Richards, 1997b), that have not been previously tested with preterm infants. Using the background television paradigm of Setliff and colleagues (2007; 2008), one could also test whether ELGA infants were more focused in toy exploration in the face of a potentially distracting stimulus, as the infants in the studies by Setliff et al., who showed greater heart rate deceleration in the presence of background television.

While the finding from studies of this nature would shed light on the important links between attention/arousal regulation and premature birth, further work is also needed to examine the contexts that contribute to, and possible reasons for, the differences in reactivity in preterm infants that may affect long-term cognitive, behavioural functioning, and possible associations with later health outcomes. Hyper-responsive change in heart rate (decelerations) may improve the capacity to attend, or compensate for deficits in information processing, however, this may occur at some metabolic cost. The fact that there are recent findings that suggest cardiovascular differences, such as higher blood pressure in adolescents and young adults born at very low birthweights emphasizes the importance of further investigation in this area. (e.g., Doyle, Faber, Callanan, & Morley, 2003; Hack, Schluchter, Cartar, & Rahman, 2005).

Furthermore, there are many contextual influences affecting the development of attentional processes of preterm infants that need to be considered. In ELGA preterm infants, maternal stress and sensitivity were found to moderate the relationship between early experience and infant independent focused toy exploration (Petrie Thomas & Grunau, 2004; Tu et al., 2007a). For preterm infants and toddlers, in the interactive play context, maternal enjoyment and responsiveness have been found to elicit positive behaviours (Petrie Thomas, Grunau, Whitfield, & Fay, 2003) and higher play competence (Fewell, Casal, Glick, Wheeden, & Spiker, 1996) as well as increased in infant attention to toys (Landry et al., 1988). In term-born infants, moderate (but not high) adult interventions have been found to effectively increase infant attention during exploratory play (Belsky, Goode, & Most, 1980; Parrinello & Ruff, 1988a) with most impact on low attenders (Parrinello & Ruff, 1988b). Importantly, in preterm infants, qualities of the home environment and caregiver responsiveness have been shown to moderate continuity between infant attention and later intellectual outcome (e.g., Sigman, Cohen, & Beckwith, 1997). Many studies have demonstrated the positive effects of optimal parenting or negative impact of adverse or social risk environments on the behavioural and developmental trajectories of preterm infants, including attention regulation (Robson et al., 1998; Robson & Pederson, 1997b) as well as cognitive and behavioural outcomes (Hack et al., 1992a). Furthermore, there is a longstanding suggestion that preterm infants may be more vulnerable to environmental adversity than full-term babies (Escalona, 1982). Over the first year of life, research also supports the view that characteristics of parental interaction may influence infant cardiac response and regulation. For example, research in term-born infants has linked parent responsiveness to greater infant regulation of heart rate in response to stress, such as the still-face procedure (Haley & Stansbury, 2003) and synchronous patterns of co-regulation during mother-infant play have been associated with greater infant parasympathetic regulation (Porter, 2003b). Feldman (2007) has emphasized the ecological significance of physiological synchrony in parent-infant interactions, as the basis for the organization and development of relational behaviours and response patterns.

Limitations

There are a number of important points to be made about this study. First it should be emphasized that because the sample for this study consisted of relatively healthy extremely and very preterm infants, one cannot generalize the results to the full range of very preterm infants typical of these cohorts. In contrast to previous studies of premature infants, in the present study the sample of relatively healthy extremely low and very low gestational age infants was chosen deliberately in order to assess focused attention without other confounding factors. For these infants who escape the more adverse outcomes of significant sensory, motor or cognitive impairment that are generally identified early in life, the subtle deficits in learning are generally not recognized until school entry, if not later childhood. A second limitation is that the measure of heart rate variability used was the standard deviation of heart rate. As described in the review, there are other methods of measuring heart rate variability that are more directly linked to the neural substrates that control autonomic function. A third limitation is that contextual factors such as parenting or mother-infant interaction, which may moderate the relationship between prematurity, infant focused attention and cardiac autonomic arousal, were not examined. As noted in the above section on "future directions" this is an extremely important and potentially fertile area of study, which I hope to explore in future studies.

