# Measures of frontal functioning and the emergence of inhibitory control processes at 10 months of age

By: Kimberly Cuevas, Margaret M. Swingler, Martha Ann Bell, Stuart Marcovitch, Susan D. Calkins

## Abstract:

During the first year, infants begin to exhibit initial evidence of working memory and inhibitory control in conjunction with substantial maturation of the frontal cortex and corresponding neural circuitry. Currently, relatively little is known about the neural and autonomic resources that are recruited in response to increased executive demands during the first year of development. To this end, we recorded electroencephalogram (EEG; 6‑9 Hz) and electrocardiogram from 10-month-olds during a working memory and inhibitory control task (looking A-not-B). Analyses compared measures of frontal functioning (EEG power, EEG coherence, heart rate) during nonreversal (working memory) and reversal (working memory + inhibitory control) trials. The increased cognitive demand of inhibitory control processing was associated with increases in heart rate and frontal coherence (medial frontal‑lateral frontal, medial frontal‑temporal, medial frontal‑medial parietal, and medial frontal‑occipital electrode pairs). Thus, synchronized activity across distributed cortical regions appeared to be essential to inhibitory control processes during infancy. The addition of inhibitory control processes, however, was not associated with any changes in neuronal activity (EEG power). These findings are discussed in relation to other neuroscience findings and provide insight into the development of integrated frontal functioning in infancy.

**Keywords:** Working memory | Inhibitory control | EEG power | EEG coherence | Heart rate | Infants

## Article:

Executive functions (i.e., higher order cognitive and self-regulatory processes that underlie goal-directed behavior), such as working memory (WM) and inhibitory control (IC), are intricately

linked to activity and development of the frontal cortex (Hwang et al., 2010 and Osaka et al., 2003). Developmental cognitive neuroscientists have posited that the maturation of the frontal cortex and associated neural circuitry late in the first year underlies the emergence of higher order cognitive processes, such as executive functions (Colombo and Cheatham, 2006 and Diamond, 1990b). Indeed, infants exhibit initial behavioral evidence of WM (i.e., active maintenance and manipulation of information) and IC (i.e., withholding of a prepotent response) near the end of the first year (Diamond, 1990a and Diamond, 1990b) in conjunction with substantial maturation of the frontal cortex (Chugani et al., 1987, Deoni et al., 2011 and Tsekhmistrenko et al., 2004). In the present study, we examined changes in 10-month-olds' frontal functioning during a WMIC task (i.e., A-not-B) by comparing psychophysiological measures during WM trials[1] and WM + IC trials. Differences between WM and WM + IC processing reveal which frontal resources are uniquely recruited in response to additional IC demands. These findings will provide insight into the psychophysiological processes that support the development of integrated frontal functioning near the end of the first year. In the following paragraphs, we briefly review the A-not-B task and then discuss our psychophysiological measures as well as other, related, neuroscience findings.

During the "standard version" of the A-not-B task, infants watch as an experimenter hides a desirable object at one of two possible locations (A; nonreversal trials); their gaze to the hiding location is broken during a brief delay; and then infants are allowed to search (i.e., look, reach) for the object (Bell and Adams, 1999). If infants respond correctly on two consecutive nonreversal trials, the hiding location is switched (B; reversal trials). It has long been theorized that the A-not-B task requires both WM and IC (Bell and Adams, 1999, Diamond, 1990b and Diamond et al., 1997). WM is required during all trials; the infant must maintain the memory of the location of the reward for a matter of seconds while attention is distracted. During reversal trials, the infant must also use IC to overcome a prepotent response—repeating the previously rewarded response (Bell and Adams, 1999). Thus, with similar WM demands for both types of trials, infants typically succeed on nonreversal trials and fail at reversal trials (i.e., A-not-B error), presumably because of increased IC demands on reversal trials. The present study directly compares the psychophysiological correlates between nonreversal (WM) and reversal (WM + IC) trials. This comparison will provide insight into the specific changes in neural activity (electroencephalogram [EEG] power), functional connectivity (EEG coherence), and autonomic activity (heart rate [HR]) associated with the additional IC demands at 10 months of age.

There is converging biobehavioral evidence that the frontal cortex is a major contributor to A-not-B task performance during infancy (EEG: Bell, 2001, Bell, 2002, Bell, 2012, Bell and Fox, 1992 and Bell and Fox, 1997; near-infrared spectroscopy: Baird et al., 2002; phenylketonuria: Diamond et al., 1997; nonhuman primates: Diamond, 1990b and Diamond and Goldman-Rakic, 1989). Likewise, functional magnetic resonance imaging (fMRI) research has indicated developmental changes in fronto-parietal brain activity and functional connectivity

underlying IC (Durston et al., 2002, Hwang et al., 2010 and Rubia et al., 2006). Although fMRI has optimal spatial resolution, it is extremely sensitive to motor artifacts. Thus, during infancy, EEG is the preferred brain imaging technique because of its superior temporal resolution, noninvasive procedures, and relative resistance to motor artifacts (Casey and de Haan, 2002).

EEG power and coherence each provide unique information about frontal functioning. EEG coherence (range: 0–1) measures the synchrony of activation at the scalp level between two underlying brain regions (i.e., a measure of functional connectivity; Thatcher et al., 1987), while EEG power measures the amount of neuronal activation at a specific scalp location. An fMRI comparison of functional connectivity during reflexive and IC eye movements revealed stronger connectivity during IC movements for children and adults (Hwang et al., 2010). Likewise, children and adults exhibit increased activity in frontal and parietal regions during IC trials of a go/no-go response inhibition task compared to non-IC trials (fMRI: Durston et al., 2002).

