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Magnitude comparison and automaticity in number processing in adolescents with prenatal alcohol exposure: An event-related potentials study

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Abstract

Background: Individuals with fetal alcohol spectrum disorders (FASD) may exhibit a distinct pattern of dysmorphic facial features, growth restriction, and cognitive deficits, particularly in arithmetic. Magnitude comparison, a fundamental element of numerical cognition, is modulated by the numerical distance effect, with numbers closer in value more difficult to compare than those further apart, and by the automaticity of the association of numerical values with their symbolic representations (Arabic numerals).

Methods: We examined event-related potentials (ERPs) acquired during the Numerical Stroop numerical and physical tasks administered to 24 alcohol-exposed adolescents (8 fetal alcohol syndrome (FAS), 8 partial FAS (PFAS), 8 heavily-exposed (HE) nonsyndromal) and 23 typically developing (TD), same age controls. The distance effect was assessed on the numerical task to examine differences in reaction time (RT) and accuracy when two numbers are close in value (e.g., 1 vs. 2) compared to when the numbers are less close (e.g., 1 vs. 6). Automaticity was assessed in the physical task by examining the degree to which RT and accuracy are reduced when the relative physical size of two numerals is incongruent with their numerical values (e.g., 1 vs. 6).

Results: Adolescents in all four groups performed behaviorally as expected on these relatively simple magnitude comparison tasks, but accuracy was poorer and RT was slower on both tasks in the FAS and PFAS than the HE and TD groups. At the neurophysiological level, in the numerical

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task, a higher level of prenatal alcohol exposure was associated with smaller P2p amplitude. In the physical task, only the TD and nonsyndromal HE groups exhibited the expected smaller P300 amplitude in the incongruent compared with the congruent condition.

Conclusions: These findings suggest that magnitude comparison in alcohol-exposed individuals may be mediated by recruitment of alternative neural pathways that are likely to be inefficient when number processing becomes more challenging.

Keywords

Numerical Stroop; prenatal alcohol exposure; number processing; event-related potentials; fetal alcohol spectrum disorders; fetal alcohol syndrome

Introduction

Fetal alcohol spectrum disorders (FASD) is an umbrella term that encompasses fetal alcohol syndrome (FAS) and other disorders attributable to prenatal alcohol exposure (PAE). Individuals who are diagnosed with FAS, the most severe of the FASD, display three sets of abnormalities: (a) a characteristic pattern of craniofacial dysmorphology (short palpebral fissures, thin upper lip (vermilion), flat philtrum); (b) pre- and/or postnatal growth restriction, and (c) small head circumference (Hoyme et al., 2005; S. Jacobson et al., 2021). Individuals with partial FAS (PFAS) exhibit a similar pattern of craniofacial dysmorphic features and either growth restriction or small head circumference. Nonsyndromal heavily exposed (HE) individuals do not show the distinctive pattern of dysmorphic features but may exhibit cognitive and behavioral impairment (Stratton et al., 1996). These impairments include lower IQ scores (e.g., Jacobson et al., 2004; Mattson et al., 1997; Streissguth et al., 1990; J. Jacobson et al., 2021), slower cognitive processing speed (e.g., Burden et al., 2005a; Jacobson et al., 1993), impaired eyeblink conditioning (S. Jacobson et al., 2008, 2011a), poor learning and memory (e.g., Mattson and Roebuck, 2002; Lewis et al., 2015; Dodge et al., 2019) and deficits in executive function (e.g., Kingdon et al., 2016; Burden et al., 2005b). Individuals with FASD may also exhibit deficits in emotional and behavioral self-regulation, which can lead to secondary problems in adulthood, including higher incarceration rates, psychiatric confinement, job instability, and inappropriate sexual behavior (Nash and Davies, 2017).

Among the cognitive deficits seen in FASD, arithmetic is a particularly sensitive endpoint (Streissguth et al., 1990, 1994; Jacobson et al., 2004). In 6.5-year-old children, low-to-moderate PAE was related to poorer performance in reading, spelling, and arithmetic, but only the effect on arithmetic was dose-dependent and remained significant after statistical adjustment for IQ (Goldschmidt et al., 1996). In a study comparing adolescents with alcohol-related dysmorphic features to non-alcohol-exposed adolescents in special education classes, the special education students were more impaired in basic reading and spelling, whereas the alcohol-exposed adolescents were more impaired in mathematics (Howell et al., 2006). In a sample of adolescents and adults diagnosed with FASD, arithmetic scores were significantly lower than those for reading or spelling (Kerns et al., 1997). Impairment has been demonstrated in calculation, estimation (Kopera-Frye et al., 1996), and symbolic (Burden et al., 2005b) and non-symbolic (Woods et al., 2017) number comparison.

PAE-related deficits in numerosity were already detected in infants with PAE compared to controls from the cohort in the present study and were predictive of their performance on Number/Quantity and Digit Span (but not Vocabulary or Fine Motor function) on the Junior South African Intelligence Scale at 5 years of age (S. Jacobson et al., 2011b; also see Berger et al., 2019).

Magnitude comparison is one of the most fundamental elements of numerical cognition. Research by Dehaene and colleagues has identified a brain region in the anterior portion of the horizontal intraparietal sulcus (IPS) that plays a critical role in magnitude comparison (Dehaene, 1996, 2001; Dehaene et al., 2003). In a study examining number processing in adolescents with PAE and/or attention deficit hyperactivity disorder (ADHD), J. Jacobson et al. (2011) found that both were associated with poorer calculation, but PAE was more strongly related to magnitude comparison. Whereas the effect of ADHD on arithmetic calculation was statistically mediated, in part, by deficits in executive attention, the effect of PAE on calculation was fully mediated by the alcohol-related deficit in magnitude comparison.

Magnitude comparison

Symbolic magnitude comparison (i.e., comparison of Arabic numerals) is strongly associated with mathematical competence (Schneider et al., 2017). Symbolic comparisons are affected by the numerical distance between the compared quantities, a phenomenon referred to as the “numerical distance effect” (Moyer and Landauer, 1967). In typically developing (TD) individuals, the distance effect is manifested by increased reaction time (RT) and poorer accuracy when the numerical distance is small (e.g., 3 vs. 4), compared to when it is large (e.g., 2 vs. 7; Ansari et al., 2010, 2006; Maloney et al., 2010; Pinel et al., 2001). Dehaene and colleagues have proposed a model of number representation, the analogue number system (ANS), wherein numbers are represented in the IPS along an analog to the number line, and suggest that the distance effect is due to a noisy or overlapping signal from two adjacent numbers (Dehaene, 2001, 1996; Dehaene et al., 2003). A recent meta-analysis supported the hypothesized activation during symbolic number processing across the left and the right parietal cortices and right frontal superior gyrus (Sokolowski et al., 2017). The discrete semantic system, an alternative model to the ANS, proposes that numbers are stored in a network of nodes and attributes the observed distance effect to stronger neural connections between adjacent digits (Krajcsi et al., 2016).

