Published in final edited form as:

Alcohol Clin Exp Res. 2011 January ; 35(1): 69–82. doi:10.1111/j.1530-0277.2010.01323.x.

The effects of maternal binge drinking during pregnancy on neural correlates of response inhibition and memory in childhood

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Abstract

Background—Although an extensive literature has documented a broad range of cognitive performance deficits in children with prenatal alcohol exposure, little is known about how the neurophysiological processes underlying these deficits may be affected. Event-related potentials (ERPs), which reflect task-specific changes in brain electrical activity, provide a method for examining multiple constituents of cognitive processing at the neural level.

Methods—We recorded ERPs in 217 children from Inuit communities in Arctic Quebec (*M*age = 11.3 yr) during two different tasks—Go/No-go response inhibition and continuous recognition memory. Children were classified as either alcohol-exposed (ALC) or controls (CON) depending on whether the mother reported binge drinking during pregnancy.

Results—Both groups performed comparably in terms of accuracy and reaction time on the tasks, and both tasks elicited the expected effects on ERPs when responses were compared across conditions. However, the ALC group showed slower P2 latencies on Go/No-go, suggesting an altered neurophysiological response associated with initial visual processing of the stimuli. On the memory task, the ALC group showed reduced FN400 amplitude to new items, known as the familiarity effect, and reduced amplitude for the late positive component, possibly reflecting impairment in memory retrieval.

Conclusions—These findings show that, even in tasks in which alcohol-exposed children exhibit behavioral performance that is comparable to controls, fetal alcohol exposure is associated with altered neurophysiological processing of response inhibition and recognition memory. The data suggest that fetal alcohol exposure is associated with reduced efficiency in the initial extracting of the meaning of a stimulus, reduced allocation of attention to the task, and poorer conscious, explicit recognition memory processing.

Keywords

Prenatal alcohol exposure; fetal alcohol spectrum disorders; event-related potentials; response inhibition; recognition memory

INTRODUCTION

Fetal alcohol syndrome (FAS) was first described in the United States by Jones and Smith (1973), who identified a distinctive set of facial anomalies in children whose mothers drank heavily during pregnancy, accompanied by prenatal and/or postnatal growth retardation and cognitive/behavioral problems. The term fetal alcohol spectrum disorder (FASD) refers collectively to the effects seen on the continuum of prenatal alcohol exposure, with an incidence of nearly 1 in 100 live births affected (Sampson et al., 1997). In addition to the global impact on intellectual function typically documented in cases of FAS, children with prenatal alcohol exposure show particular difficulties with short-term memory (Burden et al., 2005b; Streissguth et al., 1994), arithmetic (Burden et al., 2005a; Goldschmidt et al., 1996; Howell et al., 2006; Jacobson et al., 1998; Meintjes et al., 2007; Streissguth et al., 1994), and information processing speed (Burden et al., 2005a; Jacobson et al., 1993, 1994; Kable and Coles, 2004).

Although detailed prospective reports of prenatal alcohol exposure obtained during pregnancy have been shown to provide the most sensitive indicators of exposure (Jacobson et al., 2002), recent evidence suggests that dichotomous measures derived from retrospective reports may also provide a valid indicator of prenatal exposure (Chiodo et al., 2009), particularly when very heavy or binge drinking is involved. Several studies have shown that binge drinking during pregnancy has particularly detrimental effects on the developing fetus (Jacobson et al., 2008; Streissguth et al., 1994). Experimental animal studies have reported that ingestion of a given dose of alcohol over a short period of time generates a greater peak blood alcohol concentration and greater neuronal (Bonthius and West, 1990) and behavioral impairment (Goodlett et al., 1987) than when the same or even a larger dose is ingested gradually over several days. Analyses of data from our Detroit longitudinal study indicate that functionally significant deficits are seen primarily in infants born to mothers who average at least 5 drinks/occasion during pregnancy (Jacobson et al., 1998). Similarly, Streissguth et al. (1989, 1994) found that number of drinks/occasion provided the most sensitive predictor of attention and memory deficits in exposed children at 7- and 14-years of age. Thus, data from previous studies suggest that a retrospective dichotomous measure of binge drinking during pregnancy can provide a particularly useful measure of prenatal alcohol exposure.

Numerous studies have documented a broad range of cognitive performance deficits in children with prenatal alcohol exposure using traditional cognitive and neuropsychological assessments. A few recent studies have used structural and functional magnetic resonance imaging (MRI) to identify impairment in brain structures and regions that may be involved in these alcohol-related deficits in cognitive function (e.g., Archibald et al., 2001; Fryer et al., 2007; Meintjes et al., 2007; Sowell et al., 2001). One methodology for examining the neural correlates underlying observed cognitive deficits that is particularly under-represented in the FASD literature is event-related potentials (ERPs). ERPs, which are derived from an electroencephalogram (EEG) recording, reflect task-specific changes in brain electrical activity (i.e., activity associated with stimulus or response onset). By contrast to the superior spatial resolution of MRI, ERPs provide a millisecond precision with which multiple constituent processes underlying cognitive function can be identified, essentially capturing the neural signature associated with a given process as it reaches the scalp recording electrodes.

In the alcohol literature, ERP studies have been conducted primarily on adults with chronic alcoholism (e.g., Begleiter et al., 1984; 1987). One consistent finding has involved a reduction in the P3 component on the auditory oddball paradigm, which has been found in chronic, abstinent alcoholics (e.g., Cohen et al., 1995). This finding has also been replicated

in both younger and older children at risk for developing alcoholism (Begleiter et al., 1984; 1987; Porjesz and Begleiter, 1990), suggesting that a reduced P3 may be a useful biomarker for susceptibility to alcoholism. Because these studies were concerned with understanding possible genetic contributions to the P3 in the context of a family history of alcoholism, children whose mothers drank during pregnancy were excluded, precluding information regarding the impact of prenatal alcohol exposure. In one study designed to address the question of prenatal alcohol exposure (Kaneko et al., 1996), a reduced P3 in an auditory oddball paradigm was also found to be characteristic of children with FAS. This reduction was not seen in a comparison group with Down syndrome, suggesting that ERP could have utility for differential diagnosis.

