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The Cardiac Correlates of Attention In the Denervated Heart: A Study of Infant Heart Transplant Recipients

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The Cardiac Correlates of Attention in the Denervated Heart: A Study of Infant Heart Transplant Recipients

by

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A Thesis submitted in partial satisfaction of
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Each person whose signature appears below certifies that this thesis in his/her opinion is adequate, in scope and quality, as a thesis for the degree Master of Arts.

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ABSTRACT OF THE THESIS

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Master of Arts, Graduate Program in Psychology
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The cardiac correlate of attention is a deceleration in heart rate, controlled by the parasympathetic division of the autonomic nervous system. This has been extensively studied in infants; the findings indicate that this deceleration is affected by a number of factors, several mediated by the vagus nerve. However, the effects of denervation on this response are not known. Studies with adult heart transplant recipients have shown attenuated acceleration in response to stressful mental tasks. This study investigated the cardiac response to attention in infants who had received a heart transplant, using a habituation paradigm. The hypothesis that they would show a significantly attenuated deceleration in comparison to infants who had experienced no medical complications was supported, with the habituation procedure used to verify that all of the infants had attended to the visual stimulus.

INTRODUCTION AND LITERATURE REVIEW

Attention has been an area of interest in psychology for at least a century; in 1890, William James defined attention as the "taking possession by the mind, in clear and vivid form of one out of what seem several simultaneously possible objects or trains of thought" (pp. 403-404). As early as 1901, researchers were investigating the cardiac response to different types of stimuli (Brahn, as cited in Graham & Clifton, 1966). With increasing information in the 1950's and 1960's, a distinction was made between two different autonomic influences on heart rate.

The autonomic nervous system contains two divisions that are functionally and anatomically distinct (Carlson, 1994). The sympathetic division originates in the thoracic and lumbar regions of the spinal cord, and it is associated with reactions to stress and other events that involve the expenditure of energy. These reactions include heart rate acceleration and increased rate of respiration, among others. The parasympathetic division originates in the nuclei of several of the cranial nerves and in the sacral region of the spinal cord, and it usually acts in opposition to the sympathetic system. These functions include heart rate deceleration and decreased rate of respiration, among others. Thus, when studying the relation between attention and heart rate, the effects of both of these two distinct divisions of the autonomic system must be considered. Some of the more recent research involving attention has focused on this area, particularly the changes in heart rate that accompany the orienting stage of attention.

A 1966 review of the literature by Graham and Clifton discussed several studies of attention and heart rate. Some disagreement as to the nature of the cardiac response is evident in this preliminary work. Several investigators found a diphasic response, consisting of a period of heart rate acceleration, followed by a period of deceleration (e.g. Davis, Buchwald, & Frankmann, 1955; Greer, 1964; Lang & Hnatiow, 1962; and Rudolph 1965, all as cited in Graham & Clifton, 1966), but others found only a deceleration (e.g. Kanfer, 1958; Wilson, 1964; and Zeaman, Deane, & Wenger, 1954, all as cited in Graham & Clifton, 1966).

Graham and Clifton (1966) noted that an acceleration in heart rate is almost universally associated with the defense reflex. The defense response functions to protect an organism from intense stimulation, and it is elicited by a strong stimulus that may be painful and dangerous (Stern & Sison, 1990). The physiological correlates of the defense response include acceleration of the heart rate, constriction of the peripheral and cerebral blood vessels, decreases in the sensitivity of sense organs, and physical movements such as turning away from the stimulus. The inclusion of the heart rate acceleration as an important component of the defense response led Graham and Clifton to question whether the accelerative portion of the diphasic response that was found by some attention studies might not be better described as a defense reflex. This explanation was further supported by the fact that several of the studies that found an acceleration phase in attention used auditory stimuli whose intensities ranged from 70 to 120 db. These would certainly be included in the range that

Sokolov (1963, as cited in Graham & Clifton, 1966) has classified as "'high' intensity" (p. 311); these are auditory stimuli over 70 db.

In contrast, the orienting response is elicited in the presence of novel stimuli, and it involves physiological changes that oppose those of the defense response (Stern & Sison, 1990). These changes include deceleration of the heart rate; constriction of the peripheral blood vessels, but dilation of the cerebral vessels; increases in the sensitivity of the sense organs; and physical movements such as moving the eyes toward the stimulus. Thus, Graham and Clifton (1966) propose that the cardiac component of the orienting response consists solely of heart rate deceleration, whereas heart rate acceleration is the cardiac response associated with the defense reflex. The orienting response can thus be attributed primarily to the parasympathetic nervous system, and the defense reflex can be attributed primarily to the sympathetic nervous system.

Graham and Clifton (1966) also noted that heart rate acceleration is found in the startle reflex as well. The startle response is elicited by the sudden onset of a stimulus (Stern & Sison, 1990). The physiological components include acceleration of the heart rate, constriction of the cerebral blood vessels, and dilation of the peripheral blood vessels. The distinction between the startle and defense reflexes may be due, at least in part, to the "suddenness" (Graham & Clifton, p. 313) of the stimulus onset. An intense stimulus with a slow "rise time" (p. 313) may fail to elicit startle but could elicit a defense reflex; alternatively, a mild stimulus with a rapid rise time could elicit a startle reflex but not a defense reflex.

As a final note, Graham and Clifton (1966) reviewed the relevant literature on heart rate change studied specifically in infants, citing several studies indicating that no heart rate deceleration had been found in human newborns. However, an experiment by Lipton and Steinschneider (1964, as cited in Graham & Clifton) indicated that although heart rate deceleration may be difficult to elicit in the newborn, it can be seen within the first few months of life. For example, Kagan and Lewis (1965, as cited in Graham & Clifton), found that 6-month-old infants presented with a variety of visual stimuli did show a heart rate deceleration.

In the years since this review, much research has been conducted on infants' cardiac responses associated with orienting and attending to a variety of stimuli. Lewis, Kagan, and Kalafat (1966) assessed the cardiac correlates of attention in 24-week-old infants. They presented three patterns of blinking lights to the infants, for a duration of 30 seconds each, with a rest period of the same duration. They found a slight acceleration during the first 10 seconds, a slight deceleration during the middle 10-second period, and a significant deceleration during the last 10 seconds. Their overall finding was that the most common cardiac reaction to relatively long periods of visual fixation is a deceleration. Thus, their study focused more on sustained attention than on the initial orienting response. Unfortunately, there were some methodological problems with their study. First, they determined the heart rate of each 10-second period by computing the mean of the five lowest heart beats during that period; this is not a precise, or necessarily accurate, procedure. Another problem was that they did not make a clear distinction between the time of presentation of the stimulus and the initial orienting response to that stimulus; the observed heart rate changes in the first 10-second period may not include a full 10 seconds of fixation.

These methodological problems have been addressed in other studies. One study compared infants' heart rate responses to presentation of auditory and visual stimuli, as well as the responses of orienting to the visual stimuli (Lewis and Spaulding 1967). The analysis was conducted on a beat-by-beat level, which is more precise than that used in the earlier study. In a comparison of responses to initial presentation of the stimuli, they found that the heart rate deceleration was not as immediate in visual presentation as it was in the auditory presentation. However, when they compared the responses to the visual presentation against the actual orientation to the visual stimuli, they found that the orientation curve showed a significantly lower trough, indicating that a greater deceleration of the heart rate had occurred. They also found that the latency to the deceleration is faster with orientation than with presentation, which emphasizes the importance of measuring when attention actually begins, rather than when the stimuli are presented. Thus, in comparing the responses to auditory presentation with those to orientation to visual stimuli, they found no significant differences. These findings demonstrate that the deceleration occurs at the point of orientation to the stimulus. The response is more immediate with auditory stimuli because there is no delay between presentation and orienting; the stimuli are available independently of where the infant is gazing at the time. The orienting response may be delayed with the presentation of visual stimuli because if the infant is gazing elsewhere when the stimulus is presented, there will be a delay before the infant perceives and orients toward the stimulus. The authors propose that this may indicate a

> two-phase process of attending . . . where the initial response to stimulus presentation may be an alerting or startle response with a cognitive element of "What's happening?" and a cardiac response of acceleration. . . . The second phase would be orientation and absorption of the stimulation resulting in cardiac deceleration (p. 236).