The Numerical Stroop paradigm (Besner and Coltheart, 1979; Henik and Tzelgov, 1982) assesses two aspects of numerical processing: (1) the distance effect (i.e., mental representation of relative magnitude) and (2) automaticity. In this paradigm, number comparison is assessed using pairs of digits that differ in numerical value and/or physical size. In the numerical task, participants indicate which of the two digits is larger in value, ignoring their physical size; in the physical task, participants indicate which digit is physically larger, ignoring their numerical value. Each task includes three different congruency conditions: *incongruent*, in which physical size and numerical value do not match (e.g., 9 vs. 1), *congruent* where they match (e.g., 9 vs. 1), and *neutral*. In the neutral condition in the numerical task, the font size of the two digits is the same (e.g., 1 vs. 9); in the physical task, the numerical value of the pair is the same (e.g., 9 vs. 9).

Among TD individuals performing the physical task in the incongruent condition, the value of the stimulus interferes with the speed and/or accuracy of identifying which number is physically larger, providing evidence that the processing of the numerical values of the stimuli is “automatic” in that it overrides the perception of physical size. This phenomenon is known as the “size congruity effect” and is calculated as the difference in performance between the congruent and incongruent conditions. Since the Numerical Stroop paradigm also includes a neutral condition, two other size-congruency effects can be addressed: an *interference* effect, defined as the difference between the incongruent and neutral conditions, and a *facilitation* effect, defined as the difference between the neutral and congruent conditions (Henik et al., 2017; Henik and Tzelgov, 1982; Tzelgov et al., 1992).

In fMRI studies in which the numerical task is used, TD individuals show increased activation in the IPS when the numerical distance is small (i.e., when the comparison is more difficult) compared to a larger distance (Ansari et al., 2006; Kaufmann et al., 2005). At the electrophysiological level, an event-related potential (ERP) component known as second posterior positivity (P2p) has been shown to have larger amplitude when the distance between the compared numbers is smaller (Ansari, 2007). Because the left hemisphere typically exhibits functional specialization for symbolic number representation, this component is usually found at left parietal electrodes. The component appears 180–250 ms after the stimuli are presented, and its neural generator seems to be the IPS (Dehaene, 1996; Libertus et al., 2007; Turconi et al., 2004).

The cognitive conflict elicited in the physical task by the incompatibility between the numerical and physical dimensions has been linked to increased activation in the dorsolateral prefrontal cortex and anterior cingulate cortex (ACC) for the incongruent trials, compared to the congruent and neutral trails (Ansari et al., 2006; Kaufmann et al., 2005). At the electrophysiological level, this incompatibility is indicated in the P300 ERP component (measured at mid-parietal electrodes, 300–600 ms after stimuli presentation), in which mean amplitude for the incongruent trials is smaller than for the neutral trials and smaller for the neutral than the congruent trials (Kadosh et al., 2007). This pattern was replicated in a recent study, which also indicated via source localization algorithms (dipole fitting and independent component analysis clustering) that the anterior cingulate and the posterior cingulate cortex are the neural generators of this component (Beldzik et al., 2015).

FASD impairment in numerical processing

Evidence of impaired numerical processing at the brain level in FASD comes from structural and functional studies. For example, alcohol-exposed adolescents failed to show the negative correlation between mathematical achievement test scores and the surface area of the inferior and superior parietal lobule and the postcentral gyrus seen in TD adolescents (Glass et al., 2017). In an fMRI study, Woods et al. (2015) found that, although PAE was not related to behavioral performance on relatively easy magnitude comparison and exact addition tasks, higher levels of PAE were associated with less activation in the region of the IPS known to mediate mental representation and manipulation of quantity.

By contrast to TD children, children with FAS and PFAS showed greater activation in the left angular gyrus during the symbolic magnitude comparison task. The increased activation of the angular gyrus, which is adjacent to the perisylvian language processing network and is associated with the verbal processing of numbers, suggests that children with FAS and PFAS may rely on verbal recitation of the numbers to solve magnitude comparison problems to compensate for functional deficits in the IPS. In another study, young adults with PAE-related dysmorphology showed decreased neural activation in the inferior parietal region during a subtraction task, whereas a TD group did not (Santhanam et al., 2009).

Although there is substantial evidence linking FASD to impaired numerical processing, to the best of our knowledge, no previous study has specifically examined the effects of PAE on (1) the "distance effect," which assesses the function of the mental number line, or (2) automaticity in number processing. Our study used an ERP version of the Numerical Stroop task to examine these phenomena. Non-exposed TD adolescents were compared with three groups with PAE: FAS, PFAS, and heavily exposed (HE) nonsyndromal adolescents. Because neurobehavioral and brain structural and functional impairment is generally more severe in individuals with FAS and PFAS than in nonsyndromal HE and TD individuals (e.g., Cheng et al., 2014; Dodge et al., 2019; Lewis et al., 2015, 2021; Lindinger et al., 2016, 2021), we expected to see the greatest impairment in the FAS and PFAS groups.

In the **numerical task** we hypothesized that all participants would exhibit numerical distance and size congruency effects at the behavioral level; that is, for comparisons between closer numbers (smaller distance), RTs would be longer and accuracy lower. We further hypothesized that, due to inefficient neural processing (Meintjes et al., 2010; Woods et al., 2015; Santhanam et al., 2009), participants with FAS and PFAS would show an inflated numerical distance effect, compared with HE and TD participants, and that poorer performance would be correlated with increased severity of diagnosis. At the electrophysiological level, we predicted that the FAS and PFAS groups would not display the typical distance effect in the P2p component or the typical congruency effects in the P300 component. In the **physical task** we hypothesized that all participants would perform better (greater accuracy and shorter RTs) in the congruent than the neutral condition and better in the neutral than the incongruent. At the electrophysiological level, we hypothesized that mean amplitudes in the P300 component would be larger in the congruent than the neutral condition and larger in the neutral than the incongruent. At the behavioral and electrophysiological levels, we predicted that the difference in P300 amplitude would be smaller in the FAS and PFAS than in the HE and TD groups and that degree of impairment would be proportional to severity of FASD diagnosis and/or quantity of alcohol consumed by the mother during pregnancy.