Regardless of specific task requirements, ERPs often elicit a P2-N2-P3 complex, a series of voltage fluctuations (positive-negative-positive) that follow the onset of the stimulus, with each component reflecting different processes associated with task demands (e.g., Kalayam et al., 1998). In visual tasks, P2, a positive voltage deflection over frontal-central scalp that occurs ~200 ms after stimulus onset, is thought to play a role in visual selection, comparison, analysis, and integration (Barcelo et al., 1997). P2 is generally considered to be an obligatory component that primarily reflects perceptual processes related to stimulus identification (Kranczioch et al., 2003), but it may reflect both exogenous (i.e., stimulus-related) and endogenous (e.g., attentional) processes (Fabiani et al., 2000). We have recently reported ERP data from a visual Go/No-go task, indicating that slower P2 latency is characteristic of children with FAS or partial FAS (PFAS). These data suggest that children with fetal alcohol exposure may be slower in the initial analysis of stimulus meaning necessary to determine whether to execute or inhibit a response (Burden et al., 2009).

By contrast, the subsequent frontally-oriented negative deflection, N2, is generally associated with cognitive control, including the focusing of attention and suppression of competing information from distracter stimuli (Luck and Hillyard, 1994). There is debate in the literature as to whether N2 in a response inhibition paradigm reflects the active inhibition of a response (Falkenstein et al., 1999; Jodo and Kayama, 1992), other processes related to stimulus evaluation and decision-making (Nakata et al., 2005; Nieuwenhuis et al., 2003), or both. FN400 is an N2-like component elicited in visual memory paradigms, which also appears to play a general role in cognitive control/decision-making (Rugg and Curran, 2007). The FN400 is a negative deflection seen when contrasting responses to new vs. old items and is thought to reflect the process of familiarity, which varies on a continuum of signal strength in determining whether or not an item is recognized.

The P3, which has a number of different names depending on its scalp orientation, peak latency, and relation to task demands (e.g., P3a, P3b, P300, P450), is generally thought to serve as an index of the processing demands placed on the participant, thereby reflecting the relative amount of attention allocated to the task (Donchin et al., 1986). The positive-deflecting P3 typically occurs 300-600 ms after stimulus presentation and is often maximal at the parietal scalp region. In response inhibition tasks, amplitude differences in P3 also appear to reflect inhibitory control (e.g., Bokura et al., 2001; Burden et al., 2010; Davis et al., 2003; Eimer, 1993). In memory tasks, the P3-like component tends to occur somewhat later in relation to stimulus onset, and, due to its purported functional role in the memory retrieval process and distinct morphology, is typically referred to as the late positive component (LPC). Consistent with the general notion of P3, the larger LPC amplitude seen for old items vs. new, unfamiliar ones suggests that increased activation of this component reveals recognition memory (Rugg and Curran, 2007). By contrast to the FN400 familiarity effect, the LPC old-new effect is believed to be associated with the conscious and explicit recollection aspect of memory (Rugg and Curran, 2007).

We have previously used an ERP Go/No-go task to examine response inhibition in two samples of individuals with prenatal alcohol exposure. The first sample consisted of 7 heavily exposed 11-year-old children from Cape Town, South Africa, with FAS or PFAS and 6 age-matched non-exposed controls; the second, 31 young adults from Detroit, Michigan, who were prenatally exposed to alcohol at moderately-to-heavy levels and 47 whose mothers abstained or drank only minimally during pregnancy. In the heavily exposed Cape Town cohort, the children with FAS or PFAS showed a slower latency to P2, suggesting less efficient processing of visual information, and smaller P2 and N2 amplitudes, the former suggesting less efficient perceptual discrimination, the latter a less well-defined, coherent strategy in decision and execution of response inhibition (see Burden et al., 2009). Both groups showed the expected larger P3 amplitude during response inhibition (the “No-go” condition), but the FAS/PFAS group also showed a more prolonged late positive slow wave, suggesting increased cognitive effort. By contrast, the exposed and control groups did not differ on the ERP wave forms in the Detroit cohort (Burden et al., 2010), either because the participants were less heavily exposed and/or because they were older.

In this study, we examine behavioral performance and ERPs in a sample of 11-year-old Inuit children from Arctic Quebec whose mothers engaged in binge drinking during pregnancy (ALC) compared with controls whose mothers did not (CON). The exposure levels were higher than in the Detroit study but lower than in Cape Town. A broad range of potential confounding influences were considered, including socioenvironmental variables and other pre- and postnatal exposures (e.g., cigarette smoking, illicit drugs, environmental neurotoxicants). Two different cognitive tasks—Go/No-go and a Continuous Recognition Memory Task (CRT)—were administered. Both of these tasks were expected to elicit a P2-N2-P3 complex, but we adopted the terms FN400 and LPC for the memory task to be consistent with existing conventions in the literature (Rugg and Curran, 2007). Based on previous studies of visual Go/No-go using the same paradigm (Burden et al., 2009; Davis et al., 2003), we expected a larger P3 amplitude to No-go vs. Go in both groups. In addition to these stimulus-locked averages based on trials with correct responses, whose timing is based on latency from onset of stimulus presentation, error processing can be studied by examining ERP responses measured immediately following incorrect button presses (see Gehring et al., 1993). The timing for error processing ERPs is response locked; that is, it is determined by latency from onset of the incorrect button press. In the Go/No-go task, we expected to see error-related negativity (ERN) and positivity (Pe) waveforms, which have been shown to be associated with error detection and awareness, respectively, in both groups (Falkenstein et al., 1999; Overbeek et al., 2005).

Based on our findings on the Go/No-go task in children with FAS and PFAS in South Africa, (Burden et al., 2009), we expected to see reduced P2 latency, reduced P2 and N2 amplitudes, and a more prolonged positive slow wave in the alcohol-exposed Inuit children in this study compared with controls. Given the evidence of memory and attention deficits in neuropsychological assessments of children with FASD, we expected the alcohol-exposed children to exhibit a smaller LPC or P3 amplitude than controls on the CRT task, reflecting poorer recognition memory.

METHODS

Participants

Two hundred seventeen Inuit children from Northern Quebec (116 girls; M age = 11.3 years, SD = 0.6, $range$ = 9.8 to 12.9 years) participated as part of a larger study on the effects of prenatal exposure to environmental contaminants (Jacobson et al., 2008; Muckle 2001a, 2001b). The children were recruited from among those whose families had participated in

the Arctic Monitoring Assessment Program, a public health surveillance program in which umbilical cord blood samples collected between 1994 and 2002 were analyzed for environmental contaminants (Muckle et al., 1998). Cord blood samples were obtained from all women who delivered their infants at one of the two hospitals located in Inuit villages in Northern Quebec. The children from 70.0% of the families invited to participate in this study were examined at school age; 1.0% had died, 13.5% refused, 5.5% had moved away from the region, and 10.0% could not be located. Data were collected in the three largest villages in the region (Puvirnituk, Inukjuak, and Kuujuaq), and children from smaller, more remote villages traveled with their caregiver by plane to the nearest large village for testing.