Concluding Comments

The infant's ability to selectively attend and to sustain attention is central to cognitive functioning. The development of infant focused attention, particularly endogenous attention involving "effortful control" in the second half of the first year of life may lay the foundation for more complex processing including executive functions (Colombo, 2001; Rothbart, Posner, & Rosicky, 1994). Thus, it is reasonable to propose that disruptions in attention regulation, or physiological systems that index attention and arousal, may underlie altered cognitive development and executive functions in very preterm infants.

In relatively healthy ELGA infants, the ability to focus attention, as indexed behaviourally and by changes in heart rate appears to be critical in relation to cognitive development. While, children born extremely premature are at higher risk for childhood cognitive, learning and attention problems e.g. (Anderson & Doyle, 2003c; Grunau, Whitfield, & Davis, 2002d; Taylor et al., 1998; Taylor et al., 2000; Taylor, Klein, Minich, & Hack, 2000c) some of these vulnerable children escape these deficits. This would likely occur more often in the relatively healthy very preterm infants who were selected rather than excluded for this study. It is possible that relatively positive outcomes seen at later ages may be mediated by the infant's ability to regulate his or her attention and cardiac response which serves as a compensatory or protective factor against the risks associated with very premature birth. For inattentive infants or those who show little heart rate response to stimuli, the lack of regulatory responses may be considered risk factors that increase the vulnerability of the adverse effects associated with an extremely premature birth.

Thus, in relatively healthy ELGA infants, there appear to be unique relationships between attention and cardiac response patterns, which may not only relate to later cognition and attention, but also reflect regulatory characteristics that underlie the ease or difficulty in which the infant acquires skills and abilities. While patterns of heart rate add important information about the regulation of infant attention, beyond that which is generally obtained through behavioural measures of focused attention (e.g., Lansink & Richards, 1997a; Richards et al., 1992), I would add that measures of heart rate may also reveal important information about the development of cognition in the extremely preterm population. In the ELGA infants, the pattern of greater magnitude of heart rate deceleration seen during focused attention may indicate a greater expenditure of effort, or greater allocation of cognitive resources to tasks. Given the central role of attention in neurodevelopment, the long-term effects of altered attention regulation, which may affect physiologic and developmental systems, warrant further study.

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APPENDIX A

Rating Focused Attention in Infants

From: Lawson and Ruff, (2001). Focused attention. In L.T. Singer & P.S. Zeskind (Eds.), Biobehavioral assessment of the infant (p. 299). New York, Guilford.

Lawson and Ruff (2001) provide "Working Guidelines for Rating Focused Attention in Infants" together with their data of the distributions of ratings obtained for Very Low Birthweight infants at 7- and 12-months of age. Further to these guidelines, training materials from their laboratory, which included further descriptions and a video with examples of infants rated along the 5-point scale were used to train coders for the current study. From Lawson and Ruff's (2001) working guidelines, a summary of the infant behaviours that distinguish each of the 5-point ratings is provided below.

Rating of 1: The infant shows "no clear evidence for investment in the object(s), with little visual engagement". Looks are mainly "to facilitate grasping/mouthing/transfer or to watch movement of toy, as in repetitive behaviours such as banging or waving" and the infant "does not focus on the properties of specific object."

Rating of 2: The infant may "invest energy in object exploration without providing clear evidence for this" and behaviours include "marginal and poorly defined attention to objects and action on objects". The "episodes do not have clear starting and ending points and are characterized by overall lack of effort and organization."

Rating of 3: Infant behaviours include "clear demonstration of the ability and inclination to attend to objects during object exploration and other actions on objects" and "at least a few clear examples of focused attention".

Rating of 4: "A greater proportion of the available time is devoted to focused attention toward the object(s) and actions on the objects". The episodes are "longer and clear-cut, with starting and ending points easily determined".