Methods

Participants

Participants were recruited from the Cape Coloured (mixed ancestry) community in Cape Town, South Africa, where there is a very high prevalence of FASD (13.6–20.9%; May et al., 2013) due to high levels of alcohol consumption during pregnancy by some members of the community. Pregnant women were interviewed at their initial visit to a prenatal clinic by a research nurse using a timeline follow-back procedure (Jacobson et al., 2002) regarding their alcohol consumption during a 2-week period at time of recruitment and a 1-week period around time of conception (Jacobson et al., 2008). Volume was recorded for each type of beverage consumed each day and converted to ounces (oz) of absolute alcohol (AA; 1 oz AA ≈ 2 standard drinks). Any woman who reported engaging in binge drinking (≥ 5 drinks/occasion) or drinking at least 14 standard drinks/week (≈ 1 oz AA/day) was invited to participate in the study. Women who reported abstaining or drinking no more than minimally were recruited as controls. Mothers were also interviewed regarding smoking (cigarettes/day) and illicit drug use (marijuana, cocaine, opiates, methaqualone) during pregnancy. Maternal exclusionary criteria were younger than 18 years of age, multiple gestation pregnancy, illicit drug use, and the following medical conditions: diabetes, HIV infection, epilepsy, or chronic cardiac problems. Infants with neural tube defects, major chromosomal anomalies, and seizures were also excluded from the study.

A second 2-week timeline follow-back interview was conducted at mid-pregnancy and a third was conducted at 1-month postpartum to provide information about drinking during a typical 2-week period in the latter part of pregnancy. Data from the three interviews were used to derive three continuous measures of PAE: AA/day, AA drinking/occasion, and frequency of alcohol use (days/week).

Procedure

In October 2005, when the children in this sample were 5.2±0.8 (mean±standard deviation) years of age, we conducted a clinic in which each child was examined for alcohol-related anomalies and growth by two U.S.-based expert dysmorphologists (H.E. Hoyme and L.K. Robinson) using a standard diagnostic protocol (Hoyme et al., 2005). There was substantial inter-examiner agreement on the assessment of the principal fetal alcohol-related dysmorphic features (Jacobson et al., 2008). Case conferences including the dysmorphologists, SWJ, JLJ, and CDM were held to reach consensus regarding diagnosis of FAS and PFAS. Those who did not meet criteria for FAS or PFAS were categorized as heavily exposed (HE) nonsyndromal or TD controls. The children were re-assessed for FASD in clinics at ages 9.0±0.9, 13.0±0.9, and 16.0±0.9 years, in which Dr. Hoyme was one of two dysmorphologists who examined each of the children. Dr. Hoyme subsequently reviewed the diagnoses from all four assessments in a consensus conference with SWJ, JLJ, and R. Colin Carter and assigned a final diagnosis for each participant (S. Jacobson et al., 2021).

Participants were assessed at school age and adolescence on a comprehensive battery of cognitive tests, including the Wechsler Intelligence Scale for Children, 4th ed., IQ test at 10±0.9 years of age and the Wechsler Individual Achievement Test (WIAT) at 16±0.9 years.

Experimental tasks.—In the Numerical Stroop, the participant was asked to determine which of two numbers displayed horizontally on a computer screen is larger either in terms of its numerical value (numerical task) or its physical size (physical task) (Henik and Tzelgov, 1982; see Fig. 1). In both tasks, the participant was presented with a pair of single-digit numbers and asked to respond by pressing the left or right button on a serial response box. The three congruency conditions—congruent, incongruent, and neutral—are described above. The numerical distance between the two digits was manipulated and could be either 1 (e.g., 7 vs. 8) or 5 (e.g., 1 vs. 6). A trial began with the display of a fixation cross for 500 ms, followed by display of a blank screen during a randomly selected inter-stimulus interval of 300, 500, or 700ms. A pair of numbers was then presented until the participant responded or failed to respond within 2500 ms. The inter-trial interval was 1000 ms. Each task consisted of two blocks of 96 trials each. The three task conditions were equally distributed across the block and presented in random order.

The Numerical Stroop tasks were administered on two different days. In the first session, participants performed the physical task; in the second session, the numerical task. Before each task, the participant was administered five practice trials, in which visual feedback was given (in the form of happy/sad emojis. Testing was not initiated until it was clear to the experimenter that the participant understood the task. The tasks were programmed in E-Prime II (Psychology Software Tools, Inc., Pittsburgh, PA).

EEG system and data acquisition parameters.—EEGs were recorded using an EGI HydrocCel Geodesic Sensor Net and system (Electrical Geodesics, 2003). 129 electrodes were distributed on the scalp according to an adapted 10–20 method (Fig. 2) and were sampled at a rate of 250 Hz (Tucker, 1990). Recording frequency band was constant at 0.01 to 100 Hz. The electrode impedance level was kept under 40 KΩ, which is an acceptable level for this system (Ferree et al., 2001). During EEG recording, all measures were referenced to an electrode located above Cz (according to the 10–20 method).

EEG preprocessing.—Preprocessing was performed using the EEGLAB toolbox (version 14; Delorme and Makeig, 2004), operating in the MATLAB environment (version 2015a), and was comprised of seven stages. In the first stage, the continuous EEG data were band-passed (0.5–40.0Hz) filtered with a finite impulse response filter and re-referenced to the average of the channels. Then the continuous data files were segmented into 1000ms stimulus-locked segments, starting 200ms before and ending 800ms after stimulus onset. Segments were next baseline-corrected by subtracting mean amplitude based on a 200ms period prestimulus-to-stimulus onset. The third step consisted of manual artifact inspection and removal of trials and electrodes that contained large and visible artifacts. This stage was followed by an independent components analysis, conducted using EEGLAB’s runica algorithm. Components that contained blinks, oculomotor artifacts, or other artifacts that could be clearly distinguished from genuine neural activity signals were removed from the data.

In the fifth stage, the data were subjected to automatic trial-by-trial bad artifact detection. Electrodes that exhibited a min-max difference of 100μV in 30% of the trials were removed and trials in which 10 channels exceeded a min-max difference of 100μV were removed, followed by manual verification of the EEG data. The incidence of bad trials was very low: 3.2% and 1.8% for the numerical and physical tasks, respectively, and did not differ by diagnostic group on either task: $F(3,44) = 0.84$ and $F(3,46) = 1.34$, respectively, both p’s > 0.20. In the sixth stage, missing or rejected electrodes were spherically interpolated based on activity from neighboring channels. In the last pre-analysis step, the segmented data were averaged within each of the experimental conditions.