Previous infant A-not-B research has revealed baseline-to-task increases in 6–9 Hz EEG power (all electrodes; Bell and Wolfe, 2007 and Cuevas et al., in press) and frontal coherence (medial frontal–posterior pairs; Bell, 2001 and Cuevas et al., in press). However, there have been no within-task comparisons of EEG measures during reversal and nonreversal trials. Our data provide the unique opportunity to examine the neural correlates in response to added IC demands during infancy. Because infants' power and coherence values increase from a resting level during WM + IC processing (i.e., when reversal and nonreversal trials are combined), we predict that a comparison of the two trial types will exhibit a similar pattern of change: EEG power (all electrodes) and coherence (medial frontal–posterior pairs) values will be higher during WM + IC processing as compared to WM processing. On the other hand, our data capture the emergence of IC and it is plausible that the cortical resources recruited for WM + IC processing during the emergence period are not initially different than those recruited for WM processing.

Autonomic measures, such as HR, also provide infant researchers with a noninvasive method for examining physiological responses associated with cognitive processing (see Reynolds and Richards, 2008, for review). According to the neurovisceral integration model, the prefrontal cortex interacts with other cortical (i.e., cingulate cortex, insula cortex) and subcortical areas (i.e., amygdala) to modulate autonomic activity via direct and indirect pathways (see Thayer and Lane, 2009, for review). Pharmacological and neuroimaging research have provided empirical support of hypothesized prefrontal-autonomic associations (e.g., Ahern et al., 2001 and Gianaros et al., 2004). Accordingly, we conceptualize HR as a potential indicator of frontal functioning; however, we acknowledge that additional cortical and subcortical structures may also contribute to changes in HR.

HR typically increases during tasks requiring cognitive processing (i.e., information processing and manipulation; Lacey and Lacey, 1974). Research with children has found task-related increases in HR during challenging WMIC tasks (Wolfe and Bell, 2004). Infant A-not-B

research has also revealed changes in HR during task performance (Bell, 2012); however, comparisons have not been made between reversal and nonreversal trials. We posit that the additional cognitive demands required during WM + IC processing (as compared to WM processing) will be associated with increased HR.

Currently, little is known about the neural and autonomic resources that are recruited in response to increased executive demands during the first year of development. Our goal here was to examine the potential use of measures of frontal functioning (EEG power, EEG coherence, HR) to distinguish trials that require additional IC processing during A-not-B performance at 10 months of age.

## 1. Method

### 1.1. Participants

As part of a longitudinal study examining individual differences in the development of executive functions across early development, 365 healthy full-term 10-month-olds[2] (181 girls, 184 boys; 20 Hispanic, 345 Non-Hispanic; 292 Caucasian, 43 African American, 27 Multi-Racial, 1 Other, 2 Not Reported) visited one of the two research locations (Blacksburg, VA; Greensboro, NC), with each location recruiting half of the total sample. For parents who reported educational information (363 mothers, 353 fathers), 98% of mothers and fathers graduated from high school (7% and 7% technical degree; 44% and 33% bachelor's degree; 23% and 25% graduate degree; respectively). Mothers and fathers were approximately 30 and 32 years old ($SD = 6$ and 7), respectively, when the infants were born. Infants were recruited via commercial mailing lists, newspaper birth announcements, and word of mouth. Infants' mean age (in days) was 313 ($SD = 8$). Informed consent for participation was provided by the infants' parents. Parents were paid for each laboratory visit.

The experimental protocol was approved by the University Institutional Review Boards at each research location (Blacksburg; Greensboro). Data were collected in both research locations using identical protocols. Research assistants from both locations were trained together on protocol administration by the third author as well as behavioral and psychophysiological coding. To ensure that identical protocol administration was maintained between the labs, the Blacksburg team periodically viewed DVD recordings and psychophysiology files collected by the Greensboro lab. To ensure that identical coding criteria were maintained between labs, the Blacksburg lab provided reliability coding for all behavioral data collected by both labs and verification of artifact screening for psychophysiology data collected and coded by the Greensboro lab.

### 1.2. Procedure

#### 1.2.1. EEG recording

Recordings were made from 16 left and right scalp sites: frontal pole (Fp1, Fp2), medial frontal (F3, F4), lateral frontal (F7, F8), central (C3, C4), temporal (T7, T8), medial parietal (P3, P4), lateral parietal (P7, P8), and occipital (O1, O2). All electrode sites were referenced to Cz during recording. EEG was recorded using a stretch cap (Electro-Cap, Inc.) with electrodes in the 10/20 system pattern (Jasper, 1958 and Pizzagalli, 2007). After the cap was placed on the infant's head, recommended procedures regarding EEG data collection with infants were followed (Pivik et al., 1993). Specifically, a small amount of abrasive was placed into each recording site and the scalp gently rubbed. Following this, conductive gel was placed in each site. Electrode impedances were measured and accepted if they were below 10 K ohms.

The electrical activity from each lead was amplified using separate SA Instrumentation Bioamps (San Diego, CA) and bandpassed from .1 to 100 Hz. Activity for each lead was displayed on the monitor of an acquisition computer. The EEG signal was digitized on-line at 512 samples per second for each channel so that the data were not affected by aliasing. The acquisition software was Snapshot-Snapstream (HEM Data Corp.; Southfield, MI) and the raw data were stored for later analyses.

1.2.2. EEG analysis

EEG data were examined and analyzed using EEG Analysis System software developed by James Long Company (Caroga Lake, NY). First, the data were re-referenced via software to an average reference configuration (Lehmann, 1987). Average referencing, in effect, weighted all the electrode sites equally and eliminated the need for a noncephalic reference. Active (F3, F4, etc.) to reference (Cz) electrode distances vary across the scalp. Without the re-referencing, power values at each active site may reflect interelectrode distance as much as they reflect electrical potential. The average reference configuration requires that a sufficient number of electrodes be sampled and that these electrodes be evenly distributed across the scalp. Currently, there is no agreement concerning the appropriate number of electrodes (Davidson et al., 2000,Hagemann et al., 2001 and Luck, 2005), although the 10/20 configuration that we used does satisfy the requirement of even scalp distribution.