This is one potential explanation for the initial acceleration sometimes seen in infants, particularly newborns (e.g. Lipton, Steinschneider, & Richmond, 1966).

An alternative explanation, that some of the variation in the heart rate responses seen in infants may be the result of development and maturation, is supported by a series of experiments conducted by Graham et al. (1970). This report used data from five different age groups: newborn, 6 weeks, 12 weeks, 4 months, and adult. This study used an auditory stimulus of a 75 dB tone with a slow rise time, presented for 2 seconds. Heart rate was monitored from 1 second before the onset of the tone through 19 seconds after the onset. It was reported in the difference in heart rate at each one-second interval, measured in beats per minute. Newborn infants did not show any consistent response to the tone. Infants at 6 weeks of age showed a significant heart rate deceleration during only the second of the 10-second periods, but by the age of 12 weeks, the deceleratory response was significantly below the prestimulus heart rate during the first of the 10-second periods. The study conducted with these two age groups also found that sleepy infants' responses were primarily accelerative, whereas awake infants' responses were decelerative. Thus, state may play an important role in infants' responses to stimuli, particularly in early infancy; this is also supported by the findings of Lewis, Bartels, and Goldberg (1967). Because newborn infants have been reported to sleep at least 70 percent of the time (Parmelee, Wenner, & Schultz, 1964, as cited in Lewis, Bartels, & Goldberg), it is probable that their accelerative responses in earlier studies were primarily due to the fact that they were drowsy or asleep during at least some of the testing.

Some evidence for the importance of state was also seen in the portion of the study conducted with 4-month-old infants (Graham et al., 1970; these data were also reported later in K. M. Berg, W. K. Berg, & Graham, 1971). This study found that those infants who were alert showed a "marked and immediate" (p. 364) heart rate deceleration. This portion of the study also found that state of the infant, as well as the intensity and rise time of the stimulus, affected the heart rate response. The data collected with adults showed a deceleration in heart rate, but it was much smaller than that found in the 12- and 16-week-old infants. Graham et al. concluded with the suggestion that "the orienting system is, at best, not readily activated, or is a fragmentary system in the newborn, but that it develops rapidly over the first few months" (p. 364). A different study draws a similar conclusion, namely that "while the infant may be capable of producing an [orienting response] very early in life, it occurs only under the most optimal conditions; with development there is an increased range of conditions over which the infant can orient " (W. K. Berg 1974, pp. 311-312).

A more recent study has examined the developmental trends of heart rate in relation to attention in somewhat older infants (Richards, 1985). Using a cross-sectional design, this project studied the process by which sustained visual attention develops, by assessing infants between 14 and 26 weeks of age. Richards compared the heart rate responses to visual stimuli whose duration was either controlled by the infant's looking away, or interrupted by the experimenter's introducing a flashing light at the side of the monitor. He found that the 14-week-old infants showed "nearly identical patterns of heart rate responses" (p. 415) to the two types of trials. However, with both the 20- and 26-week-old infants, he found that the "initial heart rate decelerations during the interrupted stimulus trials were increasingly sustained. . . . Identifying these long latency responses as 'sustained attention' implies that there is an increase in sustained attention over this age period" (p. 415). Thus, as the infants grow older, they are better able to maintain a stage of sustained attention.

Another relevant finding in this study relates to the variability in the resting heart rate level (Richards, 1985). This experiment confirmed the findings of several other studies (e.g. Porges, Arnold, & Forbes, 1973; Porges, Stamps, & Walter, 1974; and Vranekovic, Hock, Isaac, & Cordero, 1974) that the "level of heart rate variability is correlated with the attentional responsivity of the infant" (p. 414). Thus, greater variability is associated with more consistent and greater heart rate decelerations during attention. These are both associated with respiratory sinus arrhythmia, which is the "variability in heart rate that occurs at the same frequency as breathing, with heart rate acceleration shortly after the beginning of inspiration, and heart rate deceleration shortly after the beginning of expiration" (Richards & Casey, 1991, pp. 43-44); it can be used as an "index of cardiac vagal tone" (Richards, 1985, p. 415). Thus, the vagus nerve appears to play a significant role in the heart rate deceleration associated with attention.

A later study further investigated the relationship between heart rate variability, respiratory sinus arrhythmia, and attention (Richards and Casey, 1991). The baseline level of respiratory sinus arrhythmia appears to index the magnitude of the heart rate deceleration during the period of sustained attention. It is also significant that the heart rate response could be used to define distinct phases of attention. The authors of this study speculate that the "large deceleration of heart rate during stimulus orienting, and the sustained lowering of heart rate during sustained attention, is consistent with the hypothesis that attention-linked heart rate responses are caused by large vagal outflow increasing the period of the heart rate" (p. 49).

Many of their findings also support a recent model by W. K. Berg and Richards (1997), which posits a series of stages in the process of attention; the first stage is the "transient-detecting reaction" (p. 348). Graham (1992) proposed that this process "permits rapid transmission of the information that a stimulus has been *detected*, but not necessarily identified or discriminated" (p. 7). W. K. Berg and Richards note that although the response has been considered preattentive, it "involves some basic information processing and might be considered as part of an *automatic interrupt system* that at least momentarily disengages the infant from the stimuli currently undergoing processing and prepares the infant for subsequent processing" (p. 349).

The second stage in this model is the orienting response, which is defined as the "shift of fixation (or shift of attention) to a new stimulus" (W. K. Berg and Richards, 1997, p. 349). Thus, the distinction drawn by Graham and Clifton (1966) between the orienting response and the defense reflex remains useful. Graham (1979) notes that the orienting response is associated with heart rate deceleration, whereas the defensive reaction is associated with acceleration.

The third stage of attention, according to this model, is "sustained attention" (W. K. Berg & Richards, 1997, p. 349). Richards and Casey (1992) describe this stage as the holding of attention, or the duration of the fixation. Richards and Casey (1991) found that sustained attention could be identified by a continued decelerated heart rate. They "speculate [that] . . . the sustained lowering of heart rate during sustained attention . . . is consistent with the hypothesis that attention-linked heart rate responses are caused by large vagal outflow increasing the period of the heartbeat" (p. 49).

The vagus nerve, as part of the parasympathetic system, is also postulated to contribute to the final stage of W. K. Berg's and Richards' model of the attention process, namely that of attention termination, which is defined as the "heart rate returning to its prestimulus level following sustained attention" (1997, p. 353). In discussing their experiment, Richards and Casey (1991) propose that the "heart rate activity during attention termination is consistent with vagal efferent flow diminished below prestimulus levels, allowing heart rate to increase above prestimulus levels" (p. 49). Thus, the parasympathetic system is associated with the changes in heart rate which typically accompany the orienting response, sustained attention, and the termination of sustained attention.