Task-relevant ERP components for each of the tasks were then extracted. In the physical task, the mean amplitude of the P300 component was calculated for each of the congruency conditions. Based on previous literature (Kadosh et al., 2007; Szűcs and Soltész, 2008) and visual inspection of the waveforms, these mean amplitudes were calculated at 11 middle-central electrodes located between Oz and Pz (indicated in green in Fig. 2) within a time window of 320–450ms post-stimulus. In the numerical task, the amplitude of the P2p component was calculated for each of the two numerical distance conditions (1 and 5). Based on previous literature (Ben-Shalom et al., 2013; Dehaene, 1996; Libertus et al., 2007; Parnes et al., 2012) and visual inspection of the waveforms, we calculated mean amplitude for four left parietal electrodes located between O1, P3, and PZ (indicated in green in Fig. 2) within a time window of 230–250 ms post-stimulus.

Data Analysis

All statistical analyses and plotting were conducted in R (R Core Team, 2018), using the corr version 0.3.0 package for correlations and the afex R package for analysis of variance (ANOVA) and analysis of covariance (ANCOVA; Singmann et al., 2018). Violation of the sphericity assumption was corrected by applying Greenhouse-Geisser correction. Group comparisons were conducted using the emmeans R package (Lenth, 2018). Tukey tests were used to assess *post hoc* comparisons. η_p^2 effect sizes and confidence intervals (CIs) were estimated following the procedure described by Ben-Shachar et al. (2020a).

Trials in which RT was unusually fast (RT < 100) or slow (RT > 2000) were considered outliers and excluded from the analysis. Because there was a speed/accuracy trade-off (speed was negatively correlated to accuracy in the physical task, $r = -0.34$, $p < 0.05$), inverse efficiency score (IES) was used as the dependent behavioral measure (Townsend and Ashby, 1983). IES was calculated as follows: $\left(\frac{mean\ \ reaction\ \ time}{1 - mean\ \ proportion\ \ of\ \ errors}\right)$ for each participant in each condition; poorer performance resulted in a higher IES. To make the results easier to interpret, the IES measure was also calculated for the numerical task even though speed and accuracy were only weakly correlated in that task ($r = -0.11$, $p = 0.47$).

The IES measures were analyzed using repeated measures ANOVA. For the numerical task, diagnostic group was the between-subject factor; congruency and numerical distance were within-subject factors. Because a distance effect is not seen in the neutral condition of the physical task, numerical distance was not included in the analyses of that task. The ERP results were also analyzed using repeated measures ANOVA. In the numerical task, P2p and P300 amplitude were examined in separate analyses. In the P2p analysis, group was the between-subject factor; numerical distance, the within-subject factor. In the P300 analysis, group was the between-subject factor; congruity condition, the within-subject factor. In the physical task, P300 amplitude was the dependent measure; diagnostic group, the between-subject factor; congruency, the within-subject factor. Given the small sample size, particularly for the three alcohol-exposed groups, group differences were examined in exploratory analyses. Because, as noted above, we have generally found more severe neurobehavioral and brain structural and functional impairment in individuals with FAS and PFAS than in TD and nonsyndromal HE individuals, the primary group comparisons were of the FAS and PFAS groups with the TD and HE groups. Pearson *r* was used to examine the relations of the behavioral and ERP outcome variables to maternal alcohol consumption during pregnancy and to participant's IQ and math scores. 90% CIs were computed for the ANOVAs, as recommended by Steiger (2004); 95% CIs were computed for Pearson *r*'s.

Seven control variables were assessed: maternal age at delivery, socioeconomic status (Hollingshead, 2011), years of education, and smoking (cigarettes/day) during pregnancy and participant's sex, years of education, and age at assessment. Since a control variable cannot be the cause of an observed deficit unless it is related to both exposure and outcome (Schlesselman, 1998), association with either exposure or outcome can be used as the criterion for inclusion in multivariate analyses to control for potential confounders. In this study, we selected control variables in relation to outcome, which has the additional advantage of increasing precision by also including covariates unrelated to exposure (Kleinbaum et al., 1988). Pearson *r* was calculated to examine the relation of each control variable to each IES and ERP outcome measure. We considered any control variable that was even weakly related to a given outcome (at $p < 0.10$) to be a potential confounder of the effect of diagnostic group on that outcome and included any potential confounders as covariates in the data analysis. In the numerical task, mother's cigarettes/day during pregnancy ($r = 0.37$, $p < 0.05$) and participant's years of education ($r = 0.41$, $p < 0.05$) qualified as potential confounders in the analyses of IES, which were, therefore, run using ANCOVA rather than ANOVA. None of the control variables met criterion for inclusion as potential confounders in any of the other analyses.

For the ERP analyses, in addition to the ANOVAs, we applied nonparametric time-point cluster analyses for each group to rule out the possibility that the between-group differences were due to slow processing speed or plausible differences in the suitable time window of the effects. This procedure was performed *post hoc* for both tasks. The time-point clusters were defined as at least two temporally adjacent time points at which t was < 0.05 after correction for multiple comparisons. The *t*-distribution was drawn from 5,000 Monte Carlo permutations, conducted for the averaged amplitude of the previously selected electrodes at each time point between 300–500ms (P300 time window). In each permutation, congruent and incongruent conditions were randomly swapped, and a one-tailed hypothesis-based (congruent > incongruent) *t*-test was performed (Maris and Oostenveld, 2007). This procedure was not performed for the P2p, which is a much more specific and shorter component.

Results

Sample Characteristics

Of the 51 adolescents who were assessed on the ERP tasks, 3 were excluded due to maternal illicit drug use during pregnancy and 1 withdrew prior to completion of the ERP assessments. The final sample for the physical task consisted of 23 TD (12 males; M_{age} = 16.3, SD = 0.7); 8 HE (4 males; M_{age} = 16.2, SD = 0.5); 8 PFAS (4 males; M_{age} = 16.6; SD = 0.8); and 8 FAS (3 males; M_{age} = 16.4, SD = 0.5). One participant from the PFAS group was excluded from the electrophysiological analysis because the EEG recording file was corrupted. The final sample for the numerical task consisted of 45 participants; 23 TD (11 males; M_{age} = 16.2; SD = 0.6); 7 HE (4 males; M_{age} = 16.2; SD = 0.6); 8 PFAS (4 males; M_{age} = 16.6; SD = 0.8); and 7 FAS (2 males; M_{age} = 16.5; 0.8). Two participants (1 from the FAS and 1 from the HE group) were excluded from the behavioral and electrophysiological analyses because their accuracy levels were below chance. An additional 3 participants were excluded from the electrophysiological analysis (2 from the TD group and 1 from the HE group) due to extremely noisy or corrupted EEG recordings. Socioeconomic status, maternal education, and adolescent IQ scores were low in all four groups but lower in the FAS and PFAS than the TD (Table 1). Mothers of participants in the FAS, PFAS, and HE groups drank heavily during pregnancy; all mothers of the TD participants reported abstaining throughout pregnancy, except for one who reported 2 drinks on 3 occasions. The groups did not differ by sex or age at EEG assessment.