The re-referenced EEG data were artifact scored for eye blinks using Fp1 and Fp2 (Myslobodsky et al., 1989) and for gross motor movements; these artifact-scored epochs were eliminated from all subsequent analyses. The data then were analyzed with a discrete Fourier transform (DFT) using a Hanning window of 1-s width and 50% overlap. Power and coherence were computed for the 6‑9 Hz frequency band. The 6‑9 Hz frequency band has been used by infant EEG researchers to investigate both cognitive and emotional processing (Bell, 2001, Bell, 2012, Fox et al., 2001 and Orekhova et al., 2001). Power was expressed as mean square microvolts and the data were transformed using the natural log (ln) to normalize the distribution. Coherence between medial frontal and all other electrode sites within each hemisphere was computed using an algorithm by Saltzberg et al. (1986). We chose to only examine medial frontal pairings

because of the well-established role of the frontal cortex during the A-not-B task and to limit the potential number of electrode pairings for statistical analysis.

### 1.2.3. Electrocardiogram (ECG) recording

ECG was measured from two neonatal disposable electrodes using modified lead II (right collarbone and lower left rib; Stern et al., 2001), grounded at the scalp near electrode site Fz. The cardiac electrical activity was amplified using a SA Instrumentation Bioamp and the QRS complex was displayed on the acquisition computer monitor along with the EEG data. The cardiac signal was digitized at 512 samples per second. The acquisition software was Snapshot-Snapstream (HEM Data Corp.) and the raw data were stored for later analyses.

### 1.2.4. ECG analysis

Heart data were examined and analyzed using IBI Analysis System software developed by James Long Company. First, R waves were detected and movement artifact, designated by the absence of at least three consecutive R waves, was scored. These artifact-scored epochs were eliminated from all cardiac calculations. HR was calculated as beats per minute (bpm).

### 1.2.5. Data available for analysis

Of the 365 10-month-olds who visited the lab, behavioral data were available for 364 infants (one infant's data was lost due to fussiness), EEG and ECG electrodes were accepted by 363 infants, and psychophysiological data were available for 353 infants (i.e., losses due to low-quality physiological recordings [$n = 7$]; equipment failure [$n = 2$]; experimenter error [$n = 1$]). Although the majority of infants had artifact-free EEG ($\geq$10 dfts; $n = 307$) and ECG ($\geq$ 10 s; $n = 309$) during nonreversal trials, fewer infants had artifact-free EEG ($n = 173$) and ECG ($n = 224$) during reversal trials. By nature of task design (see Section1.2.6), infants received more nonreversal trials ($M = 10.1$; $SD = 3.1$) than reversal trials ($M = 2.5$; $SD = 1.2$). Thus, subsequent analyses included the 173 and 223 infants who had artifact-free EEG and ECG, respectively, for both trial types.

### 1.2.6. Looking A-not-B task

Details about the procedure for the looking A-not-B task can be found elsewhere (Bell and Adams, 1999 and Bell, 2002). The testing apparatus was a table (90 cm $\times$ 60 cm $\times$ 75 cm) and the hiding sites were bright orange and blue plastic tubs (diameter: 17 cm; depth: 11 cm). The infant sat on the parent's lap 1.1 m from the edge of the testing table as the experimenter manipulated a toy and hid it under one of the two (17.5 cm on either side of midline) tubs.

Initial side of hiding was counterbalanced among infants and the pattern of toy placement was determined by the infant's performance. After the toy was hidden, the infant's gaze to the hiding site was broken and brought to the experimenter's face at midline by the experimenter calling the infant's name and asking, "Where's the toy?". The direction of the infant's first eye movement

after being brought to midline was scored as either correct or incorrect. Two consecutive successful eye movements toward the same side (i.e., nonreversal/WM trials) resulted in the toy then being hidden under the opposite tub (e.g., Right‑Right‑Left). Regardless of whether or not the infant was successful on the reversal (WM + IC) trial, new nonreversal trials commenced at the reversal site and continued until two consecutive correct responses, initiating another reversal (i.e., L‑L‑R). Most infants were not flawless in performance and some needed multiple nonreversal trials in order to achieve two consecutive correct responses prior to reversal trials.

Infants who were correct on two out of three reversal trials were then tested with a delay ($n = 210$; artifact-free EEG and ECG: $n = 122$ and 159, respectively). The delay was initiated during the time the infant's gaze to the hiding site was broken. The experimenter called the infant's name, counted out the delay period, and then asked, "Where's the toy?". Delay was incremented in 2-s intervals until the infant looked at the incorrect tub in two out of three reversal trials at any given delay. In practice, there was a brief delay in the "no delay" trials at the beginning of the assessment when gaze to the tub was broken and brought to midline. This brief delay was unavoidable because of the necessity of breaking the infant's gaze so that the direction of their first eye movement could be determined.

An event marker was used in conjunction with the EEG/ECG recordings so that it was possible to mark which portions of the electrophysiological record were associated with WM and WM + IC (Bell, 2001 and Bell, 2002). The task-related EEG/ECG started with the covering of the hiding sites, continued through the distraction and delay periods, and stopped when the experimenter lifted a tub prior to giving the infant appropriate verbal feedback. Thus, electrophysiological data *not* included in the analyses were those recorded when the experimenter was (a) manipulating the toy prior to hiding it and (b) giving appropriate feedback to the infant after the infant's eye movement to one of the hiding sites. Because we were primarily interested in the psychophysiological correlates associated with increased IC processing, the artifact-free EEG/ECG data from all trials, correct and incorrect, were used in the analyses. [3]

1.3. Statistical analysis

We completed separate repeated-measures multivariate analyses of variance (MANOVAs) for each of our EEG measures with region/regional pair, hemisphere, and trial type as within-subjects factors. Of major interest were main effects and interactions involving the trial type (nonreversal vs. reversal) factor. Region and regional pairs were of interest for all EEG power and coherence analyses, respectively. A Holm‑Bonferroni procedure (Holm, 1979) was adopted for follow-up comparisons to limit the familywise Type I error rate ($\alpha = .05$). A paired *t*-test was used to compare HR values as a function of trial type.