Of the 217 children who participated, 5 (2%) declined the ERP capping procedure and were not tested. Of the 212 children tested, 134 (63%) provided a sufficient number of trials after artifact rejection/correction for ERP analyses related to correct (≥ 10) and incorrect (≥ 8) trials on the Go/No-go task (further details provided in Data Analysis below). For the CRT task, 143 (67%) children had acceptable ERP data relating to correct responses.¹ The percentage of children providing usable ERP data on these tasks compares favorably with other ERP studies performed at this age (e.g., Coch et al., 2002; Czernochowski et al., 2005; Hepworth et al., 2001). Among the children with acceptable ERP data, maternal reports of drinking during pregnancy were available for all but 32 (23 who were adopted and 9 who were accompanied to the 11-year assessment by the father, grandparent, or other relative). Among the 134 children with acceptable Go/No-go data, 27 were missing maternal alcohol reports, for a total of 107. Among the 143 with acceptable CRT data, 29 were missing, for a total of 114. Sample characteristics are described for the 139 children whose prenatal alcohol exposure was documented and provided usable data on one or both of the tasks.¹

Each mother was interviewed at the 11-year assessment regarding her alcohol consumption during pregnancy, using a timeline follow-back approach to determine incidence and amount of drinking on a day-by-day basis during a typical week (Jacobson et al., 2002; Sokol et al., 1985). Volume was recorded for each type of beverage consumed and converted to oz of absolute alcohol (AA), using multipliers developed by Bowman et al. (1975). Based on these data, we computed a summary measure of average oz AA per day across pregnancy. Average alcohol consumed per occasion was measured by dividing total AA by number of drinking days during the pregnancy. Among the 139 children whose data were analyzed in this study, 59 (42.4%) of the mothers reported drinking on at least one occasion during pregnancy and, among these, 38 (64.4%) reported one or more incidents of binge drinking (≥ 4 drinks per occasion). Given that the pattern of drinking in this community primarily involves binge drinking, we compared children born to binge drinkers (referred to as the alcohol-exposed or "ALC" group) with those whose mothers did not binge during pregnancy (the control group, referred to as "CON"). Eighty (79.2%) of the mothers in the control group abstained from drinking alcohol during pregnancy, and the other 21 drank only minimally. Median exposure for the children born to light drinkers was 2.4 drinks consumed on a median of 3 occasions during pregnancy. By contrast, median exposure for those born to binge drinkers was 7.6 drinks on a median of 24 occasions.

¹The 139 children with acceptable ERP data whose prenatal alcohol exposure was documented did not differ from the 39 children with exposure data whose ERP data were not acceptable in terms of prenatal alcohol exposure, gender, age at assessment, village of residence (local vs. remote), SES, maternal age at delivery, maternal intellectual competence (Peabody Picture Vocabulary Test; Raven Progressive Matrices), or prenatal or current DHA (all p 's $> .20$). The principal differences were higher IQ scores for those with acceptable data ($M = 93.3$ vs. 84.7 , $t = 3.66$, $p < .001$) and higher years of maternal education ($M = 8.9$ vs. 8.1 , $t = 1.98$, $p < .05$). The children with acceptable data also had lower levels of prenatal exposure to PCBs ($t = 2.41$, $p < .05$), mercury ($t = 2.48$, $p < .05$), and lead ($t = 2.78$, $p < .01$) and lower levels of current maternal smoking ($t = 2.32$, $p < .05$).

ERP Tasks

Go/No-go—The Go/No-go task used in this study was based on a functional MRI paradigm used by Casey et al. (1997) to assess response inhibition, which was subsequently adapted for ERP by Davis et al. (2003). Children were instructed to press a button to all individually-presented letters (the “Go” trials) except the target “X” (the “No-go” trials). Stimulus presentation proceeded at a set rate, with the stimulus on screen for 500ms, off for 1100ms, and an average random intertrial interval (ITI) of 200ms (range: 100-300 ms). Children were presented with 220 total consecutive trials. The first block consisted of 40 Go trials, which served to prime Go responses within the second 180-trial block. This second block, referred to as the response inhibition condition (Casey et al., 1997; Davis et al. 2003), consisted of 126 Go trials (70%) randomly intermixed with 54 No-go trials (30%).² Data from the initial block of 40 Go trials were not analyzed. All responses occurring between 100 and 1600 ms post-stimulus onset were considered valid.

CRT—For the CRT task, the child pressed either a “New” or “Old” response button depending on whether s/he remembered seeing the picture in a previous trial. Stimuli, which consisted of both abstract (unnamable) and concrete (namable) objects, were on for 500 ms, off for 3000 ms, with an average random ITI of 200ms (range: 100-300 ms), and presented in continuous fashion over 3 blocks of 89 trials. The analyses focused on the 120 stimuli that were presented twice within each block at lags of 2, 5, or 10 intervening items, equally counterbalanced across blocks. “New” items were counted as those that were seen for the first time; “Old” items, the second time. The additional 27 filler items (e.g., presented only one time or at a different lag) were not analyzed. All responses occurring between 100 and 2000 ms post-stimulus onset were considered valid.

Task Procedure

Each child was seated 57cm from a 17-inch LCD flat panel monitor on which the stimuli were displayed, centered on screen within a 7-cm² space. A short practice round was administered prior to each task to ensure that the child understood the instructions, repeated if necessary. The child was instructed to respond as quickly and accurately as possible and to sit still and not make any sounds during testing. The entire Go/No-go task, including instructions and practice, took approximately 10 minutes to complete; the entire CRT task, 25 minutes.

Electroencephalogram (EEG) Collection and ERP Derivation

EEGs were recorded from 26 scalp electrodes mounted in a close-fitting cap (Electro-Cap International) using an array based on the 10-20 system (Jasper, 1958). The electrodes comprised anterior-frontal (AF3, AF4, AF7, AF8, F7, F8) frontal (F3, Fz, F4), fronto-central (FC1, FCz, FC2), central (C3, Cz, C4), temporal (T3, T4, T5, T6), parietal (P3, Pz, P4), parieto-occipital (POz), and occipital (O1, Oz, O2) scalp sites plus the left and right mastoids (M1, M2), earlobes (A1, A2), nose, and a ground electrode. Cz was the reference lead during acquisition. Electrooculogram (EOG) was recorded from bipolar miniature electrodes placed vertically above and below the right eye for the purpose of artifact detection. Impedance for all scalp and EOG electrodes was kept below 10 kOhm. EEG and EOG were acquired using a Grass Neurodata Acquisition System and amplified using Model

²Of the 212 children tested, the first 38 were presented with only 150 total trials, but the ratio of Go to No-go trials was the same: 40 Block 1 Go (100%), 77 Block 2 Go (70%), and 33 Block 2 No-go (30%). The task was extended to 220 trials to allow additional opportunities for errors, thus increasing the number of children who made enough errors to enable us to analyze ERPs in relation to incorrect as well as correct responses. Alcohol exposure was distributed similarly in the 38 children who completed the shorter and the 174 who completed the longer version of the task, $\chi^2(1) = 1.37, p > .15$, and the two groups did not differ on any of the ERP latency and amplitude measures presented in Table 2 (all p 's $> .15$).