Numerical Task

Behavioral results.—There was a main effect for distance, indicating, as expected, that overall performance of the participants was better (i.e., lower IES) when the distance between the compared numbers was 5 rather than 1, $F(1,39) = 113.96$; $p < 0.001$; $\eta_p^2 = 0.75$; 90%CI [0.62, 0.82] (Table 2). The main effect for diagnostic group fell short of conventional levels of statistical significance, $F(3,39) = 2.40$; $p = 0.08$; $\eta_p^2 = 0.16$; 90%CI [0.00, 0.30]. The TD and HE groups performed better (lower IES) than the FAS and PFAS groups, $t(40) = 2.01$; $p = 0.05$; $\eta_p^2 = 0.09$; 90%CI [0.00, 0.26], and there was a significant linear trend across the three PAE groups: (FAS > PFAS > HE), $t(40) = 2.29$; $p < 0.05$; $\eta_p^2 = 0.13$; 90%CI [0.01, 0.28].

The difference in performance (i.e., IES scores) between the two numerical distance conditions (distance 1 minus distance 5) was correlated with both frequency of maternal drinking (days/week), $r = 0.34$, 95%CI [0.03, 0.59]; $p < 0.05$, and dose/drinking occasion during pregnancy, $r = 0.33$, 95%CI [0.02, 0.58]; $p < 0.05$, such that, the more often and the greater the amount of alcohol/occasion the mother drank during pregnancy, the higher the IES when the numerical distance was 1, compared to 5. The difference in IES between the two numerical distance conditions was negatively correlated with the adolescents' IQ scores, $r = -0.46$, 95%CI [−0.67, −0.17]; $p > 0.005$, and marginally related to performance on WIAT math reasoning, $r = -0.31$, 95%CI [−0.57, 0.00]; $p = 0.066$, indicating that a larger difference between distance 1 and distance 5 was related to lower IQ and poorer math reasoning.

We also found an effect for congruency, $F(2,78) = 72.20$; $p < 0.0001$; $\eta_p^2 = 0.65$; 90%CI [0.54, 0.72], for the sample as a whole; that is, participants performed better in the congruent than in the neutral condition and better in the neutral than in the incongruent condition, indicating that the physical size of the stimuli was processed automatically and either facilitated or interfered with the processing of the numerical dimension. Tables 2 and 3 and Figure 5 show that in all four groups, the physical size of the stimuli facilitated or interfered with the processing of the numerical dimension; that is, physical size processing was not altered by PAE in the congruent or incongruent conditions, respectively.

ERP results.—There was no main effect on P2p amplitude for group, $F(3,38) = 0.28$; $p > 0.80$; $\eta_p^2 = 0.02$; 90%CI [0.00, 0.07], or distance, $F(1,38) = 0.03$; $p > 0.80$; $\eta_p^2 < 0.01$; 90%CI [0.00, 0.05], and the interaction between group and distance was not significant, $F(3,38) = 1.02$; $p > 0.20$; $\eta_p^2 = 0.07$; 90%CI [0.00, 0.19]. The P2p effect, that is, a larger amplitude when the numerical distance is 1 compared to 5, fell short of statistical significance in the TD group, $t(38) = 1.71$; $p < 0.10$; $\eta_p^2 = 0.07$; 90%CI [0.00, 0.23], and was not seen in any of the three PAE groups, all p's > 0.20 (Fig. 4). However, P2p amplitude difference (distance 1 minus distance 5) was inversely correlated with oz AA/drinking occasion, $r = -0.33$, 95%CI [−0.58, −0.02]; $p < 0.05$, and AA/day, $r = -0.30$, 95%CI [−0.56, 0.01]; $p = 0.058$, during pregnancy, such that higher levels of alcohol consumption during pregnancy were related to a lower amplitude difference (i.e., a weaker distance effect).

With respect to congruency effects, we examined P300 amplitude to determine whether the physical size of the digits was implicitly processed and interfered with the explicitly required numerical processing. There were main effects for distance, $F(1,38) = 11.23$; $p < 0.005$; $\eta_p^2 = 0.23$; 90%CI [0.06, 0.41], with larger P300 amplitude at distance 5 compared to 1, and for congruency, $F(2,76) = 11.39$; $p < 0.001$; $\eta_p^2 = 0.23$; 90%CI [0.10, 0.35], with larger P300 amplitude in the congruent compared to the neutral and incongruent conditions (see Table 2 and Fig. 3), and a marginally significant interaction for group X distance $F(3,38) = 2.56$; $p = 0.068$; $\eta_p^2 = 0.17$; 90%CI [0.00, 0.32]. The P300 distance effect was significant only in the FAS group, $t(38) = -3.51$; $p < 0.005$; $\eta_p^2 = 0.24$; 90%CI [0.07, 0.42]. All groups showed the size congruity effect; TD: $t(38) = -2.80$; $p < 0.001$; $\eta_p^2 = 0.17$; 90%CI [0.03, 0.35]; HE: $t(38) = -2.00$; $p = 0.052$; $\eta_p^2 = 0.09$; 90%CI [0.00, 0.26]; PFAS: $t(38) = -2.71$; $p < 0.01$; $\eta_p^2 = 0.16$; 90%CI [0.02, 0.34]; FAS: $t(38) = -2.61$; $p < 0.05$; $\eta_p^2 = 0.15$; 90%CI [0.02, 0.33]. The size congruity effect was also apparent in the significant time-point cluster comparison (Fig. 5). The TD group was the only one to show a facilitation effect: $t(38) = -2.81$; $p < 0.05$; $\eta_p^2 = 0.12$; 90%CI [0.03, 0.35], and none of the groups exhibited interference effects, all p's > 0.20.

Physical Task

Behavioral results.—There was a main effect for congruency, $F(2,86) = 56.31$; $p < 0.001$; $\eta_p^2 = 0.57$; 90%CI [0.45, 0.65], with participants performing better in the congruent than in the neutral condition and better in the neutral compared to the incongruent condition. The effect for diagnostic group fell short of significance, $F(3,43) = 2.26$; $p = 0.10$; $\eta_p^2 = 0.14$; 90%CI [0.00, 0.27] (see Table 4 and Fig. 4), and the group by congruency interaction was not significant, $F(6,86) = 1.52$; $p = 0.20$; $\eta_p^2 = 0.10$; 90%CI [0.00, 0.16]. Group comparisons showed that IES was higher in the FAS and PFAS groups than in the TD and HE groups, $t(40) = -2.08$; $p < 0.05$; $\eta_p^2 = 0.10$; 90%CI [0.00, 0.26], and there was a linear trend among the PAE groups, with IES increasing with severity of the diagnosis: FAS > PFAS > HE $t(43) = 2.40$; $p < 0.05$; $\eta_p^2 = 0.12$; 90%CI [0.01, 0.28].