Another interesting finding from this study (Richards and Casey, 1991) is the existence of a refractory period. They monitored heart rate deceleration during stimulus presentation; when the heart rate returned to the prestimulus level, a second stimulus was presented with either a 0-, 3-, 6-, or 9-second delay. They found that for both the 0- and 3-second delay conditions, "the magnitude of heart rate deceleration was smaller than the heart rate orienting response to the first stimulus" (p. 336), whereas "the heart rate response to the second stimulus onset on the 6- and 9-second delay trials was not significantly different from the first stimulus onset response" (p. 337). Thus, there is a brief period, associated with attention termination, during which heart rate deceleration does not occur, or is significantly attenuated; Casey and Richards note that one reason this occurs could be a depression of vagal activity during attention termination. They propose that "vagal activity may take several seconds to return to prestimulus levels, and has a 'refractory period' during which the response to new stimulation is attenuated " (p. 49). The vagus nerve thus appears to play a critical role in the deceleration of the heart rate associated with the orienting response.

Although others agree that the vagus nerve plays a critical role in the changes in heart rate, as is evident in chemically blocking vagal innervation of the heart (Obrist, 1981; Porges, 1992), there has not been agreement about the precise role of this vagal innervation and its decelerative response associated with attention. Lacey and Lacey (1970) stated that the cardiac deceleration might play an initiating or feedback role in the psychophysiological attention response. However, Obrist, Webb, Sutterer, and Howard (1970) found that in a reaction time task with varying preparatory intervals, pharmacologically blocking the heart rate deceleration did not have a significant impact on the performance of the task. Therefore, they argued that the cardiac and other somatic effects of attention are manifestations of a “centrally initiated efferent process” (p. 703) and play no feedback role.

Evidence for the importance of innervation of the heart in changing the heart rate can also be seen in studies with people who have had heart transplants; one used a mentally stressful arithmetic task to assess the effects of cardiac denervation in heart transplant recipients (Shapiro, Sloan, Horn, Myers, and Gorman, 1993). The subjects in this study were assessed 7 to 15 days after surgery. An electrocardiographic recording was made while subjects subtracted by 7's from a four-digit number; the results showed that the "differences in [heart rate] were greater in the native atrial remnant than in the graft heart" (p. 277). Thus, the remaining portion of the original heart, which was still innervated, was more responsive, and responded more quickly, than the donor heart. This indicates that the innervation plays a critical role in controlling heart rate. Other studies have also reported significantly attenuated cardiac responsivity in adult recipients of heart transplants (e.g., Shapiro, Sloan, Bagiella, Bigger, & Gorman, 1996; Shapiro, Sloan, Bigger, Bagiella, & Gorman, 1994; and Sloan, Shapiro, and Gorman, 1990).

Although the accelerative heart rate response can be controlled either by the activation of the sympathetic nervous system or by the withdrawal of the parasympathetic nervous system, there is evidence that these changes, in heart transplant recipients, are solely through the former. A study designed to investigate the relationship between heart rate responsivity and the time interval since the transplant found that the duration of this interval did seem to influence the extent of heart rate acceleration, mediated by the sympathetic nervous system (Doering, Dracup, Moser, Czer, & Peter, 1996). Also, this study concluded that it would be unlikely to find reinnervation by the parasympathetic nervous system after a heart transplant.

No studies have been found that examined, in adult, child, or infant recipients of heart transplants, the decelerative heart rate response, either in the context of being controlled by activation of the vagus nerve and the parasympathetic nervous system, or of being controlled by withdrawal of the sympathetic nervous system. Most of the literature supports the former, but if the vagus nerve cannot be reattached in heart transplant recipients, leading to a denervated heart, what implications does this have for the deceleration of the heart rate usually associated with orienting and sustained attention? Two studies have found that adult heart transplant recipients showed mild impairment in "sustained concentration" (Hecker, Norvell, & Hills, 1989; and Bornstein, 1989, both as cited in Nussbaum & Goldstein, 1992, p. 478), but neither one monitored heart rate. Little is known about whether a deceleration occurs, under any conditions, in heart transplant recipients of any age.

Hypothesis

This project investigates whether there is a deceleration during attention in infants who have received heart transplants. The a priori hypothesis was that if any heart rate deceleration occurs in this population, it would be significantly attenuated in comparison to infants who experienced no complications before, during, or after birth. The most important difference between these two groups is that those infants who received a heart transplant do not have an attachment between their own vagus nerves and the donor hearts; that is, there is denervation of the heart in these of infants. The amount of change in heart rate that occurs during orienting and attention was compared between these two groups of infants.

One of the primary means of determining that an infant is orienting and attending to a stimulus has traditionally been the measurement of a deceleration in heart rate. However, because our hypothesis is that orienting and attention will produce little or no change in heart rate in the recipients of heart transplants, a different criterion for orienting and attention is necessary. In this project, a modification of an infant-controlled habituation paradigm was used as a measure of attention; in order for the infant to habituate to the stimulus, s/he must have attended to it. A visual stimulus was used in this paradigm to facilitate behavioral observations, such as visual fixation toward and away from the stimulus. Use of a visual stimulus, rather than an auditory one, was also important because the possibility that a stimulus of high intensity may elicit an accelerative response, associated with the defense or the startle reflex, has been seen more frequently in auditory stimuli.

Method

Participants

The experimental group, of 11 infant heart transplant recipients (HTR), was referred through the pediatricians of the Infant Heart Transplant Team at the Loma Linda University International Heart Institute. There were five males and six females in this group. Five of the infants had a primary cardiac diagnosis of Classic Hypoplastic Left Heart Syndrome, four of the infants had a primary cardiac diagnosis of Dilated Cardiomyopathy, and two of the infants had a primary cardiac diagnosis of Critical Aortic Stenosis. The mean age at transplant was 1 month, 24 days, and ranged from 9 days to 4 months, 10 days. For the ten infants for whom the discharge date was available, the mean time spent in the hospital after the transplant was 23 days, and ranged from 13 days to 54 days. Seven of the ten infants were released in 2-3 weeks, the other three were released after 27, 40, and 54 days. The mean time interval between the transplant and participation in the habituation portion of the study was 3 months, 29 days, and ranged from 1 month, 23 days, to 7 months, 10 days. The mean time interval between discharge from the hospital after transplant and participation in the habituation portion of the study was 3 months, 8 days, and ranged from 1 month, 10 days, to 6 months, 14 days.

The comparison group, of 10 infants who had no medical complications of any type during the prenatal period or after birth (NMC), was referred by the

Loma Linda University Faculty Medical Offices. There were two males and eight females in this group.

All infants were tested between 4 and 8 months of age. Most developmental changes in the heart rate response have already occurred at this age, so maturational factors should not have been a significant source of variance. Parent education level was considered for a possible matching variable. However, a review of the literature offered little support for a relationship between parent education level and cognitive development in infants at this age (Jacobson & Jacobson, 1992 [as cited in Jacobson & Jacobson, 1996]; Richter & Grieve, 1991). Although parent education level has been shown to be related to the child's later cognitive development, these effects are not evident until approximately two years of age (Rose & Wallace, 1985). Thus, although parent education level was measured, it was used not as a matching variable, but as an independent variable in the exploratory analyses.