2. Results

## 2.1. Behavior

We calculated the proportion of correct responses for nonreversal and reversal trials (Bell and Adams, 1999,Cuevas and Bell, 2010 and Hofstadter and Reznick, 1996). A paired $t$-test revealed that performance was higher on nonreversal trials ($M = .67$, $SD = .19$) as compared to reversal trials ($M = .41$, $SD = .35$), $t(348) = 14.78$, $p < 001$, $d = 0.79$.

## 2.2. EEG power

A repeated-measures MANOVA was completed on the ln 6‑9 Hz EEG power values. The within-subjects factors were trial type, region (i.e., frontal pole, medial frontal, lateral frontal, temporal, lateral parietal, medial parietal, or occipital), and hemisphere (i.e., left or right). For this overall MANOVA, there were main effects for region, $F(6, 158) = 248.38$, $p < .001$, $\eta^2p=.90$, and hemisphere, $F(1, 163) = 13.45$, $p < .001$, $\eta^2p=.08$, as well as a Region × Hemisphere interaction, $F(6, 158) = 2.43$, $p = .028$, $\eta^2p=.09$. The main effect and interactions involving trial type were not significant.

## 2.3. EEG coherence

A repeated-measures MANOVA was completed on the 6‑9 Hz EEG coherence values. The within-subjects factors were trial type, regional electrode pair (i.e., frontal pole-medial frontal, medial frontal‑lateral frontal, medial frontal‑temporal, medial frontal‑medial parietal, medial frontal‑lateral parietal, or medial frontal‑occipital), and hemisphere. For this overall MANOVA, there were main effects for trial type, $F(1, 163) = 23.94$, $p < .001$, $\eta^2p =.13$, and regional pair, $F(5, 159) = 353.02$, $p < .001$, $\eta^2p =.92$. There were also Trial Type × Regional Pair, $F(5, 159) = 3.54$, $p = .005$, $\eta^2p = .10$, and Regional Pair × Hemisphere, $F(5, 159) = 2.64$, $p < .001$, $\eta^2p = .08$, interactions.

Paired samples $t$-tests were completed to examine the Trial Type × Regional Pair interaction, and thus determine whether there was a main effect for trial type for all frontal coherence pairs. A Holm‑Bonferroni procedure was used to control the overall level of significance. As can be seen in Fig. 1, coherence values were higher during reversal trials as compared to nonreversal trials for medial frontal‑lateral frontal ($d = 0.23$), medial frontal‑temporal ($d = 0.56$), medial frontal‑medial parietal ($d = 0.20$), and medial frontal‑occipital ($d = 0.19$) electrode pairs.
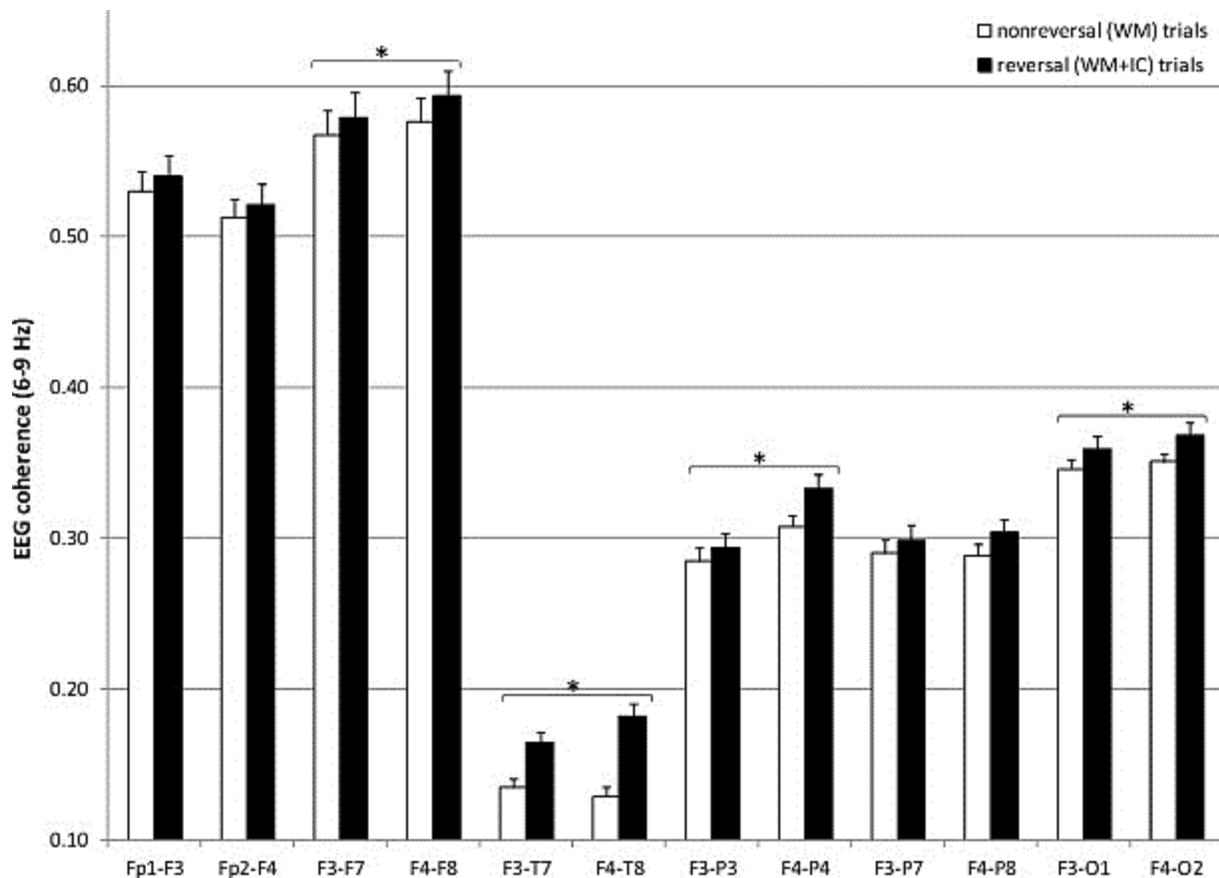
Fig. 1.