All the groups exhibited size congruity and interference effects (Table 5). However, the facilitation effect was not significant in the FAS and PFAS groups, and there was an inverse relation between AA/day and facilitation that fell short of statistical significance, $r = -0.27$, 95%CI [−0.53, 0.04]; $p < 0.10$.

ERP results.—There was a significant main effect for congruency on P300 amplitude for the sample as a whole, $F(2,84) = 7.00$; $p < 0.005$; $\eta_p^2 = 0.14$; 90%CI [0.04, 0.25], but not for group, $F(3,42) = 1.29$; $p > 0.20$; $\eta_p^2 = 0.08$; 90%CI [0.00, 0.20] or for group × congruency, $F(6,84) = 1.04$; $p > 0.20$; $\eta_p^2 = 0.07$; 90%CI [0.00, 0.11] (Fig. 7). Although the difference between P300 amplitude in the incongruent and congruent conditions was significant in the TD, $t(42) = -2.96$; $p < 0.005$; $\eta_p^2 = 0.17$; 90%CI [0.03, 0.34], and HE, $t(42) = -3.50$; $p < 0.001$; $\eta_p^2 = 0.22$; 90%CI [0.07, 0.40] groups, it was not significant in the PFAS or FAS groups, both p's > 0.10. A significant interference effect was found for the TD, $t(42) = -1.98$; $p < 0.05$; $\eta_p^2 = 0.09$; 90%CI [0.00, 0.24], and HE, $t(42) = -1.95$; $p < 0.05$; $\eta_p^2 = 0.08$; 90%CI [0.00, 0.24], groups; no interference effect was found for the PFAS group, $t(42) = -0.50$; $p > 0.20$; $\eta_p^2 < 0.01$, 90%CI [0.00, 0.10], and the effect for the FAS group fell just short of significance, $t(42) = -1.651$; $p = 0.053$; $\eta_p^2 = 0.06$; 90%CI [0.00, 0.21]. The facilitation effect was not significant for any of the groups, all p's > 0.20. Time-point cluster analysis based on nonparametric statistics for the size congruity effect produced significant time-point clusters only for the TD group (from 308 ms to 440 ms; $p < 0.001$) and the HE group (from 300 ms to 460 ms; $p < 0.0005$) (Fig. 7).

Discussion

This study used the Numerical Stroop tasks to examine behavioral performance and electrophysiological activity patterns in adolescents who were heavily exposed to alcohol during pregnancy compared to TD controls. These tasks enabled us to investigate deficits in two specific aspects of numerical cognition: (1) magnitude comparison (indicated by the distance effect), which reflects representation of numbers along a mental number line; and (2) automatic processing of the numerical value of digits, as indicated by the facilitation and interference effects in the physical task.

The FAS and PFAS groups performed more poorly than the HE and TD groups on both the numerical and physical tasks, a pattern consistent with previous studies showing number processing deficits in dysmorphic individuals with PAE (Ben-Shachar et al., 2020b; Santhanam et al., 2009). While all four groups exhibited distance effects behaviorally in the numerical task, the FAS and PFAS groups showed a stronger distance effect, indicating greater impairment in the ability to discriminate numbers whose values are closer together, compared with the TD and HE groups.

The expected increased amplitude in the P2p component when the distance between the compared numbers is smaller fell short of statistical significance in the TD group and was not seen in any of the PAE groups. However, in correlational analyses, higher levels of PAE were associated with a smaller amplitude difference. Given that the IPS appears to be the neural generator of P2p (Dehaene, 1996; Libertus et al., 2007; Turconi et al., 2004), this finding is consistent with fMRI studies linking PAE to reduced activations in the IPS during symbolic (Meintjes et al., 2010; Woods et al., 2015) and non-symbolic (Woods et al., 2017) magnitude comparison tasks. Since all four diagnostic groups showed a numerical distance effect behaviorally but the region of the IPS involved in magnitude comparison is functionally impaired in FASD, fetal alcohol exposed individuals likely rely on different neural mechanisms, such as long-term memory of the ordinal relation between small numbers. Our findings resemble those seen in individuals with developmental dyscalculia, who show a numerical distance effect behaviorally (Rubinsten and Henik, 2006) but do not exhibit the expected activation within the IPS (Price et al., 2007).

The behavioral and P300 data from the numerical task confirm previous reports that alterations in physical size create a size-congruency conflict in a task in which the subject has been instructed to focus on numerical values (Beldzik et al., 2015; Kadosh et al., 2007). All four groups had higher IES scores when the physical size of the number was not congruent with the numerical value of the stimulus. In studies of numerical cognition, the interference effect by the numerical values during the physical task is interpreted as indicating that automatic strong associations have been established between digits and their numerical values through learning, which leads the number's value to interfere with the perception of its physical size (Henik et al., 2017; Henik and Tzelgov, 1982; Tzelgov et al., 1992).

Although all four groups showed an interference effect behaviorally on the physical task, only the TD and HE groups showed smaller P300 amplitudes for the incongruent compared to the congruent trials, suggesting an impairment in the neural mechanisms that mediate automaticity in the FAS and PFAS groups. Behaviorally, all four groups showed size congruency and interference effects, but a facilitation effect was seen only in the TD and HE groups. The pattern seen in the FAS and PFAS groups is similar to that seen in young children prior to the 3rd grade, who also show a lack of facilitation despite an overall size congruency effect (Rubinsten et al., 2002). A similar pattern has been reported for developmental dyscalculia, where interference and facilitation effects were seen in the numerical task but the facilitation effect was not seen in the physical task (Ashkenazi et al., 2009; Rubinsten and Henik, 2006).

The principal limitation of this study is small sample size, which increases the risk of undue influence by outliers. For this reason, we have included confidence intervals for all effect size estimates to provide information regarding their precision (Rothman and Greenland, 2018). Given the small sample size, particularly of the three PAE groups, the study findings should be interpreted with caution and replication in a larger sample is needed. A second limitation is the use of only two numerical distances (1 vs. 5) because additional conditions would have made the task too long. In addition, because of the speed-accuracy trade-off found in some of the groups, we used the IES as our behavioral measure, which did not allow for differentiation between poor accuracy and long RT. Despite these limitations, the high temporal precision of EEG added substantially to our understanding of the deficits in magnitude comparison seen in FASD and mechanisms that may mediate these deficits. The observed associations cannot be attributed to confounding by the control variables that we examined (i.e., participant's years of education, sex, and age at EEG recording and maternal years of education, socioeconomic status, smoking during pregnancy, and age at delivery) because none of these variables were related to any of the behavioral or neurophysiological outcomes, except for two that were related to IES on the numerical task and were controlled statistically. Nevertheless, as in all correlational studies, it is always possible that other unmeasured variables confounded the effects that we have reported.