Rating of 5: The infant shows "longer periods of absorption in the object(s) and actions on the objects, with focused attention episodes long and clear-cut and extraneous behaviors reduced still further or non-existent".

APPENDIX B

Preliminary Analyses

Preliminary Focused Attention Measures

Overview

As noted in the results section, separate ANOVAs were conducted for the four preliminary measures comparing the average time to organize a focused response (Latency), the total number of focused episodes (Number of Focused Episodes), the total number of times toys were thrown (Toys Thrown) and total duration of focused attention (Duration Focused Attention) over the exploratory play sequences by group (ELGA, VLGA, Term-born) and sex. The data for each of these four preliminary measures are shown in Table 4, together with the summary of the preliminary results provided in the main section. Bivariate correlations were also carried out between preliminary and main focused attention measures, again by group and sex, in order to illustrate the nature of focused attention in 8-month infants according to gestational status and sex, and to examine the overlap of data for data reduction.

Latency

Latency to the first focused attention period represents the time it takes to organize a focused response. To replicate and extend previous findings, it was hypothesized that preterm infants would take longer to organize a focused response. Only 51% of the

ELGA infants, 58% of the VLGA infants, and 61% of the Term-born infants showed focused attention for every toy exploration sequence.

There was a lot of individual variation in average Latency, with a range of 2 to 44 seconds (overall mean 12.8, *SD* 9.5). Surprisingly, there were no significant Group differences in average Latency (F [2,123] = .073, p = .930). Nor were there any significant effects of Sex on average Latency, where girls took an average of 15 seconds (SD 12) and boys took an average of 19 seconds (SD 15) to focus following the toy presentations (F [1,123] = 2.345, p = .128), and no significant Group by Sex interaction (F [1,123] = .152, p = .859).

Relating Latency to Global Focused Attention and Peak Focus

Latency was examined in relation to the main focused attention variables (Global Focused Attention and Peak Focus). Correlations were run only for sequences where infants showed focused attention and thus where Latency scores could be derived. The relationship between average Latency and average Global Focused Attention differed between the ELGA infants versus the other two infant Groups (ELGA, r = -.22, p = .213; VLGA, r = -.56, p < .0001, Term-born, r = -.33, p = .024). Considering sex of the infant separately, average Latency and average Global Focused Attention were significantly correlated for girls (r = -.35, p =.007) and boys (r = -.33, p =.008).

The correlations between average Latency and average Peak Focus were significantly correlated for all infants groups (ELGA, r = -.38, p = .029; VLGA, r = -.48, p= .001, Term-born, r = -.45, p = .002), and for girls (r = -.48, p <.0001) and boys (r = -.39, p= .001).

In summary, the moderate association of Latency and Global Focused Attention (inverse relationship) suggests that in general, at least for the VLGA and Term-born infants, and for both sexes, infants who showed focused attention more quickly after the toys were presented were also rated as having higher focused attention. The relative lack of association between Latency and ratings of Global Focused Attention for the ELGA infants, in contrast with the other groups, is interesting and suggests that the time that ELGA infants take to organize a focused response is not consistently related to overall attentiveness. There was a consistent relationship between the time taken to organize a focused response (Latency) and the average length of longest focus (Peak Focus) for all infant groups.

Number of Focused Episodes

There were no significant differences in total Number of Focused Episodes by Group (F [2,123] = .971, p = .392). However, there were significant Sex differences, with girls showing a greater total Number of Focused Episodes across the four exploratory Toy Sequences consisting of a total of 10.3 focused episodes versus 8.3 focused episodes for the boys (F [1,123] = 5.595, p = .020). There was no significant Group by Sex interaction (F [2,123] = 1.928, p = .150).

Relating Number of Episodes to Peak Focus and Global Focused Attention

There were significant positive correlations between Number of Focused Episodes and ratings of Global Focused Attention for each infant Group (ELGA: r = .74; VLGA: r

=.69; Term-born: r = .59, p < .0001) and for both sexes (Girls: r = .62; Boys: r = .70, p< .0001).