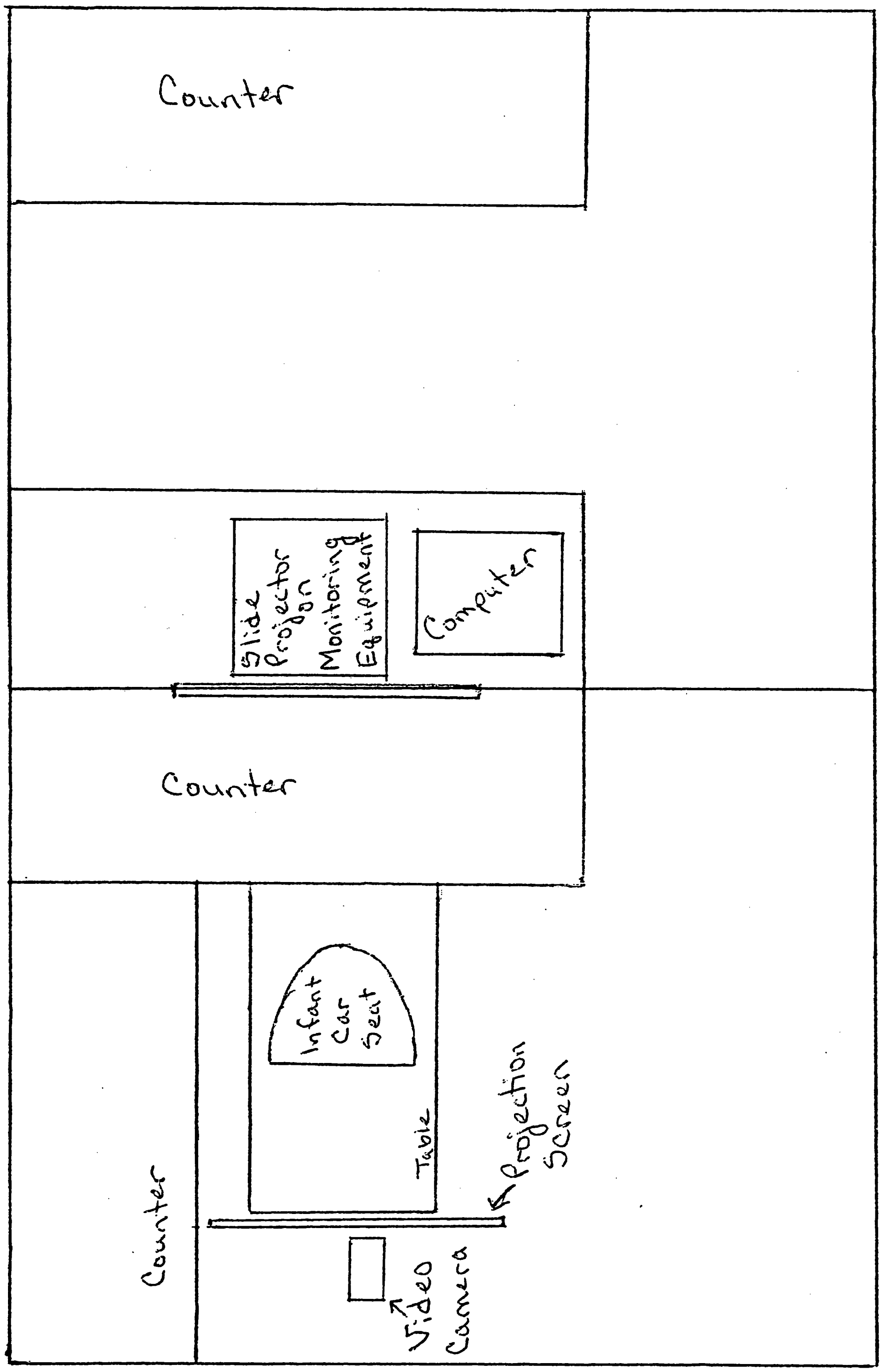
Materials

The habituation procedure used was a modification of one described by L. C. Mayes (e.g. Mayes & Kessen, 1989). A 37" square projection screen subtended a visual angle of 30 degrees. A reclined car seat, strapped to a 24" by 60" table, secured the infant, who faced the screen. Shoulder and lap straps were used to secure the infant, with the leads for the physiological monitoring equipment placed behind the infant. Directly beneath the bottom edge of the screen, a video camera was mounted on a tripod. This was focused on the infant's face and allowed for monitoring and recording of eye movements as well as the current state of the infant. The infant was observed on a television in an adjoining room, which allowed continuous observation of the infant's orienting toward or looking away from the screen. The infant faced away from a window to the adjoining room, through which a projector was used to project the appropriate slides over the car seat and onto the projection screen. Also in this other room was a computer to record heart rate and respiration, as well as the onset and termination of the stimulus presentations and the infant's orientation toward or away from the stimulus. (Please see Figure 1.)

A demographic questionnaire was used to obtain information about the infant's caregivers, such as their ages and education levels, as well the infant's general medical history (see Appendix A). The medical history was used to ensure that the comparison group of healthy infants met the criteria for inclusion.

The second edition of the Bayley Scales of Infant Development (Bayley – II; Bayley, 1993) was used to assess the cognitive and motor development of each infant. This scale is widely used for the developmental assessment of both non-clinical and clinical populations of infants and toddlers. It has demonstrated adequate test-retest reliability, as well as concurrent validity with other nationally standardized measures. It provides several scales. The Mental Developmental Index (MDI) assesses the development of cognitive skills, and the Psychomotor Developmental Index (PDI) assesses the development of physical and motor skills. Additionally, the Behavior Rating Scale (BRS) assesses several areas of behavior and personality development. For infants 5 months of age or younger, there is an Attention/Arousal (A/A) factor. For infants 6 months of age or older,

Figure 1. Scaled representation (top view) of the rooms and equipment used during the habituation procedure.


Counter
Slide Projector on Monitoring Equipment
Computer
Counter
Infant Car Seat
Table
Projection Screen
Counter
Video Camera

there are an Orientation/Engagement (O/E) factor and an Emotional Regulation Factor. For all infants, there are a Motor Quality (MQ) factor and a Total Score (TS) as well.

Procedure

Parents of HTR infants were contacted by telephone to schedule the developmental assessment, which is routinely done with all infants who receive heart transplants at Loma Linda University. While the parents were on the phone, they were told about the additional study of attention and asked to participate; none refused. Parents of NMC infants were recruited by a pediatrician in the Loma Linda University Faculty Medical Offices. (See Appendix B for the recruiting notice.) If the parents indicated that they would be willing to participate in the study, they were contacted by telephone to offer more information and to schedule an appointment.

When the infants arrived, the procedure was explained to their caregivers, who provided informed consent for the procedure as well as for the videotaping (see Appendices C and D). The three electrodes were attached to the infant's chest (one over each collarbone and one over the lowest left rib) and the pneumatic chest cuff was placed around the infant's upper torso. The infant was secured in the car seat and the lights were dimmed. The caregiver remained in the room with the infant until the habituation procedure began in order to maintain the infant in a calm state. The caregiver then moved to the adjacent room to monitor the infant from the video monitor. The infant remained alone in the testing room to minimize distractions. If the infant showed signs of fussiness, soothing was sometimes done, such as verbally reassuring the infant, or taking a break from the experiment so that the caretaker could hold and calm the infant; this was done for the sake of the infant and because it was important for the infant to be in an awake, alert state during testing for optimal results. At times, however, no soothing procedures could be used or they were not effective; in these cases, the experiment continued if the infant continued to look at the slides. Unfortunately, no pacifier could be used during the study because sucking causes an acceleration in heart rate (Nelson, Clifton, Dowd, and Field, 1978, as cited in Von Bargen, 1983), and this would add unnecessary error variance. Because fussing and crying also cause heart rate acceleration, the videotape of the infant was used to assess fussiness; data were only used from trials where the infant was alert or fussing mildly.