15A54 quad AC amplifiers with a gain of 50,000 for scalp leads and 5,000 for EOG. The bandpass filter was 0.1-30 Hz, and a 60-Hz notch filter was engaged. Data were sampled every 5 ms (200 Hz).

ERP data were digitized online and then edited by computer algorithm. Prior to averaging, trials with excessive artifact (i.e., EEG > ± 125 mV) were rejected. Data were then re-referenced to linked earlobes, and EOG-related artifact was corrected (Gratton et al., 1983). There was a baseline recording period of 100 ms prior to stimulus onset, and individual trials were baseline corrected and subsequently averaged for each participant within each condition. Based on visual inspection of individual and averaged waveforms, individual cross-averages were accepted or rejected on the basis of excessive ear (linked earlobes), eye (vertical EOG), or suspected movement artifact that appeared to bias the waveform. A minimum of 10 usable ERP trials across conditions was imposed for analyses relating to correct responses in both tasks; a minimum of 8 usable ERP trials was required for inclusion in the error-related analyses on Go/No-go. All criteria were imposed blind with respect to alcohol group status.

Automatic detection was used to identify peak amplitude or area (μ V) and latency to peak (ms) associated with the stimulus-locked P2-N2-P3 complex elicited by both tasks at central (C3, Cz, C4), frontal (F3, Fz, F4), and parietal (P3, Pz, P4) scalp electrodes, respectively. Component windows for peak and latency detection were specified as follows: for Go/No-go, P2 (200 to 400 ms), N2 (325 to 500 ms); for CRT, P2 (250 to 400 ms), N2 (or FN400; 300 to 500 ms). Area measures (i.e., average μ V within the specified window) were used for Go/No-go P3 (400 to 700 ms) and CRT P3 (or LPC; 500 to 800 ms). For error-related analyses on Go/No-go, response-locked averages were used to compare peak ERN (incorrect No-go, 0 to 125 ms) at frontal leads (F3, Fz, F4) and Pe (incorrect No-go, 100 to 500 ms) at central leads (C3, Cz, C4). Stimulus-locked components were segmented 100 ms before and 1,000 ms after the onset of the stimulus; response-locked components were segmented 300 ms before and 500 ms after button press. Peak amplitude measures represent mean activity surrounding the peak (± 5 ms) within the component's specified time window.

Data Analysis

For Go/No-go, accuracy (% correct) and reaction time (RT) were computed for the Go and No-go conditions; ERP analyses focused on these two conditions as well as on a comparison of incorrect No-go vs. correct Go. For CRT, correct Old (old item, response = "old") and false alarms (FA; new item, response = "old") were used to compute d' -prime (discrimination) and C (bias) for behavioral performance measures. D' -prime measures number of correct button presses, adjusted for false alarms, to correct for any tendency to press the same button regardless of whether the stimulus being displayed is old or new. Bias measures the tendency to press the same button repeatedly without regard to the stimulus displayed. RT was also measured in both conditions. ERPs were examined for correct Old and correct New (new item, response = "new"). Preliminary analyses showed that the abstract-concrete and three lag conditions all produced very similar Old-New effects. The Old and New items were, therefore, collapsed across item type and lag in the data analysis.

All statistical analyses were conducted using SPSS 9.0. Mixed design repeated measures analysis of variance (ANOVA) was used to assess behavioral task performance for correct responses (%) and mean reaction time (RT) in separate 2 (group: ALC, CON) $\times$ 2 (condition) analyses, with group as the between-subjects factor and condition as the within-subjects factor. The repeated factor was used to evaluate overall condition effects on the task; planned group comparisons were made separately for individual conditions. For ERPs, mixed design repeated measures analysis of variance (ANOVA) was used to assess peak or

average amplitude (μV) and latency to peak (ms) of each component of interest, with group as the between-subjects factor and electrode region and condition as within-subjects factors. The electrode region in the analysis was either frontal (F3, Fz, F4), central (C3, Cz, C4), or parietal (P3, Pz, P4), depending on where the response involving the component in question appeared maximal. All F - and p -values are Greenhouse-Geisser adjusted to correct for lack of homogeneity in the variances among multiple scalp recording sites, as is commonly applied in ERP studies assessing component differences at multiple leads. Although multiple interactions often emerge when analyzing multiple electrodes that differ across conditions, these interactions can be ambiguous and are not readily interpretable (see Luck, 2005; McCarthy and Wood, 1985); therefore, even though the full model was retained in the ANOVA model from which results are reported, we only present relevant within-subjects effects for the sake of parsimony. For all analyses, partial η^2 was used as the measure of effect size.

To account for possible confounding influences, outcomes that were identified as being sensitive to prenatal alcohol exposure group were also tested in relation to 22 control variables. Twelve child control variables were assessed: gender; age at assessment; IQ assessed on the Wechsler Intelligence Scales for Children, 4th edition (WISC-IV), adapted for Inuit culture³; village of residence (local, i.e., where testing took place, vs. remote, i.e., flown in by airplane); and pre- and postnatal exposure to three environmental contaminants (polychlorinated biphenyls (PCBs), mercury (Hg), and lead (Pb) and an omega-3 fatty acid (docosahexaenoic acid (DHA) prevalent in the Inuit diet that has been shown to be important for cognitive development (Colombo et al., 2004; Jacobson et al., 2008; O'Connor et al., 2001). The contaminant and DHA exposures were assessed in umbilical cord and 10-year blood samples obtained from the children. Eleven maternal control variables were assessed: age at delivery, marital status, socioeconomic status (SES; Hollingshead, 1975), years of education, verbal competence (Peabody Picture Vocabulary Tests score), nonverbal intellectual competence (Raven Progressive Matrices), prenatal and current use of cigarettes and marijuana, and current binge drinking (present/absent) (see Table 1). For each outcome measure on which the exposure groups differed, the mixed-design repeated measures ANOVA was re-run as an analysis of covariance (ANCOVA) that adjusted statistically for all control variables that differed even marginally (at $p < .10$) between the groups. Given the potential for multicollinearity between prenatal alcohol exposure and current maternal drinking, current drinking was not treated as a routine control variable. Because current drinking was not related to any of the ERP outcomes associated with binge exposure during pregnancy (all p 's $> .10$), it was not considered a potential confounder of any of the observed effects.