The Number of Focused Episodes and average Peak Focus were highly correlated for each infant Group (ELGA, r = .75, VLGA, r = .63, and Term-born, r = .62, p < .0001), and for girls (r = .68) and boys (r = .63), (p< .0001). Summarizing these results, there were no group differences in number of focused episodes, however overall girls had a greater number of focused episodes than boy. Generally, infants who sustained their focus for longer periods also tended to be rated higher on focused attention.

Toys Thrown

Toy throwing is a behaviour that is generally inversely related to infant focused attention. For total number of Toys Thrown, there were no significant Group differences (F [2,123] = 1.093, p = .338). However, there were significant Sex differences, where boys threw toys off the table more than girls (F [1,123] = 4.957, p = .028). There was no significant Group by Sex interaction (F [2,123] = .447, p = .641).

Toy throwing behaviour is within the normal developmental repertoire of this age group. As this data shows, 73 (56.6%) of the 129 infants in the sample threw at least one toy throughout the four 90-second exploration sequences. Considering only the infants who threw toys, there was a large variation of throwing; 43% of infants (24% of entire sample) threw toys either one or two times, and 44% of infants (25% of entire sample) threw toys 3 to 9 times over the entire exploration period. Of the 129 infants, less than 1% of infants threw toys more than ten times. With regards to Sex, 67.2% of the boys in the entire sample threw toys and 45.2% of the girls threw toys. For boys, toys were thrown an average total of 3.9 times (SD 5.3) over the entire toy exploration period, whereas girls threw toys a mean of 2.1 times (SD 4.0).

Relating Toys Thrown to Global Focused Attention and Peak Focus

There was a general pattern of more toys thrown to lower ratings of Global Focused Attention. For Term-born and ELGA infants, the more toys were thrown, the lower the average Global Focused Attention rating (ELGA; $r = -.48$, $p = .004$; Term-born; $r = -.474$, $p = .001$). For the VLGA infants, the relationship between Toys Thrown and Global Focused Attention approached significance ($r = -.28$, $p = .059$). Considering Sex of the infants, the pattern or more toy throwing and lower ratings of Global Focused Attention was also seen in girls ($r = -.30$, $p = .016$), and boys ($r = -.38$, $p = .001$).

Greater number of Toys Thrown was related to shorter duration of average Peak Focus for Term-born infants ($r = -.343$, $p=.020$). However, there was no significant relationship between Toys Thrown and Peak Focus for the ELGA or VLGA infants ($p>.1$). Toys Thrown and Peak Focus were correlated for girls ($r = -.30$, $p=.014$) but not boys ($p>.1$).

Though toy throwing is within the normal behavioural repertoire of this age group (Ruff et al., 1991), more toy throwing is generally associated with less focused attention. This inverse relationship is not surprising as by definition, greater focused attention is generally accompanied and characterized by a reduced motor activity (Ruff, 1986v). In a similar vein, as was evident in the Term-born infants, one would also expect to see a relationship between more toys thrown and shorter duration of average peak focus. The fact that the ELGA and VLGA preterm infants did not show this pattern is interesting and may reflect slight differences in integrity of response.

Duration of Focused Attention

There were no significant differences in total Duration of Focused Attention by Group ($F [2,123] = .415$, $p = .661$). However, there were significant Sex differences, with girls showing a greater total Duration of Focused Attention across the 6-minute four exploratory Toy Sequences, consisting of a total of 68.5 seconds (SD 49.7) of focused attention for the girls versus 50.5 seconds of focused attention (SD 38.3) for the boys ($F [1,123] = 5.091$, $p = .026$). There was no significant Group by Sex interaction ($F [2,123] = 1.075$, $p = .344$).

Relating Duration to Global Focused Attention and Peak Focus

As would be expected, there were significantly positive correlations, across Groups and Sex, between total Duration of Focused Attention and Global Focused Attention for each of the four Toy Sequences. Averaged across all four toys, correlations between Global Focused Attention and total Duration were $r = .75$ for the ELGA Preterm infants, $r = .78$ for the VLGA infants and $r = .69$ for the Term-born infants, ($p < .0001$). Correlations for girls and boys were $r = .69$, and $r = .74$ respectively ($p < .0001$).