The three slides were shown in a specified order, for a total of seven presentations. The first slide and last slide were the same colorful geometric pattern; this allowed the infant's looks at the beginning and end of the habituation to be compared and to "assess whether or not looking time at the end of the trial [was] comparable to that at the beginning" (Yale Child Study Center, n.d., p. 7). The slide of an "affectively neutral woman's face" (Yale Child Study Center, n.d,) was shown in the second, fourth, and sixth positions. The third slide, a different geometric pattern, appeared in the third and fifth positions. The criterion for habituation to a particular presentation of a slide was set at two gazes in a row that were both shorter in duration than 50% of the mean of the duration of the first two gazes to the habituation stimulus. Thus, there were at least four looks to each slide. When this criterion for habituation had been satisfied, the next slide was presented.

In the procedure described by Mayes, the habituation stimulus was constantly present on the screen throughout the habituation phase; the duration of the infant's looks toward and away from the stimulus were monitored. Because there is a refractory period at attention termination during which the heart rate does not decelerate (Richards & Casey, 1991), this aspect of Mayes' procedure was modified. In the present experiment, the slide projector was blocked for 10 seconds each time the infant looked away. At the end of the 10-second period, the projector again displayed the stimulus on the screen; however, the infant may or may not have re-oriented quickly toward the stimulus. Because the presentation of a visual stimulus may not coincide with orientation toward it, as Lewis and Spaulding (1967) noted, each infant was carefully observed on the monitor to ensure accurate measures of the duration of looks toward or away from the stimulus. Although this modification may have lead to somewhat different results than those obtained by Mayes, habituation still occurred to the individual slides. However, the ten-second delay may have increased the fussiness of the infants (Colombo & Horowitz, 1985). Overall, the use of this procedure facilitated measurements of heart rate changes in response to orienting and attention, and it also provided evidence that any attenuation in the decelerative heart rate response in transplant recipients was not due to a failure to attend to the stimulus. There is preliminary evidence that behavioral indices, such as visual fixation on a target stimulus, are not always reliable indicators of sustained attention (Richards, 1995, as cited in W. K. Berg and Richards, 1997), and it is not known how this may relate to the orienting response. Both of these considerations indicated that it would be necessary to provide evidence that the infant had attended to the stimulus presented in this study, and the habituation paradigm did so.

The habituation data gathered included the number of looks to reach criterion for each slide, the duration of each look, the total duration of looking, and the overall pattern of habituation. The physiologic data gathered during the habituation procedure included heart rate, measured in beats per minute, during each 0.5 second interval, obtained through the electrodes and the electrocardiogram (EKG); as well as respiration rate and quantity, obtained with the pneumatic chest cuff.

An attenuated heart rate deceleration during attention among heart transplant recipients may indicate that the vagus nerve is not attached, which in turn may be associated with a less efficient ability to attend. In turn, this could lead to delayed cognitive development, because information is gained and processed primarily during periods of sustained attention.

In order to assess development, after the habituation paradigm, the Bayley – II was used to estimate each infant's progress in reaching age-appropriate cognitive and motor developmental milestones. This assessment is already routine for the HTR infants, and it was used as an incentive for the NMC infants. Also, if significant differences had been found between the groups on any of the relevant scales, there would have been less confidence in the results of the study. If any delays or other developmental concerns were noted during the assessment, the parent was referred for appropriate early intervention services.

Results

At the time of habituation, the average age of the HTR infants was 5.8 months, and of the NMC infants, 6.7 months (see Table 1). This difference was not statistically significant. One infant in the HTR group was born 5 weeks premature; no infants were born prematurely in the NMC group. However, Bonin, Pomerleau, and Malcuit (1998) found that, using corrected age, "healthy preterm infants perform[ed] as well as full-term infants on specific measures . . . such as length of fixation and response decrement to a repeated stimulus in habituation" (p. 115).

Table 1: Age, Bayley Scores, and Demographic Data

	HTR			NMC						
Variable	n	M	SD	n	M	SD	t	χ^2	df	p
Habituation Age	11	5.81	1.34	9	6.73	1.11	-1.67		17.99	.112
Bayley Age	11	5.65	1.09	9	6.70	1.12	-2.12		17.02	.049 *
MDI score	11	93.81	6.97	9	96.78	5.36	-1.07		17.95	.297
PDI score	11	83.82	12.47	9	97.11	10.74	-2.56		17.93	.020 *
A/A percentile	5	65.00	13.27	1	78.00		- .90		4	.422
ER percentile	6	58.67	31.82	7	38.86	29.70	1.15		10.42	.274
O/E percentile	6	69.67	21.89	7	48.57	30.50	1.45		10.73	.177
MQ percentile	10	12.90	11.07	8	37.38	20.08	- .31		10.34	.011 *
TRS percentile	10	43.80	32.87	8	40.12	28.45	.25		15.86	.803
Father's Age	11	32.64	7.92	8	30.50	4.10	.76		15.70	.456
Mother's Age	11	28.27	5.61	8	28.88	4.70	-2.54		16.56	.803
Father's Ed. Level	10			8				6.27	5	.280
Mother's Ed. Level	11			8				3.82	3	.281
Primary Caregiver	10			8				1.32	1	.250

* $p < .05$

The HTR and NMC groups differed in their performance on the Bayley Psychomotor Development Index scores and in their Motor Quality percentiles (see Table 1). Also, although there was a significant difference in the average age at the time of the Bayley administration, with the NMC infants older than the

HTR infants. There were no significant differences between the groups on the other Bayley scales, including the Mental Developmental Index and the other behavioral factors. There were also no significant differences between the groups on the demographic variables, including parents' ages and education levels.

The a priori hypothesis of a significant attenuation of the decelerative heart rate response during orienting in the HTR infants was tested with several repeated measures analysis of variance (ANOVA). The ANOVAs were run for the first two looks (during habituation, the looks are often progressively shorter) to the first two slides (fussiness increased as time passed). The quasi-independent variables of interest in this analysis were group, either HTR or NMC, and the time interval during the look, segregated into 0.5-second intervals, from 2 seconds before to 10 seconds after orientation toward the stimulus. Casey and Richards (1991) report that the deceleration process usually lasts about 5 to 6 seconds; therefore, this 12-second interval included the deceleration period of interest.

The dependent variable of interest was the change in heart rate, in beats per minute, for each .5-second interval. This was calculated from the data recorded with the EKG during the habituation procedure. The repeated measures, mixed between-within ANOVA used to investigate the a priori hypothesis was a 2 (group) X 24 (each 0.5-second interval) design, with change in heart rate as the dependent variable.

The EKG data recorded were not usable for every subject. From the HTR group, one participant was excluded because her EKG showed premature ventricular contractions. Excessive artifact rendered the EKG data unusable for two more, and for a third, EKG data from two trials were unusable for this reason. From the NMC group, the EKG data from two participants were not recorded, due to computer error. The EKG data from two more were unusable due to excessive artifact. For one additional participant, no state assessment could be made due to the lack of a video recording; no data were used because no ratings of her fussiness during each look could be made. Finally, data were not used for the first look of one subject; the heart rate showed an acceleration of 14 beats per minute, indicating that the initial presentation of the slide elicited a startle response, rather than an orienting of attention. Depending on how fussy the infants were at various times during the habituation, data were usable for different numbers of them on the various different looks.

The EKG data from the majority of the other participants showed some error due to artifact; this was corrected by averaging from the data points on either side of the affected intervals. In cases where the artifact occurred at the beginning or the end of the gaze, it was averaged based on the two closest available data points. The heart rates for each .5-second interval were then converted to difference scores. The heart rate for the interval immediately before the onset of the look was determined to be the zero point; this was subtracted from the heart rate for each of the other intervals of that look. This was done to reduce error variance added by the differences in the initial heart rates and to standardize the heart rate change to facilitate the statistical analyses.