EEG coherence values (*S.E.*) at 6‑9 Hz for nonreversal (working memory processing) and reversal (working memory and inhibitory control processing) trials at 10 months of age. Asterisks represent significant difference (following a Holm‑Bonferroni procedure to limit familywise Type I error rate; $\alpha = .05$) in coherence values as a function of trial type.

## 2.4. ECG

A paired samples *t* test revealed that HR was higher during reversal trials ($M = 123.56$, $SE = .66$) than during nonreversal trials ($M = 122.53$, $SE = .64$), $t(222) = 4.41$, $p < .001$, $d = 0.30$.

## 3. Discussion

The maturation of the frontal cortex and associated neural circuitry late in the first year is posited to underlie the emergence of executive functions (Colombo and Cheatham, 2006 and Diamond, 1990b). Yet, little is known about the neural and autonomic resources that are recruited in response to increased executive demands during the first year of development. The data in the present study permitted comparison of dynamic changes in frontal functioning (i.e., EEG power, EEG coherence, HR) associated with WM and WM + IC processing during infancy. Our findings

reveal valuable information regarding increased IC demands and associated frontal functioning. By 10 months of age, infants recruit distinct frontal resources during task trials that require additional IC processing as compared to trials that primarily require WM.

The A-not-B task requires infants to constantly update their memory of where a desirable object was hidden through a series of displacements (i.e., WM) and to inhibit looking back toward a previously rewarded hiding place (i.e., IC; Bell and Adams, 1999 and Diamond, 1990b). Although behavioral data suggest that both WM and IC are essential to A-not-B performance (Bell and Adams, 1999, Cuevas and Bell, 2010 and Diamond et al., 1997), the present study provides initial psychophysiological evidence of dissociation between processing used during nonreversal (WM) and reversal (WM + IC) trials. It is particularly interesting that this psychophysiological dissociation occurs very early in development−10 months of age−near the same time that infants initially exhibit evidence of executive processes.

Research with older children and adults has indicated increases in frontal and parietal brain activity (fMRI:Durston et al., 2002 and Rubia et al., 2006) and functional connectivity (Hwang et al., 2010 and Stevens et al., 2007) during IC processing. As hypothesized, 10-month-olds in the present study exhibited increased HR and increased frontal EEG coherence (i.e., medial frontal‐lateral frontal, medial frontal‐temporal, medial frontal‐medial parietal, and medial frontal‐occipital electrode pairs) during reversal (WM + IC) trials as compared to nonreversal (WM) trials. There were, however, no changes in neuronal activity (i.e., EEG power) as a function of task trial type. Our neuronal activity findings are similar to event-related potential (ERP) EEG findings with young children. In one such study, 6-year-olds exhibited similar amounts of neuronal activity at parietal regions when "go" and "no-go" (IC) trials were intermixed−similar to the intermixing of reversal and nonreversal trials in the present study (Davis et al., 2003). Based on the aforementioned EEG and fMRI findings, it appears that changes in neuronal activity during IC processing do not occur until middle childhood (i.e., after 6 years of age). This conclusion must be considered with caution, however, because our cross-study comparisons are limited by differences in developmental populations (i.e., infants, young children, older children), IC tasks, and brain imaging techniques.

Increasingly, cognitive neuroscientists have focused on interactions among various brain regions −as opposed to examining activation of brain regions in isolation−because functional neural networks are presumed to reflect how the brain interacts as a whole to permit higher order cognitive processes (Stevens, 2009). In the present study, 10-month-olds exhibited synchronized activity across distributed cortical regions in response to additional IC demands. An examination of effect sizes reveals that the magnitude of difference between WM and WM + IC in EEG coherence was largest for medial frontal‐temporal electrode pairs. This finding might reflect the regional differences in frontal axon growth and myelination (Deoni et al., 2011 and Tsekhmistrenko et al., 2004) that are essential to executive processes.

Our coherence findings are consistent with evidence that fronto-posterior connectivity is essential to IC during childhood and adulthood (fMRI: Hwang et al., 2010 and Stevens et al., 2007), and provide initial evidence that similar functional connections might underlie the emergence of IC processes during infancy. However, adult-like IC abilities are not found until adolescence. Luna and Sweeney (2004) have proposed that changes in brain network dynamics (e.g., synaptic pruning, myelination) are essential to adult-like IC. During the first 2 years of postnatal development, there is considerable structural growth in the frontal axons and in the myelination of these projections (Deoni et al., 2011 and Tsekhmistrenko et al., 2004), which contribute to more efficient neural communication. For instance, during the first year of postnatal development, the number of neurons in the frontal cortex decreases while the number of frontal axonal fibers increases (Tsekhmistrenko et al., 2004). Likewise, glucose metabolism in the frontal cortex reaches adult levels at 12 months (Chugani et al., 1987), and a comparison of 7- and 13-month-olds revealed increased cerebral blood flow to the prefrontal cortex by 13 months (Wang et al., 2008). Myelination of frontal axons does not begin until 6–8 months, and myelination is only halfway complete by 18 months of age (Deoni et al., 2011). Myelination of axons, such as the superior longitudinal fasciculus, which are part of the fronto-parietal feedback loop are likely essential for executive processes development (Colombo and Cheatham, 2006). We posit that the aforementioned structural changes—which are likely reflected in measures of functional connectivity—are associated with the emergence and development of IC processes as well as other executive and regulatory processes during infancy (Colombo and Cheatham, 2006 and Diamond, 1990b).