RESULTS

Background Characteristics

Table 1 provides information on the demographic characteristics for the 139 children whose prenatal alcohol exposure was documented and provided usable ERP data on the Go/No-go and/or CRT tasks. Although the two groups were generally similar in terms of child characteristics, the CON group showed higher values than the ALC group on prenatal exposure to both PCBs, $F(1,132) = 7.57, p < .01, \eta_p^2 = .05$, and Hg, $F(1,135) = 10.24, p < .01, \eta_p^2 = .07$; the higher PCB level in the CON group was also seen at the 11-year assessment, $F(1,134) = 6.27, p < .05, \eta_p^2 = .05$. Regarding maternal characteristics, mothers

³Seven WISC-IV subtests were administered to assess Perceptual Reasoning, Working Memory, and Processing Speed. Because the WISC-IV Verbal Comprehension subtests were not appropriate for Inuit culture, verbal comprehension was assessed using the Boston Naming Test and Delis-Kaplan Verbal Fluency Test, which were adapted by substituting culturally-relevant vocabulary where necessary.

in the ALC group were, on average, 4 years younger at delivery than those in the CON group, $F(1,137) = 14.52$, $p < .001$, $\eta_p^2 = .10$. The analyses in Table 1 were also run breaking down maternal drinking during pregnancy into three groups: abstainers, light drinkers, and binge drinkers. The only group differences were those that had already been seen in the two-group comparison shown in Table 1. In post hoc analyses comparing abstainers vs. light drinkers on those measures, no differences were seen between the abstainer and light drinker groups (all p 's $> .10$).

Although no data regarding changes in pattern of drinking across pregnancy are available for this sample, in a sample of binge drinkers from another cohort from this population (Jacobson et al., 2008), frequency of binge drinking declined from a median of 4.7 binges/month prior to pregnancy recognition to 1.3 and 1.2 binges/month during the first and second trimesters, respectively. Binge drinking declined further to a median of 0.6/month during the third trimester, increasing to 1.2/month at the end of the first postpartum year. By the 11-year assessment in the present sample, current maternal binge drinking in the CON group had increased to become as prevalent as in the ALC group during pregnancy (i.e., ~2 binges/month), while frequency of binge drinking in the ALC group had increased to more than twice that in the CON group at 11 years, $F(1,137) = 19.20$, $p < .001$, $\eta_p^2 = .12$ (see Table 1).

Go/No-go

Behavioral performance—There were significant main effects of condition for both accuracy and RT but no alcohol exposure group differences for the Go/No-go behavioral performance measures. Overall, children were less accurate at correctly inhibiting No-go ($M = 65.2\%$) compared to correctly pressing the button to Go ($M = 92.6\%$), $F(1,105) = 516.12$, $p < .0001$, $\eta_p^2 = .83$, and failures to inhibit to the No-go stimulus (false alarms) were faster ($M = 393$ ms) than correct presses to Go ($M = 462$ ms), $F(1,105) = 173.93$, $p < .0001$, $\eta_p^2 = .62$. Means (SDs) for each group and the group difference statistics are presented in Table 2.

ERP findings—Figure 1 shows the ERP waveforms for correct Go and No-go responses by group. P2 peak amplitude (μV) at the central leads (C3, Cz, C4) was larger for No-go ($M = 10.7$) vs. Go ($M = 9.5$), $F(1,105) = 6.90$, $p < .01$, $\eta_p^2 = .06$. There was also an overall effect on P2 latency (ms), with Go ($M = 258$) faster than No-go ($M = 265$), $F(1,105) = 4.46$, $p < .05$, $\eta_p^2 = .04$. The groups differed in P2 latency averaged across condition, with the ALC group ($M = 270$) showing a slower P2 than CON ($M = 253$), $F(1,105) = 8.42$, $p < .01$, $\eta_p^2 = .07$. ANOVAs conducted separately for the two conditions showed that this alcohol effect was present for both Go and No-go (see Table 2). There were no effects on N2 amplitude. N2 latency (ms) for No-go ($M = 364$) was faster than Go ($M = 387$), $F(1,105) = 11.96$, $p < .001$, $\eta_p^2 = .10$, and there was a group $\times$ condition interaction, $F(1,105) = 4.00$, $p < .05$, $\eta_p^2 = .04$, which was due to a larger Go vs. No-go difference in N2 latency for ALC (M difference = 36 ms) vs. CON (M difference = 10 ms) (see Table 2). For P3 area (μV), the expected condition difference was present, with No-go ($M = 7.1$) larger than Go ($M = 2.5$), $F(1,105) = 58.67$, $p < .0001$, $\eta_p^2 = .36$. There were no group differences at the parietal leads (see Table 2). There were also no group effects for ERN or Pe amplitudes (Table 2)—both groups showed large, robust error-related responses (see Figure 2).

As seen in Table 1, the ALC and CON groups differed on four potential confounding variables unrelated to alcohol use—prenatal PCBs, prenatal Hg, 11-yr PCBs, and maternal age. After controlling for these potential confounders simultaneously in ANCOVAs, the slower P2 latency seen the ALC group continued to be significant in both conditions: Go, $F(1,96) = 5.76$, $p < .05$, $\eta_p^2 = .06$; No-go, $F(1,96) = 6.63$, $p < .05$, $\eta_p^2 = .07$.

Although the groups did not differ in No-go P3 amplitude at the parietal leads where the ERP response appeared maximal, we conducted an exploratory post hoc analysis based on visual inspection of electrodes Cz and C4, a region in which the ALC group appeared to show a diminished No-go response (see Figure 1). After controlling for the four potential confounders on which the ALC and CON groups differed, the adjusted mean No-go P3 (μV) was significantly smaller in this right-central region for the ALC ($M = 5.1$) vs. CON group ($M = 7.8$), $F(1,96) = 4.23$, $p < .05$, $\eta_p^2 = .04$.

The ERP components with significant group differences were re-examined in bar graphs to compare the responses of the control children born to mothers who drank only at low levels during pregnancy with those whose mothers abstained and those who binge drank (Figure 3). In three of the four comparisons, the responses of the children of the light drinkers were more similar to those of the children born to abstainers than to those whose mothers engaged in binge drinking during pregnancy. None of the effect sizes for alcohol exposure in these three-group comparisons differed from the effect sizes for the two-group analyses by more than 1%.