Assumptions for the ANOVA were violated, reducing the likelihood of finding statistical significance. The assumption of normality was not met; this was due, at least in part, to the small size of the groups. Also, the assumption of homogeneity of variance was not met. This was to be expected, based on the hypothesis of the study – very little variability was expected in the heart rates of the HTR infants, whereas more variability was expected in the heart rates of the NMC infants. Because of these violations of the assumptions, it was more difficult to achieve statistical significance.

For each look analyzed, the linear trends, or one change in direction, were examined, as well as any interactions, or differences between the groups. This reflected a deceleration. Also, because the heart rates were expected to return to baseline after the termination of the look, quadratic trends, or two changes in direction, were also studied, again looking also for interactions. Finally, the overall repeated measures ANOVA was assessed, again looking for differences between the two groups. For these analyses, Greenhouse Geisser was used for the probability values, due to the assumption of sphericity having been violated in each of these.

The graphic representation of the data shows that the two groups differed in their cardiac response to the orienting of attention (see Figure 2). This appears to be most pronounced during the first look to the second slide, which was the first presentation of the face. The face was the most complex of the three visual

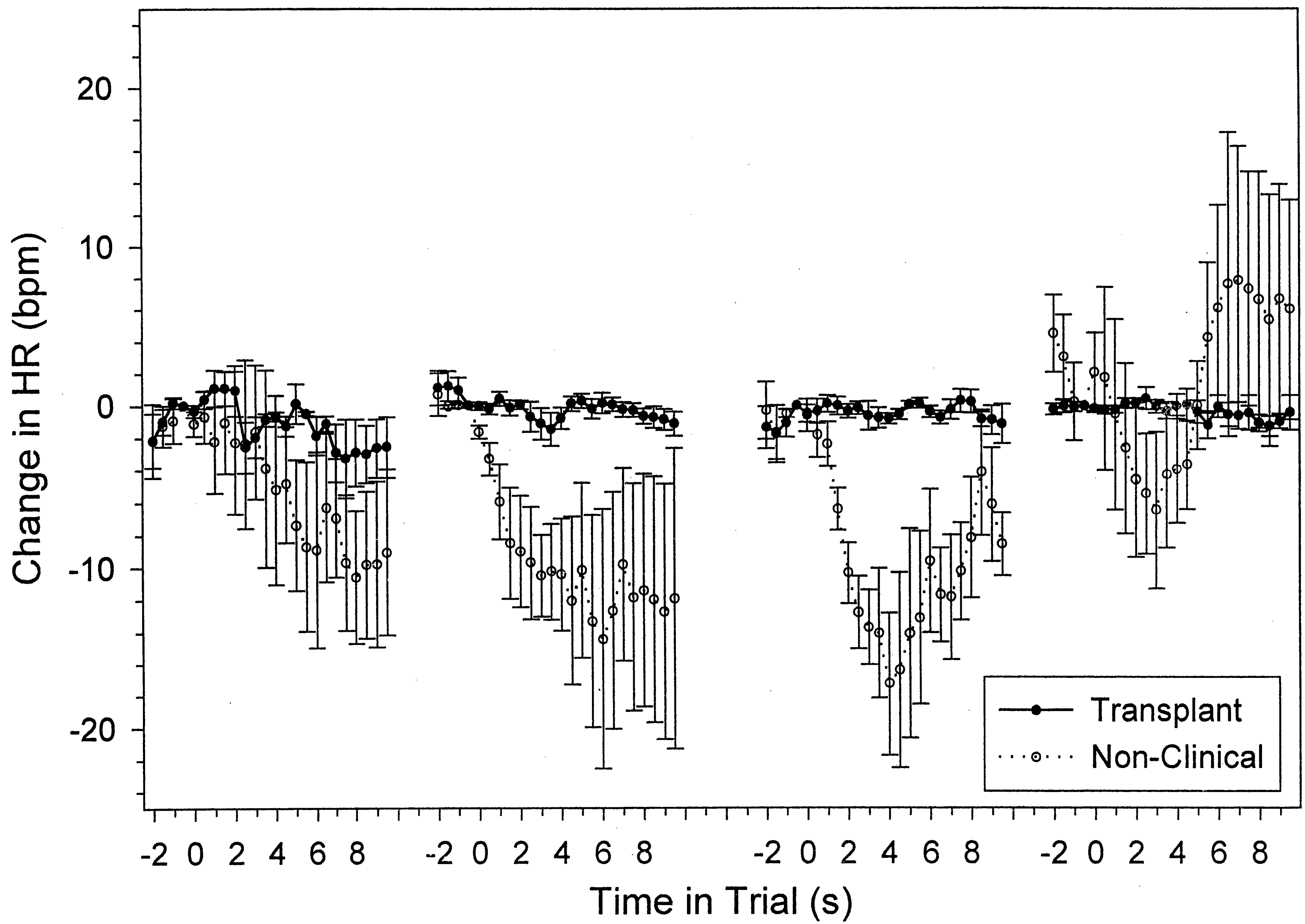


Figure 2: Graphic representation of change in heart rate during the first two looks to the first two slides.

stimuli; it was expected that this first look to it would be the one most likely to elicit a deceleration. During the first look to the slide one, the average heart rate change for the HTR infants (n = 7) remained close to zero, although it showed some variation,

whereas the average heart rate change for the NMC infants (n = 4) showed a deceleration of 8-10 beats per minute during the 6-10 seconds after the gaze onset. The graph of the heart rates of the two groups during the 12 seconds reflects this (see Figure 2). As Table 2 shows, for this first look, only the linear trend was statistically significant, and there was not a significant interaction between the groups for this look.

Table 2: Slide 1, Look 1

Comparison	F	MSE	p	η^2
Linear	11.38 (1, 9)	92.92	.008 *	.912
Linear x Group	3.91 (1, 9)	92.92	.079	.744
Quadratic	.30 (1, 9)	174.68	.598	
Quadratic x Group	0.00 (1, 9)	174.68	.975	
Overall	3.21 (23, 207)	17.29	.050 (Greenhouse Geisser)	.688
Overall x Group	1.27	17.29	.304 (Greenhouse Geisser)	.215

* $p < .05$

For the second look to slide one, the HTR infants (n = 8) again showed very little change in heart rate, and with somewhat less variability than the first look (see Figure 2). The NMC infants (n = 3) demonstrated an average deceleration of 8-14 beats per minute during the 3-10 seconds after the gaze onset. As Table 3 shows, all of the analyses were statistically significant, with the exception of an interaction between groups for the linear trend. Also, each of these accounts for at least 75 per cent of the variance for that analysis. The quadratic trend and its interaction account for 95 per cent and 93 per cent of the variance, respectively, which reflects the deceleration and a the beginning of the return to the baseline heart rate.

Table 3: Slide 1, Look 2

Comparison	F	MSE	p	η^2
Linear	6.82 (1, 9)	161.04	.028 *	.853
Linear x Group	4.62 (1, 9)	161.04	.060	.783
Quadratic	21.65 (1, 9)	11.26	.001 *	.954
Quadratic x Group	15.26 (1, 9)	11.26	.004 *	.934
Overall	5.55 (23, 207)	11.24	.013 * (Greenhouse Geisser)	.820
Overall x Group	3.94 (23, 207)	11.24	.037 * (Greenhouse Geisser)	.746

* $p < .05$

The first look to slide two again showed very little change in the heart rate for the HTR infants (n = 6) (see Figure 2). There was an average deceleration of 10-17 beats per minute during the 3-8 seconds after the gaze onset for the NMC infants (n = 4). For this look, statistical significance was seen in each of the ANOVAs, with each one accounting for at least 83 per cent of the variance for that analysis (see Table 4). Again, the quadratic trends accounted for more variance than the other analyses.