Research with adults and children has revealed that autonomic activity is related to executive processes (Marcovitch et al., 2010 and Mathewson et al., 2010). Patterns of task-related increases in HR have been found in previous WM (Gianaros et al., 2004) and IC (Mathewson et al., 2010) research with adults as well as previous developmental work during cognitively challenging WMIC tasks (Bell, 2012 and Wolfe and Bell, 2004). We found the same pattern of changes in HR at 10 months of age when additional executive processing was required. We interpret increased HR during the addition of IC processing to reflect the additional cognitive demands required during reversal trials. From the perspective of the neurovisceral integration model (see Thayer and Lane, 2009, for review), our data potentially reflect the prefrontal cortex mediating changes in HR via direct and indirect pathways to cortical and subcortical areas. To our knowledge, this is the first examination of HR measures of the relation between WM and IC processes during infancy. Although replication of these findings is essential, autonomic measures potentially provide insight into IC processes during infancy.

The majority of research on the psychophysiological correlates of IC has focused on children 6 years and older. Although this research has informed developmental cognitive neuroscientists about the neural changes that support adult-like IC, little is known about the brain-IC associations during infancy and childhood—when there is ample behavioral research on IC emergence and development. A recent study with 9-month-olds (Holmboe et al., 2010) revealed

that polymorphisms in dopamine genes with receptors in frontal cortical areas as well as subcortical areas were associated with IC as measured by the Freeze-Frame task. Thus, despite using different IC tasks and brain-behavior methods, our findings and Holmboe et al.'s (2010)both suggest that the frontal cortex mediates IC processing by 9‑10 months of age.[4] These findings set the stage for future brain-behavior examinations with older infants and toddlers. Whether IC processing is associated with increases in HR and frontal functional connectivity throughout early childhood, is a question for future research. It is plausible that advances in IC during early childhood are mediated by corresponding changes in frontal neural activity during IC processing that support the emergence of these new skills. Thus, although our study focused on one age group, our findings have direct implications for the brain-behavior relations that underlie the emergence and development of IC.

3.1. Potential limitations

Our coherence findings are potentially affected by volume conduction (i.e., cortical activity recorded at one electrical site that can also contribute to the signal at other nearby sites). However, skull thickness has been shown to have an effect on the amount of volume conduction with thicker skulls propagating more volume conduction (Nunez, 1981). The infant skull is thinner than the adult skull, and there is evidence that volume conduction effects are much smaller in infants than adults (Grieve et al., 2003). For instance, theoretical modeling using average-reference data reveal that the effect of volume conduction is relatively small at interelectrode distances of 5 and 10 cm for infants and adults, respectively (Grieve et al., 2003). Accordingly, our coherence findings for medial frontal‑lateral frontal pairs (≈4.3 cm interelectrode distance) should be interpreted with caution. On the other hand, it is unclear whether volume conduction would differ as a function of trial type, as there were no corresponding differences in neural activity.

A potential limitation of the current study is the fact that our data did not permit examination of IC processes in isolation. WM was required during both nonreversal and reversal trials, and it is plausible that our data reflect the general addition of cognitive demands rather than the specific contribution of IC processes. Although there are infant tasks that measure primarily "WM-only" or "IC-only" processes, we are unaware of any infant tasks that contain measures of both "WM-only "and "IC-only" processes within the same task. Future infant research, using either a single- or multi-task approach, with psychophysiological measures of "WM-only", "IC-only", and WM + IC processing is essential to determining how these executive processes differ in recruitment of frontal resources. Our data represent the first step to understanding the psychophysiological correlates of co-emerging executive processes during infancy.

3.2. Conclusions

Executive functions, such as WM and IC, emerge near the end of the first year and continue to develop throughout adolescence (Diamond, 1990a, Diamond, 1990b and Luna and Sweeney,

2004). The present study provides initial psychophysiological evidence that 10-month-olds exhibit different patterns of activity when IC processing is recruited in addition to primarily WM processing. Specifically, infants displayed increases in frontal functioning (i.e., EEG coherence, HR) during WM + IC processing. These findings provide insight into the development of integrated frontal functioning near the end of the first year.

Conflict of interest

The authors have no conflicts of interest to declare.

Acknowledgments

**References**

Ahern, G.L., Sollers, J.J., Lane, R.D., Labiner, D.M., Herring, A.M., Weinand, M.E., Hutzler, R., Thayer, J.F., 2001. Heart rate and heart rate variability changes in the intracarotid sodium amobarbital (ISA) test. Epilepsia 42, 912–921, doi:10.1046/j.1528-1157.2001.042007912.x.

Baird, A.A., Kagan, J., Gaudette, T., Walz, K.A., Hershlag, N., Boas, D.A., 2002. Frontal lobe activation during object permanence: data from nearinfrared spectroscopy. NeuroImage 16, 1120–1126.

Bell, M.A., 2001. Brain electrical activity associated with cognitive processing during a looking version of the A-not-B task. Infancy 2, 311–330.

Bell, M.A., 2002. Power changes in infant EEG frequency bands during a spatial working memory task. Psychophysiology 39, 450–458.

Bell, M.A., 2012. A psychobiological perspective of working memory performance at 8 months of age. Child Development 83, 251–265.

Bell, M.A., Adams, S.E., 1999. Comparable performance on looking and reaching version of the A-not-B task at 8 months of age. Infant Behav. Dev. 22, 221–235.

Bell, M.A., Fox, N.A., 1992. The relations between frontal brain electrical activity and cognitive development during infancy. Child Dev. 63, 1142–1163.