CRT

Behavioral performance—For CRT, the children were more accurate at correctly identifying New items ($M = 76.7\%$) than Old ($M = 67.5\%$), $F(1,112) = 33.98$, $p < .0001$, $\eta_p^2 = .23$. There was reliable discrimination of “old” vs. “new” responses, $d\text{-prime} = 1.31$, and little bias towards one button press or the other, overall $C = 0.16$. There was also a significant slowing down for correct Old ($M = 812$) vs. correct New ($M = 783$), $F(1,112) = 16.48$, $p < .0001$, $\eta_p^2 = .13$. As seen in Table 3, there were no differences by group on any of these behavioral measures.

ERP findings—Figure 4 shows the ERP waveforms for correct New and Old responses by group. P2 peak amplitude (μV) at the central leads (C3, Cz, C4) was larger for Old ($M = 3.3$) vs. New ($M = 0.6$), $F(1,112) = 42.45$, $p < .0001$, $\eta_p^2 = .28$, for the sample as a whole. There was also a significant group difference, with the ALC group showing a larger P2 averaged across conditions ($M = 3.2$) compared to CON ($M = 0.7$), $F(1,112) = 4.21$, $p < .05$, $\eta_p^2 = .04$. The group differences on P2 amplitude examined separately by condition fell just short of statistical significance (Table 3). There were no condition effects on P2 latency. However, there was a trend for slower P2 latency (ms) averaged across condition in the ALC ($M = 302$) vs. CON group ($M = 293$), $F(1,112) = 2.82$, $p = .10$, $\eta_p^2 = .03$, which appeared to be due primarily to an effect on responses to the New stimuli (Table 3). As expected, the FN400 peak amplitude (μV) at the frontal leads (F3, Fz, F4) was greater for New stimuli ($M = -13.7$) than Old ($M = -11.6$), $F(1,112) = 20.25$, $p < .0001$, $\eta_p^2 = 0.15$. There was also a significant effect of group on FN400 amplitude averaged across condition, with the ALC group showing a smaller FN400 ($M = -11.5$) compared to CON ($M = -13.8$), $F(1,112) = 4.21$, $p < .05$, $\eta_p^2 = .04$, a difference that was attributable solely to a group difference in response to the New items (Table 3). There were no condition or group effects on FN400 latency. Also as expected, the LPC at the parietal leads (P3, Pz, P4) showed a larger area amplitude (μV) for Old ($M = 12.3$) vs. New ($M = 9.3$), $F(1,112) = 54.02$, $p < .0001$, $\eta_p^2 = .33$. There was also a significant effect of group, with the ALC group showing a smaller LPC averaged across condition ($M = 9.6$) compared to CON ($M = 12.0$), $F(1,112) = 4.16$, $p < .05$, $\eta_p^2 = .04$, a difference that was attributable solely to the group difference on the Old items (Table 3).

After controlling for the four potential confounders identified above, the ALC group continued to show a significantly larger overall peak amplitude on P2, $F(1,102) = 4.73$, $p < .03$, $\eta_p^2 = .04$, and a smaller FN400 peak amplitude in response to the New stimuli, $F(1,102)$

$= 6.17, p < .05, \eta_p^2 = 0.06$. For the LPC Old area measure, the effect of a reduced amplitude in the ALC group fell just short of statistical significance after controlling for these potential confounders, $F(1,102) = 3.86, p = .052, \eta_p^2 = .04$.

The ERP components with significant group differences on CRT were re-examined in bar graphs to compare the responses of the control children born to mothers who drank only at low levels during pregnancy with those whose mothers abstained and those who binge drank (Figure 3). In four of the five comparisons, the responses of the children of the light drinkers were clearly more similar to those of the children born to abstainers than to the children born to mothers who binge drank. None of the effect sizes for alcohol exposure in these three-group comparisons differed from the effect sizes for the two-group analyses by more than 1%.

DISCUSSION

In this study, ERPs were measured on two different neurocognitive tasks in children whose mothers reported binge drinking during pregnancy and age-matched controls. In the Go/No-go response inhibition task, all children were more accurate in responding to the Go stimuli than in inhibiting their response to the No-go “X” stimulus, and reaction time was faster on the No-go trials in which the child failed to inhibit than on the correct Go button presses. These types of errors have been attributed to impulsive responding (Coles et al., 2001) and are likely the result of failing to extract of all the information necessary from a given stimulus prior to responding (cf. Gratton et al., 1988). Similar to previous ERP findings on this task (Burden et al., 2009; Davis et al., 2003), a large P3 effect was seen, with No-go amplitude larger than Go, presumably due to the increased attentional engagement required to actively inhibit a response (e.g., Bokura et al., 2001; Eimer, 1993). On the CRT task, the behavioral performance measures indicated reliable memory performance in both groups (i.e., more correct hits than false alarms) and, as expected, the children took more time to correctly identify old vs. new stimuli. The two expected ERP effects were also seen on this task—a larger FN400 to new vs. old items, suggesting the presence of familiarity; and a larger LPC amplitude to old vs. new items, which likely reflects the recollection of the specific item (Rugg and Curran, 2007).

The alcohol-exposed and control groups did not differ behaviorally on reaction time or accuracy on either test. The absence of behavioral differences is consistent with the findings in the more heavily exposed Cape Town cohort, where neural processing differences were found on the ERP measures even though behavioral performance was not impaired on this relatively simple response inhibition task (Burden et al., 2009). As in Cape Town, differences between the alcohol-exposed and control children were seen on several ERP measures. For Go/No-go, a slower P2 latency was seen in the alcohol-exposed children at central scalp for both the Go and No-go conditions. P2, which is thought to be involved in the initial visual processing of a stimulus (e.g., Barcelo et al., 1997), may be an index of the efficiency with which the meaning of the stimulus is extracted. Although the task used in the Cape Town study was slower paced, the stimulus-locked P2 emerging with the visual presentation of the Go and No-go stimuli was also maximal over central scalp, and the FAS/PFAS group showed the same slower P2 latency (Burden et al., 2009). This finding is also consistent with behavioral measures from several studies indicating slower information processing speed in infants and children with fetal alcohol exposure (e.g., Burden et al., 2005a; Jacobson et al., 1993, 1994; Kable and Coles, 2004; Streissguth et al., 1994). The replication and extension of this P2 latency effect from the Cape Town study in a faster-paced but highly similar response inhibition paradigm with children exposed to alcohol at lower levels suggests that slower P2 latency may warrant consideration as a potentially useful biomarker across a range of fetal alcohol exposure.