In summary, our findings add to the growing body of evidence of a specific deficit in magnitude comparison processing in individuals with PAE, particularly those with the dysmorphology and growth restriction that characterize FAS and PFAS. The P2p data from the numerical task are consistent with neuroimaging data that have linked PAE to functional deficits in a region of the IPS where numbers are represented along an analog to the mental number line. Behaviorally, the TD and alcohol-exposed participants all showed the expected size-incongruency effects in both the numerical and physical tasks. However, the FAS and PFAS groups did not exhibit a smaller P300 during the incongruent compared with the congruent condition in the physical task, suggesting alteration in the neural processes underlying the automaticity associated with over-learning of numerical values.

The numerical task findings complement recent results from another of our studies from the same cohort, showing smaller theta bursts during error detection in adolescents with FASD performing a mathematical verification task (Ben-Shachar et al., 2020b). These signals emanate from a region within the anterior cingulate cortex that has been shown (Luu et al., 2003) to mediate violation of expectations in comparisons between expected and perceived stimuli. Thus, our studies show functional alterations in brain regions known to mediate three specific aspects of number processing—magnitude comparison, automaticity, and error detection—even though behaviorally the participants were able to successfully complete the relatively easy tasks. These findings suggest that alcohol-exposed individuals recruit alternative neural pathways, which are likely to be less efficient and likely to lead to poorer performance when number processing tasks become more challenging. These data support the use of mathematical interventions, such as, Math Interactive Learning Experience (MILE; (Kable et al., 2007; Kully-Martens et al., 2018), which was designed to focus on specific deficits in magnitude comparison that we and others have shown to be altered in FASD. This intervention uses slower pacing of instructions and training with tangible objects, as well as vertical number lines as an aid in understanding that, as numbers go up, they increase in value and, as they go down, they decrease in value. Our findings suggest that individuals with FASD may also benefit from assessment of their use of the mental number line and automaticity in number processing and that new interventions focusing on error detection and automaticity in number processing are warranted.

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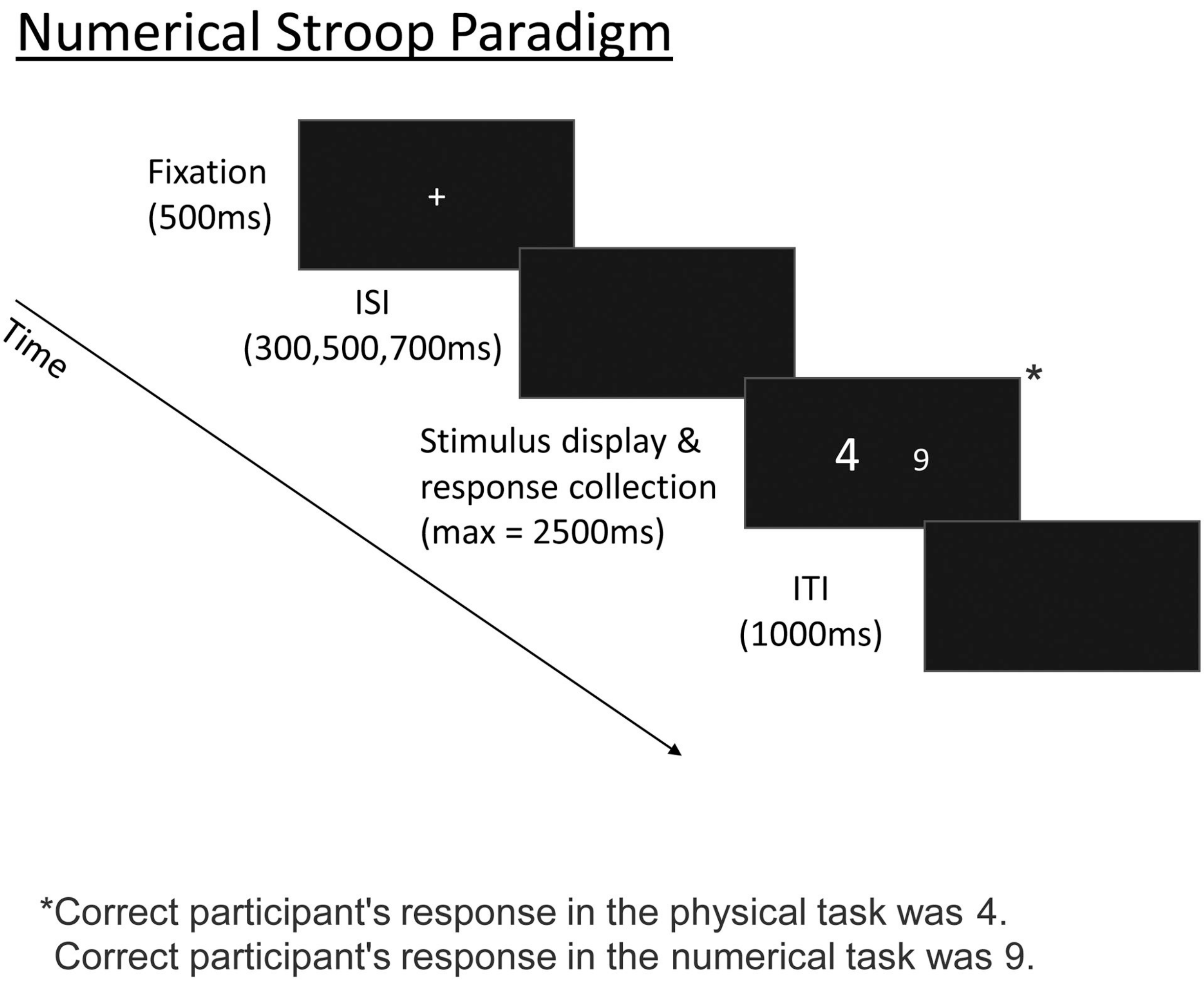

Figure 1.

Sample trial from the Numerical Stroop task. In each trial, the participant is asked to determine which of two numbers displayed horizontally on a computer screen is larger either in terms of its numerical value (numerical task) or its physical size (physical task). In both tasks, the participant is asked to respond by pressing the left or right button on a serial response box. A trial begins with the display of a fixation cross for 500ms, followed by display of a blank screen during a randomly selected inter-stimulus interval (ISI) of 300, 500, or 700ms. A pair of numbers is then presented until the participant responds or fails to respond within 2500ms. If this sample trial were presented in the physical task, the correct response would be 4; in the numerical task, it would be 9. The inter-trial interval (ITI) is 1000ms.