Average Duration of Focused Attention was highly correlated with average Peak Focus for all Groups (ELGA: $r = .91$; VLGA, $r =.92$; Term-born, $r = .88$, $p < .0001$) and for both sexes (Girls: $r = .92$; Boys: $r = .86$, $p<.0001$). This is not surprising and confirms the overlap between total Duration of Focused Attention and Peak Focus, supporting the use of only one of these variables in the main analyses.

Association of Primary Measures

Correlations between Global Focused Attention and Peak Focus

As would be expected, Average Peak Focus was highly and positively correlated with average Global Focused Attention for all Groups (ELGA, $r = .61$; VLGA, $r =.66$; Term-born, $r = .68$, $p < .0001$) and average Global Focused Attention for both sexes (Girls: $r = .68$; Boys: $r = .58$, $p < .0001$). Taken together, the longer infants sustained their focus the higher they were rated on focused attention. This pattern was consistent for all infant groups and for both boys and girls.

APPENDIX C: Summary Table of Results

Table 8: Summary of Results Comparing Gestational Age Groups and Sex

	Group Differences	ELGA vs. VLGA	ELGA vs. Term	VLGA vs. Term	Boys vs. Girls
Preliminary Analyses					
Average Latency	.930 (ns)				.128(ns)
Total # of Focused Episodes	.392 (ns)				.020*
Total # of Toys Thrown	.338 (ns)				.028*
Total Duration of Focused Attention	.661 (ns)				.026*
Primary Analyses					
Average Global Focused Attention	.050*	ns	.063 (ns)	.018*	.012*
Levels (3) of Global Attentiveness	.242 (ns)				.049*
Distributed 5-point Ratings (Lawson & Ruff, 2001)	.056 (ns)	ns	.073 (ns)	.013*	.316(ns)
Average Peak Focus	.666 (ns)				.068(ns)
Single Peak Focus	.871 (ns)				.123(ns)
Average HR across Toy Exploration	.251 (ns)				.524(ns)
Heart Rate Variability (HRSD) Baseline to Toys (mean HRSD for each 90- second sequence)	.935 (ns)				.832(ns)
Average HR Change for All Focused Episodes	.043*	.023*	ns	ns	.022*
HR Change during Peak Focus	.006**	.003**	.007**	Ns	.237(ns)
Magnitude HR Change during Peak Focus	.016*	.009**	.011*	ns	.171(ns)

* the mean difference is significant at the .05 level; ** the mean difference is significant at the .01 level

APPENDIX D: Ethics Approval

The University of British Columbia
Office of Research Services and Administration
Clinical Research Ethics Board

Certificate of Approval

PRINCIPAL INVESTIGATOR	DEPARTMENT	NUMBER
Grunau, R.	Paediatrics	**C01-0017**

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT
Children's & Women's Health Ctr
CO-INVESTIGATORS:
Oberlander, Tim, Paediatrics; Schulzer, Michael, Medicine; Singh, Avash, Paediatrics; Solimano, Alfonso, Paediatrics; Weinberg, Joanne, Anatomy; Whitfield, Michael, Paediatrics
SPONSORING AGENCIES
National Institutes of Health (US)
TITLE
Pain in Preterm Infants: Development and Effects

APPROVAL DATE	TERM (YEARS)	DOCUMENTS INCLUDED IN THIS APPROVAL:
MAY 1 8 2001	1	28 March 2001, consent forms; 19 December 2000, questionnaires

CERTIFICATION:

The protocol and consent form for the above-named project have been reviewed by the Committee and the experimental procedures were found to be acceptable on ethical grounds for research involving human subjects.

Approval of the Clinical Research Ethics Board by one of:
Dr. B. McGillivray, Chair
Dr. A. Hannam, Associate Chair
Dr. R. D.Spratley, Director, Research Services

This Certificate of Approval is valid for the above term provided there is no change in the experimental procedures