By contrast to the P2 latency effect, the relation of fetal alcohol exposure to reduced P2 and N2 amplitude found on the Go/No-go task in the Cape Town cohort (Burden et al., 2009) were not seen in the less heavily exposed Inuit children. As in both the Cape Town and Detroit cohorts, the exposed and control groups did not differ in No-go P3 amplitude measured at the parietal leads on this task which, as expected, was where the ERP response was maximal, although there was evidence of a diminished P3 response in the No-go condition at central leads, suggesting that the alcohol-exposed children were not processing the inhibition stimulus as fully or efficiently as controls. In the error-related analyses, both groups produced a similar ERN and Pe, indicating no difference in error monitoring or error awareness.

On the CRT task, the alcohol-exposed children exhibited increased P2 amplitude and reduced amplitude for both FN400 and LPC. As noted above, the FN400 on the CRT is considered equivalent to the N2 and the LPC to the P3. The larger P2 amplitude in the alcohol-exposed group suggests that these children need to exert greater cognitive effort in stimulus identification (Kranzloch et al., 2003), which is particularly challenging in this task, in which both concrete (namable) objects and abstract figures are displayed. The reduced FN400 amplitude suggests poorer selective attention in the context of stimulus evaluation and decision making (Luck and Hillyard, 1999; Rugg and Curran, 2003).

In addition to these earlier components, which are involved primarily in selective attention and perceptual processing, the alcohol-exposed children showed reduced LPC (or P3) amplitudes on the CRT task, indicating alterations in neural processing of relatively later cognitive processing, particularly memory retrieval. Although lower P3 amplitudes have been found in adults with alcoholism (Begleiter et al., 1984; 1987; Cohen et al., 1995; 1997; Porjesz and Begleiter, 1990) and children with FAS (Kaneko et al., 1995) on the auditory oddball paradigm, to our knowledge, our finding is the first to demonstrate reduced P3 amplitudes in association with binge drinking during pregnancy in children who do not meet diagnostic criteria for FAS. Although it is unclear what mechanism might be responsible for this finding, future studies using larger and denser ERP arrays may be able to use source localization to more precisely pinpoint specifically affected brain regions. At this point, we can conservatively suggest that the reduced FN400 and LPC amplitudes in the alcohol-exposed group represent a reduction in synchronous neuronal firing during processing at these key cognitive stages.

One limitation of this study is that prenatal alcohol exposure was assessed by retrospective maternal report rather than from information obtained contemporaneously during pregnancy. Although a continuous measure based on quantity of alcohol ingested would have enabled us to examine dose-response and threshold, whether the mother engaged in binge drinking during pregnancy can presumably be recalled more reliably than how much she drank per occasion when assessed 11 years after delivery. One notable strength of this study is that the ERP data go beyond standard neuropsychological tests to identify specific stages of information processing that are adversely affected by prenatal alcohol exposure. Thus, these data extend findings linking fetal alcohol exposure to poorer response inhibition to suggest that one important component of information processing that impairs response inhibition performance relates to reduced efficiency in extracting information from visual stimuli. On the other hand, contrary to what might have been expected, prenatal alcohol exposure did not predict poorer error monitoring or awareness in this study. Similarly, building upon reports linking fetal alcohol exposure to poorer declarative memory, these ERP findings identify greater cognitive effort in stimulus recognition and reduced neural activation during memory retrieval as two key elements of recognition memory processing that appear to be targeted by prenatal alcohol.

In conclusion, these findings suggest that fetal alcohol exposure is associated with altered neurophysiological processing in tasks involving both response inhibition and recognition memory even when behavioral performance is unaffected. The consideration of potential confounding by a broad range of control variables in the analyses performed in this study, including smoking and marijuana use during pregnancy, current maternal alcohol use, SES, and prenatal exposure to environmental contaminants, provides evidence that these effects are specifically attributable to prenatal alcohol exposure. Our data suggest that increased P2 latency and the reduced amplitudes associated with the later cognitive components are indicative of alterations in fundamental neural processes that may mediate the well-documented effects of fetal alcohol exposure on cognitive function.

Acknowledgments

We thank Renee Sun, Line Roy, Brenda Tuttle, Alacie Puv, and Dave Saint-Amour for their contributions in meeting the challenges involved in collecting these data in Arctic Quebec; Jocelyne Gagnon and Neil Dodge for their contributions in assembling the data set; and the Inuit community and families for their willingness to participate. Research support: grants from the NIH/National Institute of Environmental Health Sciences (R01-ES007902); Northern Contaminants Program, Indian and Northern Affairs, Canada; NIH/National Institute on Alcohol Abuse and Alcoholism National Research Service Award (F32-AA14730); and the Joseph Young, Sr., Fund from the State of Michigan.

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Fig. 1. Go/No-go stimulus-locked grand means for correct Go (gray) and No-go (black) for CON (thin) and ALC (bold) groups; y-axis, μV (positive up); x-axis (ms). Arrows illustrate example components at midline electrodes.

Fig. 2. Go/No-go response-locked grand means for correct Go (gray) and incorrect No-go (black) for CON (thin) and ALC (bold) groups; y-axis, μV (positive up); x-axis (ms). Arrows illustrate example components at midline electrodes.

Fig. 3. Comparison of ERP responses among children born to mothers who abstained, drank at low levels, or binge drank during pregnancy for the nine ERP components found to relate to binge drinking in Tables 2 and 3.

Fig. 4. CRT stimulus-locked grand means for correct New (gray) and Old (black) for CON (thin) and ALC (bold) groups; y-axis, μV (positive up); x-axis (ms). Arrows illustrate example components at midline electrodes.

Table 1

Demographic and exposure characteristics. Means (SD) or *n* (%).

	CON (<i>n</i> =101) ¹	ALC (<i>n</i> =38) ²
Child characteristics		
Gender (number of males, %)	45 (45)	14 (37)
Age at test (yr)	11.3 (0.6)	11.3 (0.6)
Estimated IQ ⁴	92.6 (12.7)	95.3 (12.0)
Village of residence (number not local; arrived by plane)	45 (45)	16 (42)
Prenatal PCBs (μg/kg) ⁵	130.5 (105.0)	81.9 (41.8) **
Prenatal Hg (nmol/L) ⁵	110.9 (92.6)	63.9 (97.9) **
Prenatal DHA (% fatty acid plasma phospholipids)	3.6 (1.3)	3.5 (1.3)
Prenatal Pb (μg/dL)	4.5 (3.0)	4.0 (2.7)
11-yr PCBs (μg/kg) ⁵	88.9 (79.7)	56.9 (61.2) *
11-yr Hg (nmol/L) ⁵	24.2 (26.8)	17.3 (16.6)
11-yr DHA (% fatty acid plasma phospholipids)	2.4 (1.0)	2.4 (0.8)
11-yr Pb (μg/dL)	2.5 (2.2)	2.6 (2.5)
Maternal characteristics		
Biological mother's age at delivery (yr)	25.2 (6.1)	21.2 (3.4) ***
Marital status at 11-yr (number married)	47 (47)	15 (40)
Socioeconomic status (SES) ⁶	28.4 (12.2)	31.1 (12.0)
Highest grade attained	8.8 (2.2)	8.9 (2.3)
Peabody Picture Vocabulary Test	87.3 (37.4)	97.4 (24.6)
Raven Progressive Matrices	36.2 (10.5)	36.9 (8.1)
Cigarettes/day during pregnancy ^{7,8}	7.0 (6.3)	6.9 (5.3)
Marijuana use (days/month) during pregnancy ⁷	1.4 (5.2)	2.7 (7.5)
Current smoking (cigarettes/day) ⁸	8.7 (7.4)	6.9 (5.1)
Current marijuana use (days/month)	5.8 (10.5)	8.5 (11.7)
Alcohol use averaged across pregnancy (AA/day) ^{5,7}	0.0 (0.0)	0.3 (0.6) ***
Alcohol use per occasion during pregnancy (AA/day) ^{5,7}	0.3 (0.6)	4.3 (1.7) ***