Bell, M.A., Fox, N.A., 1997. Individual differences in object permanence at 8 months: locomotor experience and brain electrical activity. Dev. Psychobiol. 31, 287–297.

Bell, M.A., Wolfe, C.D., 2007. Changes in brain functioning from infancy to early childhood: Evidence from EEG power and coherence during working memory tasks. Dev. Neuropsychol. 31, 21–38.

Casey, B.J., de Haan, M., 2002. Introduction: new methods in developmental science. Dev. Sci. 5, 265–267.

Chugani, H.T., Phelps, M.E., Mazziotta, J.C., 1987. Positron emission tomography study of human brain functional development. Ann. Neurol. 22, 487–497.

Colombo, J., Cheatham, C.L., 2006. The emergence and basis of endogenous attention in infancy and early childhood. In: Kail, R.V. (Ed.), Advances in Child Development and Behavior, vol. 34. Elsevier, Amsterdam, pp. 283–322.

Cuevas, K., Bell, M.A., 2010. Developmental progression of looking and reaching performance on the A-not-B task. Dev. Psychol. 46, 1363–1371, doi:10.1037/a0020185.

Cuevas, K., Bell, M.A., Marcovitch, S., Calkins, S.D. EEG and heart rate measures of working memory at 5 and 10 months of age. Dev. Psychol., doi:10.1037/a0026448, in press.

Davidson, R.J., Jackson, D.C., Larson, C.L., 2000. Human electroencephalography. In: Cacioppo, J.T., Tassinary, L.G., Berntson, G.G. (Eds.), Handbook of Psychophysiology. , second ed. Cambridge University Press, Cambridge, UK, pp. 27–52.

Davis, E.P., Bruce, J., Snyder, K., Nelson, C.A., 2003. The x-trials: neural correlates of an inhibitory control task in children and adults. J. Cogn. Neurosci. 15, 432–443.

Deoni, S.C.L., Mercure, E., Blasi, A., Gasston, D., Thomson, A., Johnson, M., Williams, S.C.R., Murphy, D.G.M., 2011. Mapping infant brain myelination with magnetic resonance imaging. J. Neurosci. 31, 784–791, doi:10.1523/JNEUROSCI.2106-10.2011.

Diamond, A., 1990a. Developmental time course in human infants and infant monkeys, and the neural basis of, inhibitory control in reaching. In: Diamond, A. (Ed.), The Development and Neural Bases of Higher Cognitive Functions. New York Academy of Sciences Press, New York, pp. 637–676.

Diamond, A., 1990b. The development and neural bases of memory function as indexed by the AB and delayed response tasks in human infants and infant monkeys. In: Diamond, A. (Ed.), The Development and Neural Bases of Higher Cognitive Functions. New York Academy of Sciences Press, New York, pp. 267–317.

Diamond, A., Goldman-Rakic, P.S., 1989. Comparison of human infants and rhesus monkeys on Piaget's A-not-B task: evidence for dependence on dorsolateral prefrontal cortex. Exp. Brain Res. 74, 24–40.

Diamond, A., Prevor, M., Callender, G., Druin, D.P., 1997. Prefrontal cortex cognitive deficits in children treated early and continuously for PKU. Monogr. Soc. Res. Child Dev. 62 (4, Serial No. 252).

Durston, S., Thomas, K.M., Yang, Y., Ulug, A.M., Zimmerman, R.D., Casey, B.J., 2002. A neural basis for the development of inhibitory control. Dev. Sci. 5, F9–F16.

Fox, N.A., Henderson, H.A., Rubin, K.H., Calkins, S.D., Schmidt, L.A., 2001. Continuity and discontinuity of behavioral inhibition and exuberance: psychophysiological and behavioral influences across the first four years of life. Child Dev. 72, 1–21.

Gianaros, P.J., Van Der Veen, F.M., Jennings, J.R., 2004. Regional cerebral blood flow correlates with heart period and high-frequency heart period variability during working-memory tasks: implications for the cortical and subcortical regulation of cardiac autonomic activity. Psychophysiology 41, 521–530, doi:10.1111/j.1469-8986.2004.00179.x.

Grieve, P.G., Emerson, R.G., Fifer, W.P., Isler, J.R., Stark, R.I., 2003. Spatial correlation of the infant and adult electroencephalogram. Clin. Neurophys. 114, 1594–1608, doi:10.1016/S1388-2457(03)00122-6.

Hagemann, D., Naumann, E., Thayer, J.F., 2001. The quest for the EEG reference revisited: a glance from brain asymmetry research. Psychophysiology 38, 847–857.

Holm, S., 1979. A simple sequentially rejective multiple test procedure. Scand. J. Stat. 6, 65–70.

Holmboe, K., Nemoda, Z., Fearon, R.M.P., Csibra, G., Sasvari-Szekely, M., Johnson, M.H., 2010. Polymorphism in dopamine system genes are associated with individual differences in attention in infancy. Dev. Psychol. 46, 404–416, doi:10.1037/a0018180.

Hofstadter, M., Reznick, J.S., 1996. Response modality affects human infant delayed-response performance. Child Dev. 67, 646–658, doi:10.1111/1467-8624.ep9605280333.

Hwang, K., Velanova, K., Luna, B., 2010. Strengthening of top-down frontal cognitive control networks underlying the development of inhibitory control: a functional magnetic resonance imaging effective connectivity study. J. Neurosci. 30, 15535–15545, doi:10.1523/JNEUROSCI.2825-10.2010.

Jasper, H.H., 1958. The ten twenty electrode system of the international federation. Electroencephalogr. Clin. Neurophysiol. 10, 371–375.

Lacey, B.C., Lacey, J.I., 1974. Studies on heart rate and other bodily processes in sensorimotor behavior. In: Obrist, P.A., Black, A.H., Brener, J., DiCara, L.V. (Eds.), Cardiovascular Psychophysiology: Current Issues in Response, Mechanisms, Biofeedback, and Methodology. Aldine, Chicago, pp. 538–564.