Table 4: Slide 2, Look 1

Comparison	F	MSE	p	η^2
Linear	5.75 (1, 8)	72.94	.043 *	.826
Linear x Group	6.75 (1, 8)	72.94	.032 *	.852
Quadratic	17.66 (1, 8)	40.25	.003 *	.943
Quadratic x Group	23.61 (1, 8)	40.25	.001 *	.958
Overall	7.27 (23, 184)	9.98	.005 * (Greenhouse Geisser)	.862
Overall x Group	7.96 (23, 184)	9.98	.003 * (Greenhouse Geisser)	.874

* $p < .05$

For the second look to slide two, there was very little change in the heart rate for the HTR infants ($\underline{n}$ = 8) (see Figure 2). The NMC infants ($\underline{n}$ = 3) showed an initial average deceleration of 6 beats per minute, followed by an acceleration to nearly 8 beats per minute above the baseline. This acceleration reflects the heart rate of one of the three infants, whose heart rate accelerated to 20 beats per minute higher than baseline. Although the infant was only mildly fussy during this gaze, the infant grew more fussy before the next gaze, indicating that this acceleration is probably due to a change in state after the termination of the look. Neither of the linear trend analyses showed statistical significance, but the other four analyses did (see Table 5). Each of these four accounted for at least 78 per cent of the variance for its analysis. Again, the quadratic trends accounted for more of the variance than the other analyses; for this look, there reflect not only the deceleration and return to baseline, but also the acceleration.

Table 5: Slide 2, Look 2

Comparison	$\underline{F}$	**MSE**	$\underline{p}$	$\underline{\eta}^2$
Linear	1.97 (1, 9)	105.69	.194	.492
Linear x Group	3.20 (1, 9)	105.69	.107	.688
Quadratic	34.25 (1, 9)	10.33	.000 *	.971
Quadratic x Group	41.64 (1, 9)	10.33	.000 *	.976
Overall	4.53 (23, 207)	9.51	.032 * (Greenhouse Geisser)	.779
Overall x Group	5.80 (23, 207)	9.51	.016 * (Greenhouse Geisser)	.828

* $\underline{p} < .05$

Two variables from the habituation data were also analyzed (see Table 6). The numbers of looks to reach habituation on each slide were analyzed with a repeated measures ANOVA; there was no significant difference between the groups. For the duration of the looks, only the first two looks to the first three slides were used. These were first divided into four categories – shorter than 1.5 seconds, 1.5 to 6.0 seconds, 6.0 to 10.0 seconds, and longer than 10 seconds. Chi-Square analyses found no significant differences between the two groups in their categorized frequencies of look durations in any of these six looks.

Table 6: Habituation Comparisons

Comparison	**F**	**MSE**	χ^2 **(n=19)**	**df**	**p**
Slide (# Looks)	.79	7.63		2, 32	.420 (Greenhouse-Geisser)
Slide x Group	.19	7.63		2, 32	.737 (Greenhouse-Geisser)
Slide 1 Look 1 Duration			1.71	2	.425
Slide 1 Look 2 Duration			.35	3	.950
Slide 2 Look 1 Duration			1.82	3	.611
Slide 2 Look 2 Duration			2.00	3	.572
Slide 3 Look 1 Duration			4.96	2	.084
Slide 3 Look 2 Duration			2.11	2	.348

Finally, a comparison of the fussiness of the infants in the two groups was made. Chi square analyses were performed for the fussiness ratings of the two groups of infants for their first two looks to each of the first three slides. No significant differences were seen between the two groups on the ratings of their fussiness for any of these six looks.

Discussion

The hypothesis of this investigation was supported in that a significant attenuation in the decelerative response associated with orientation was seen in the infants who had received heart transplants. Although this attenuation was apparent in all four of the looks shown in Figure 2, the difference between the groups was not always statistically significant. This was particularly true for the first look to slide one; this may be partially due to its being the first visual stimulus presented. One participant demonstrated a startle response; although this infant's EKG data were not used in the analysis, this shows that the first presentation of a stimulus may not have elicited an orienting of attention in all of the participants, both HTR and NMC. A second factor that may have contributed to the error variance is the procedure for timing the first look. For the subsequent looks, the slide appeared on the screen, and the duration of the look began when the infant looked at it. For the first look, however, the infant looked at the screen first, and then the slide was presented. Because of the delay of the computer processing, a few of the infants looked away from the screen before the image appeared, and they may not have looked back at the screen immediately. Finally, it can be seen that the EKG data for the HTR infants shows more variability during this look. Because it did not appear to occur systematically, (i.e. there were both small accelerations and small decelerations), this was most likely due to random or error variance. This variability may also have contributed to the lack of statistical significance.

Although the hypothesis of the study was supported, other explanations for the attenuation in the heart rate deceleration seen in the infant heart transplant recipients must be explored. One possible explanation is the age of the participants. The HTR infants were almost one month younger than the NMC infants at the time of habituation. This difference was not statistically significant; however, because of the small sample size, this may have had some practical significance. In other words, there may have been a difference large enough to affect the results, but with the small sample size, the statistical test of probability failed to detect this because of insufficient power. While possible, this seems very unlikely, because the variability in the heart rate response to orientation is fairly stable by 12 weeks of age (Graham et al., 1970), and all of the participants in this study were older – at least 16 weeks of age. The two groups did not differ on their parent's ages or education levels, nor did they differ on their primary caregiver – most often the mother. There were two differences between the groups on the Bayley-II scales. The HTR infants scored lower than the NMC infants on both the Psychomotor Development Index and on the Motor Quality factor. This is likely to reflect delayed motor skills in the HTR group, not uncommon in infants who have spent extended periods of time in the hospital. However, this delay seems unlikely to have affected the heart rate deceleration, particularly when other factors more theoretically related to attention showed no significant differences between the groups.

The most feasible alternative explanation is that the attenuation of the deceleration occurred because, for some reason, the HTR infants were less able to orient to visual stimuli. This could be a reasonable explanation, in that these infants may have learned to ignore stimuli after being over-stimulated during their stay in the busy Neonatal Intensive Care Unit, when much of their environment held little relevance for them. However, the use of a habituation paradigm has provided the necessary evidence that these infants were, indeed, attending to the visual stimuli; the infants would not have habituated to the stimulus unless they had oriented and attended to it (Mayes & Kessen, 1989). The similar performance between the two groups on both the number and duration of looks supports that both groups attended to the stimuli in a similar manner.

It is possible that the modification in the infant-controlled habituation paradigm, the 10 seconds between each stimulus presentation, may have affected the results. The most likely effect of this change was that the infants may have shown increased fussiness, compared to the traditional infant-controlled paradigm (Colombo & Horowitz, 1985). Indeed, fussiness was problematic in this study, limiting the usable data from subjects in both groups. However, this change in the paradigm seems unlikely to have contributed to a difference between the two groups, in that both groups experienced the same paradigm.

Because the infants who had received heart transplants were indeed able to orient and attend to the visual stimuli without a functional vagal connection, this connection must not be necessary for orienting and attention to occur. It may facilitate attention, but it is not required. This supports the argument by Obrist et al. (1970) that the cardiac deceleration is a "peripheral manifestation of central processes" (p. 695) and does not provide additional feedback necessary to these internal processes.

The results of this study suggest several areas in need of further exploration. One question to be addressed is whether the role of the heart rate deceleration associated with orienting and attention is more important in sustaining attention, particularly in the presence of distractions. Perhaps the deceleration is more important for sustaining attention than it is for orienting, or perhaps the deceleration facilitates the maintenance of attention on one stimulus, helping to block out other distractions. If this is found to be the case, it would offer support for the idea proposed by Lacey and Lacey (1970) that the cardiac deceleration associated with attention may precede central nervous system activity, acting as a signal or feedback mechanism.