	CON (<i>n</i> =101) ¹	ALC (<i>n</i> =38) ²
Binge drinking during pregnancy (binges/month) ⁷	0.0 (0.0)	2.1 (3.5) ***
Current alcohol use (binges/month at 11 yr)	2.0 (3.6)	5.7 (5.8) ***

¹Due to missing observations, group *n* ranges from 92 to 101.

²Due to missing observations, group *n* ranges from 37 to 38.

³From ANOVA or Chi-square.

⁴Based on 7 non-verbal WISC-IV IQ subtests and standard scores form 2 verbal tests (Boston Naming, Verbal Fluency), adapted for translation into Inuktituk.

⁵Logged values were used in the ANOVAs; unlogged means are shown here.

⁶Hollingshead four factor index of social status (unpublished manuscript).

⁷Based on retrospective report at 11-yr.

⁸Means based on winsorized values.

Note. Group differences based on *t*-tests or chi-squares are shown with asterisks.

[†]*p* < .10

^{*}*p* < .05;

^{**}*p* < .01;

^{***}*p* < .00

Table 2

Go/No-go results by exposure group.

	CON (n = 76)	ALC (n = 31)	ES ¹ ; F, p-value
Behavioral performance ²			
Go (% correct)	93.1 (6.7)	91.6 (7.8)	0.01; 1.02, p = .31
No-go (% correct)	65.1 (9.9)	65.3 (10.1)	0.00; 0.01, p = .93
Correct Go RT (ms)	465 (63)	454 (64)	0.01; 0.60, p = .44
FA (incorrect No-go) RT (ms)	395 (68)	389 (67)	0.00; 0.15, p = .70
ERP ³			
P2 peak amplitude Go (μV)	9.7 (0.4)	9.0 (0.7)	0.01; 0.70, p = .41
P2 peak amplitude No-go (μV)	10.4 (0.6)	11.0 (1.0)	0.00; 0.30, p = .58
P2 latency Go (ms)	251 (3)	265 (5)	0.05; 5.24, p < .05
P2 latency No-go (ms)	254 (4)	275 (6)	0.07; 8.00, p < .01
N2 peak amplitude Go (μV)	-5.9 (0.5)	-5.9 (0.7)	0.00; 0.00, p = .99
N2 peak amplitude No-go (μV)	-6.6 (0.8)	-5.3 (1.3)	0.01; 0.72, p = .40
N2 latency Go (ms)	380 (5)	394 (7)	0.02; 2.45, p = .12
N2 latency No-go (ms)	370 (6)	358 (9)	0.01; 1.42, p = .24
P3 area Go (μV)	3.0 (0.4)	2.1 (0.7)	0.01; 1.15, p = .28
P3 area No-go (μV)	7.7 (0.7)	6.5 (1.1)	0.01; 0.89, p = .35
ERN peak amplitude No-go (μV)	-8.5 (0.7)	-7.7 (1.1)	0.00; 0.39, p = .53
Pe peak amplitude No-go (μV)	12.7 (1.0)	12.3 (1.5)	0.00; 0.04, p = .84

¹ Effect size measure: η_p^2 .

² Mean (standard deviation).

³ Composite mean across electrodes (standard error).

Table 3

CRT results by exposure group.

	CON (<i>n</i> = 82)	ALC (<i>n</i> = 32)	ES ¹ ; <i>F</i> ; <i>p</i> -value
Behavioral performance ²			
New (% correct)	77.3 (14.9)	75.3 (13.6)	0.00; 0.45, <i>p</i> = .51
Old (% correct)	68.0 (17.4)	66.2 (16.3)	0.00; 0.25, <i>p</i> = .62
<i>d</i> -prime (discrimination)	1.36 (0.93)	1.20 (0.87)	0.01; 0.69, <i>p</i> = .41
<i>C</i> (bias)	0.16 (0.25)	0.14 (0.16)	0.00; 0.25, <i>p</i> = .62
Correct New RT (ms)	797 (182)	748 (194)	0.01; 1.63, <i>p</i> = .20
Correct Old RT (ms)	827 (190)	772 (195)	0.02; 1.95, <i>p</i> = .17
ERP ³			
P2 peak amplitude New (μV)	-0.6 (0.6)	1.8 (1.0)	0.03; 3.81, <i>p</i> = .053
P2 peak amplitude Old (μV)	2.1 (0.7)	4.5 (1.1)	0.03; 3.65, <i>p</i> = .058
P2 latency New (ms)	291 (3)	303 (5)	0.03; 3.49, <i>p</i> = .064
P2 latency Old (ms)	294 (3)	301 (5)	0.01; 1.25, <i>p</i> = .27
FN400 peak amplitude New (μV)	-15.3 (0.6)	-12.2 (1.0)	0.06; 6.94, <i>p</i> < .01
FN400 peak amplitude Old (μV)	-12.3 (0.7)	-10.9 (1.1)	0.01; 1.27, <i>p</i> = .26
FN400 latency New (ms)	405 (5)	404 (7)	0.00; 0.02, <i>p</i> = .89
FN400 latency Old (ms)	410 (4)	404 (7)	0.01; 0.56, <i>p</i> = .46
LPC area New (μV)	10.2 (0.6)	8.3 (1.0)	0.02; 2.54, <i>p</i> = .11
LPC area Old (μV)	13.7 (0.7)	10.9 (1.1)	0.04; 5.05, <i>p</i> < .05

¹Effect size measure: η_p^2 .²Mean (standard deviation).³Composite mean across electrodes (standard error)