Lehmann, D., 1987. Principles of spatial analysis. In: Gevins, A.S., Remond, A. (Eds.), Handbook of Electroencephalography and Clinical Neuropsychology, rev. ser. Vol. 1: Methods of Analysis of Brain Electrical and Magnetic Signals. Elsevier, Amsterdam, pp. 309–354.

Luck, S.J., 2005. An Introduction to the Event-Related Potential Technique. MIT Press, Cambridge, MA.

Luna, B., Sweeney, J.A., 2004. The emergence of collaborative brain function: FMRI studies of the development of response inhibition. Ann. N. Y. Acad. Sci. 1021, 296–309, doi:10.1196/annals.1308.035.

Lustig, C., May, C.P., Hasher, L., 2001. Working memory span and the role of proactive interference. J. Exp. Psychol. Gen. 130, 199–207, doi:10.1037/0096-3445.130.2.199.

Marcovitch, S., Leigh, J., Calkins, S.D., Leerkes, E.M., O'Brien, M., Blankson, A.N., 2010. Moderate vagal withdrawal in 3.5-year-old children is associated with optimal performance on executive function tasks. Dev. Psychobiol. 52, 603–608, doi:10.1002/dev.20462.

Mathewson, K.J., Jetha, M.K., Drmic, I.E., Bryson, S.E., Goldberg, J.O., Hall, G.B., Santesso, D.L., Segalowitz, S.J., Schmidt, L.A., 2010. Autonomic predictors of Stroop performance in young and middle-aged adults. Int. J. Psychophysiol. 76, 123–129, doi:10.1016/j.ijpsycho.2010.02.007.

Myslobodsky, M.S., Coppola, R., Bar-Ziv, J., Karson, C., Daniel, D., van Praag, H., Weinberger, D.R., 1989. EEG asymmetries may be affected by cranial and brain parenchymal asymmetries. Brain Topogr. 1, 221–228.

Nunez, P., 1981. Electrical Fields of the Brain. Oxford, New York.

Orekhova, E.V., Stroganova, T.A., Posikera, I.N., 2001. Alpha activity as an index of cortical inhibition during sustained internally controlled attention in infants. Clin. Neurophysiol. 112, 740–749.

Osaka, M., Osaka, N., Kondo, H., Morishita, M., Fukuyama, H., Aso, T., Shibasaki, H., 2003. The neural basis of individual differences in working memory capacity: an fMRI study. NeuroImage 18, 789–797.

Pivik, R.T., Broughton, R.J., Coppola, R., Davidson, R.J., Fox, N.A., Nuwer, M.R., 1993. Guidelines for the recording and quantitative analysis of electroencephalographic activity in research contexts. Psychophysiology 30, 547–558.

Pizzagalli, D.A., 2007. Electroencephalography and high-density electrophysiological source localization. In: Cacioppo, J.T., Tassinary, L.G., Berntson, G.G. (Eds.), Handbook of Psychophysiology. , third ed. Cambridge University Press, Cambridge, UK, pp. 56–84.

Reynolds, G.D., Richards, J.E., 2008. Infant heart rate: a developmental psychophysiological perspective. In: Schmidt, L.A., Segalowitz, S.J. (Eds.), Developmental Psychophysiology: Theory, Systems, and Methods. Cambridge University Press, Cambridge, UK, pp. 173–212.

Rubia, K., Smith, A.B., Woolley, J., Nosarti, C., Heyman, I., Taylor, E., Brammer, M., 2006. Progressive increase of frontostriatal brain activation from childhood to adulthood during event-related tasks of cognitive control. Hum. Brain Mapp. 27, 973–993, doi:10.1002/hbm.20237.

Saltzberg, B., Burton Jr., W.D., Burch, N.R., Fletcher, J., Michaels, R., 1986. Electrophysiological measures of regional neural interactive coupling. Linear and non-linear dependence relationships among multiple channel electroencephalographic recordings. Int. J. Biomed. Comput. 18, 77–87.

Stern, R.M., Ray, W.J., Quigley, K.S., 2001. Psychophysiological Recording, second ed. Oxford University Press, Oxford. Stevens, M.C., 2009. The developmental cognitive neuroscience of functional connectivity. Brain Cogn. 70, 1–12, doi:10.1016/j.bandc.2008.12.009.

Stevens, M.C., Kiehl, K.A., Pearlson, G.D., Calhoun, V.D., 2007. Functional neural network underlying response inhibition in adolescents and adults. Behav. Brain Res. 181, 12–22, doi:10.1016/j.bbr.2007.03.023.

Thatcher, R.W., Walker, R.A., Giudice, S., 1987. Human cerebral hemispheres develop at different rates and ages. Science 236, 1110–1113.

Thayer, J.F., Lane, R.D., 2009. Claude Bernard and the heart–brain connection: further elaboration of a model of neurovisceral integration. Neurosci. Biobehav. Rev. 33, 81-88, doi:10.1016/j.neubiorev.2008.08.004.

Tsekhmistrenko, T.A., Vasil'eva, V.A., Shumeiko, N.S., Vologirov, A.S., 2004. Quantitative changes in the fibroarchitectonics of the human cortex from birth to the age of 12 years. Neurosci. Behav. Physiol. 34, 983–988.

Wang, Z., Fernandez-Seara, M., Alsop, D.C., Liu, W.-C., Flax, J.F., Benasich, A.A., Detre, J.A., 2008. Assessment of functional development in normal infant brain using arterial spin labeled perfusion MRI. Neuroimage 39, 973–978, doi:10.1016/j.neuroimage.2007.09.045.

Wolfe, C.D., Bell, M.A., 2004. Working memory and inhibitory control in early childhood: contributions from physiology, temperament, and language. Dev. Psychobiol. 44, 68–83.