Finally, further investigation in this area should address the implications of attenuated heart rate deceleration in relation to both attention and learning. This study demonstrated that infants who have received heart transplants are capable of orienting to visual stimuli and sustaining that attention. However, the shifting of attention and the termination of attention were not addressed in this project. Additional study in this area may indicate that shifting and terminating attention are more difficult when the heart rate deceleration is attenuated. Regarding learning, this is best done when one is attending to the stimuli to be learned. This study has shown that the infants who received heart transplants were able to attend to the stimulus in a manner similar to those with no medical complications. However, the setting in this study was designed to minimize distractions; it is possible that in an environment with more distractions, or with more complex stimuli, it may be difficult for these infants to orient or to maintain sustained attention. If so, any intervention to remediate these potential problems would be very relevant for them. Also, this study looked at attenuation in a response that is under the control of the parasympathetic system; future research should examine any attenuation in responses under the control of the sympathetic system, such as the startle reflex or the defense reflex.

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Appendix A

Demographic Questionnaire

1. What is the current age of the baby's father? ____________

2. What is the current age of the baby's mother? ____________

3. Who is the primary caregiver? (please circle one)

   Mother Father Grandparent Other relative Foster parent

   Other (please specify _______________)

4. What is the highest year of education completed by the baby's mother?

   (please circle one)

   8th grade or below GED High school diploma Some college

   College diploma More than college

5. What is the highest year of education completed by the baby's father?

   (please circle one)

   8th grade or below GED High school diploma Some college

   College diploma More than college

6. What was your baby's gestational age? _______________

7. Does your baby have any medical conditions? Yes No

   If yes, please explain ______________________________________

8. If your baby is currently taking medication(s), please list it/them. ____________

   ____

   ____

Appendix B

Loma Linda University

Departments of Psychology and Pediatrics

Invite healthy infants

4-8 months of age

to participate in a study of

attention and development.

If you are interested in having your baby

participate in this 45-60 minute study,

please call Dr. Kiti Freier, pediatric psychologist,

at (909) 824-0800, ext. 82388.

Appendix C

Loma Linda University

Graduate School
Department of Psychology

11130 Anderson Street
Loma Linda, California 92350
(909) 558-8577
FAX: (909) 558-0171

INFORMED CONSENT

Cardiac Correlates of Attention in the Denervated Heart:

A Study of Infant Heart Transplant Recipients

Dear Parent / Guardian:

Your infant is invited to participate in a research study because s/he is in one of two groups: (1) infants who have received a heart transplant or undergone reparative heart surgery, or (2) infants who are healthy with no medical complications before, during, or after birth.

Purpose and Procedures

The purpose of this research is to study the relationship between the central nervous system and heart rate, following heart transplant. By comparing the breathing and heart rate of babies who have had heart transplants with those who have not, this research will study how the body learns to adapt to receiving a heart transplant.

Participation in this study involves several steps for your infant during one visit to this laboratory. The total study will take approximately 45-50 minutes to complete. First, three button-like sensors will be attached to your infant's chest, in order to measure heart rate. Second, a band will be put around your infant's chest, secured with Velcro. This band contains a sensor that will be used in order to measure your infant's breathing.

After these sensors have been placed, your infant will be seated in a car seat and secured gently, in order to ensure the safety of your infant. S/he will be alone in a semi-darkened room for about 10 minutes. Throughout this time, you will be able to watch your infant on a video monitor in an adjoining room. During this time, your infant will be shown a series of geometric designs and faces, which will be projected from slides onto a screen. This portion of the study will take approximately 15 minutes to complete, and then the sensors will be removed.

You will be asked to complete a brief questionnaire, which consists of several questions about your infant's caregiver(s) and a few questions about your infant's health. This will take approximately 5 minutes to complete.

During the final developmental assessment portion, you will be able to hold your infant on your lap and watch him/her play on a mat. This portion will take approximately 30 minutes to complete.

Risks

Your infant may become mildly upset during the application of the sensors or during the brief separation for viewing the slides. You will be able to offer comfort to your infant, but no pacifier will be used during the slide presentation. If your infant is not easily soothed, this stage of the research study will be discontinued. Three options are available in this case: (1) you may choose to move on to the developmental assessment portion at this time, (2) you may reschedule both portions of the assessment for a later time, or (3) you may discontinue your participation in this study. The committee at Loma Linda University that reviews human studies (Institutional Review Board) has determined that the risk resulting from such physical or emotional stress is minimal.

Benefits

If you desire, information about how your infant's development compares with national standards will be made available to you. Otherwise, you and your child will not benefit personally. However, the results of this study will be shared with healthcare providers who work with infants who have received heart transplants in order to help them to have a better understanding of the central nervous system's function, following a heart transplant.

Participants' Rights

Participation in this study is voluntary. Your decision whether or not to participate or terminate at any time will not affect your infant's present or future medical care.

Confidentiality

All results are strictly confidential. All data is kept in a locked filing cabinet and can be accessed only by authorized research personnel. In addition, if your infant has received a heart transplant, the developmental assessment is part of a routine follow-up procedure. In this case, you will be asked to sign a form that will allow the results of your infant's developmental progress to be included in his/her medical chart, so that the physicians can use this information.

Parent / Guardian Initials _______ Date _______

Costs/ Reimbursement

There is no cost to you for your infant's participation in this study. There will be no monetary reimbursement for your infant's participation in this research study.

Impartial Third Party Contact

If you wish to contact an impartial third party not associated with this study regarding any complaint you may have about the study, you may contact Jean Fankhanel, Patient Representative, Loma Linda University Medical Center, Loma Linda, CA, 92354, phone (909) 824-4647 for information and assistance.

Informed Consent Statement

I have read the contents of the consent form and have listened to the verbal explanation given by the investigator. My questions concerning this study have been answered to my satisfaction. I hereby give voluntary consent to participate in this study and for my child to participate in this study. Signing this consent document does not waive my rights nor does it release the investigators, institution, or sponsors from their responsibilities. I may call Kiti Freier, Ph.D. during routine office hours at 478-8577 if I have additional questions or concerns.

Consent Copy

I have been given a copy of this consent form.

INFORMED CONSENT: Cardiac Correlates of Attention in the Denervated Heart:A Study of Infant Heart Transplant Recipients

Signatures

I give my consent for my child ____________________ to participate in the study.

Name of infant

____ ____________________

Signature of parent or guardian Date

____

Signature of witness

I have reviewed the contents of the consent form with the person signing above.

I have explained the potential risks and benefits of the study.

____________________________ __________________ ____________

Signature of Investigator Phone Number Date

Appendix D

Loma Linda University

Graduate School
Department of Psychology

CONSENT AND WAIVER FOR AUDIO/VISUAL RECORDINGS

11130 Anderson Street
Loma Linda, California 92350
(909) 558-8577
FAX: (909) 558-0171

I ______________________________ authorize Loma Linda University,
(print name)

Department of Psychology, specifically ______________________________, and

Appropriate agents to make any of the following audio/visual recordings:

Check Box(es)

☐ Video (television) tapes

☐ Audio (sound) recordings

☐ Still photographs or slides

Of ______________________________.
(print name of subject)

These audio/visual recordings may be taken for the purpose of education. I grant to Loma Linda University, Department of Psychology and its agent the right to use these audio/visual recordings for educational purposes only. My/ The subject's name will not be disclosed with said use.

______________________________ ______________________________
Witness *Signature of subject*

______________________________ ______________________________
Date *Signature of parent or guardian (if applicable)*