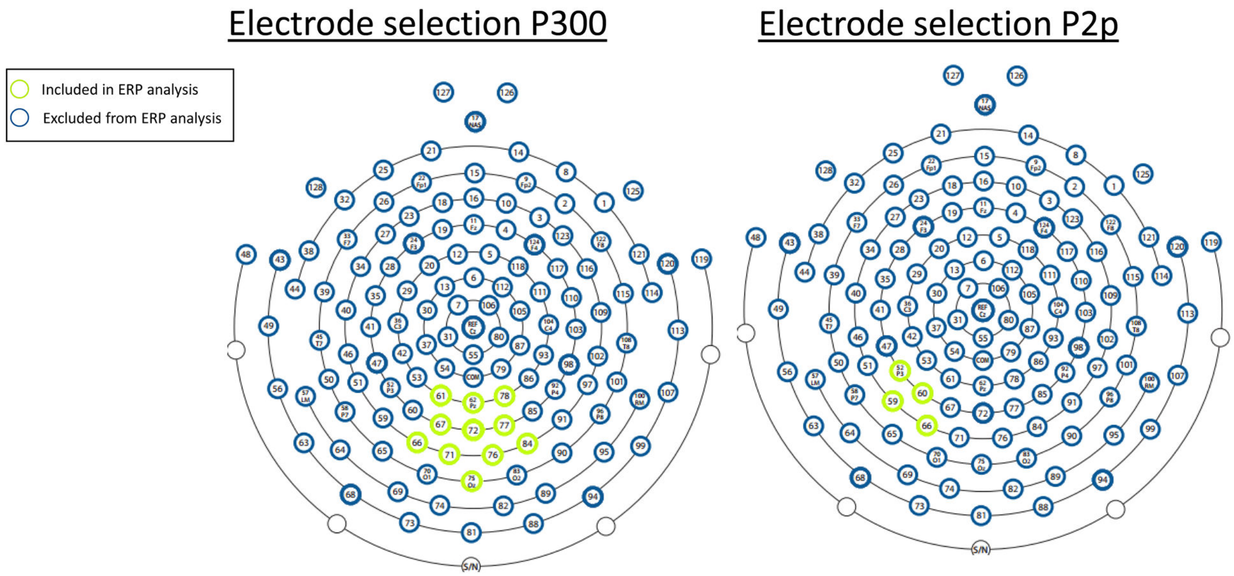

Figure 2.

EEG channels used to form the ERPs. The electrodes selected for the ERP analyses of each component are shown in the green circles.

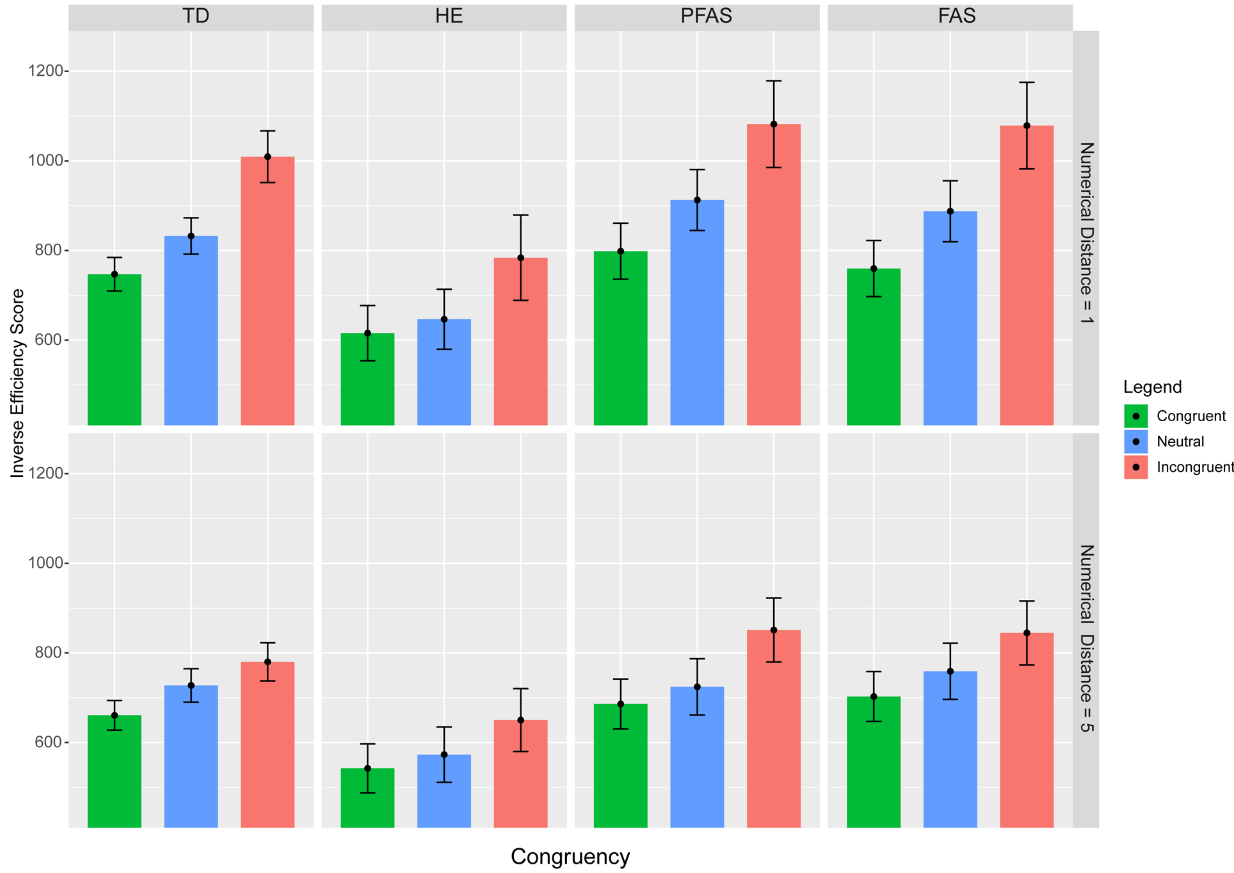

Figure 3.

Behavioral results on the numerical task. Values are inverse efficiency score (IES), which assesses reaction time and errors (mean reaction time/(1 - mean proportion of errors)). Higher IES score indicates slower reaction time and more errors. In the first row, the numerical distance between the two digits presented was 1; in the second row, it was 5. TD = typically developing controls, HE = heavily exposed nonsyndromal, PFAS = partial fetal alcohol syndrome, FAS = fetal alcohol syndrome.

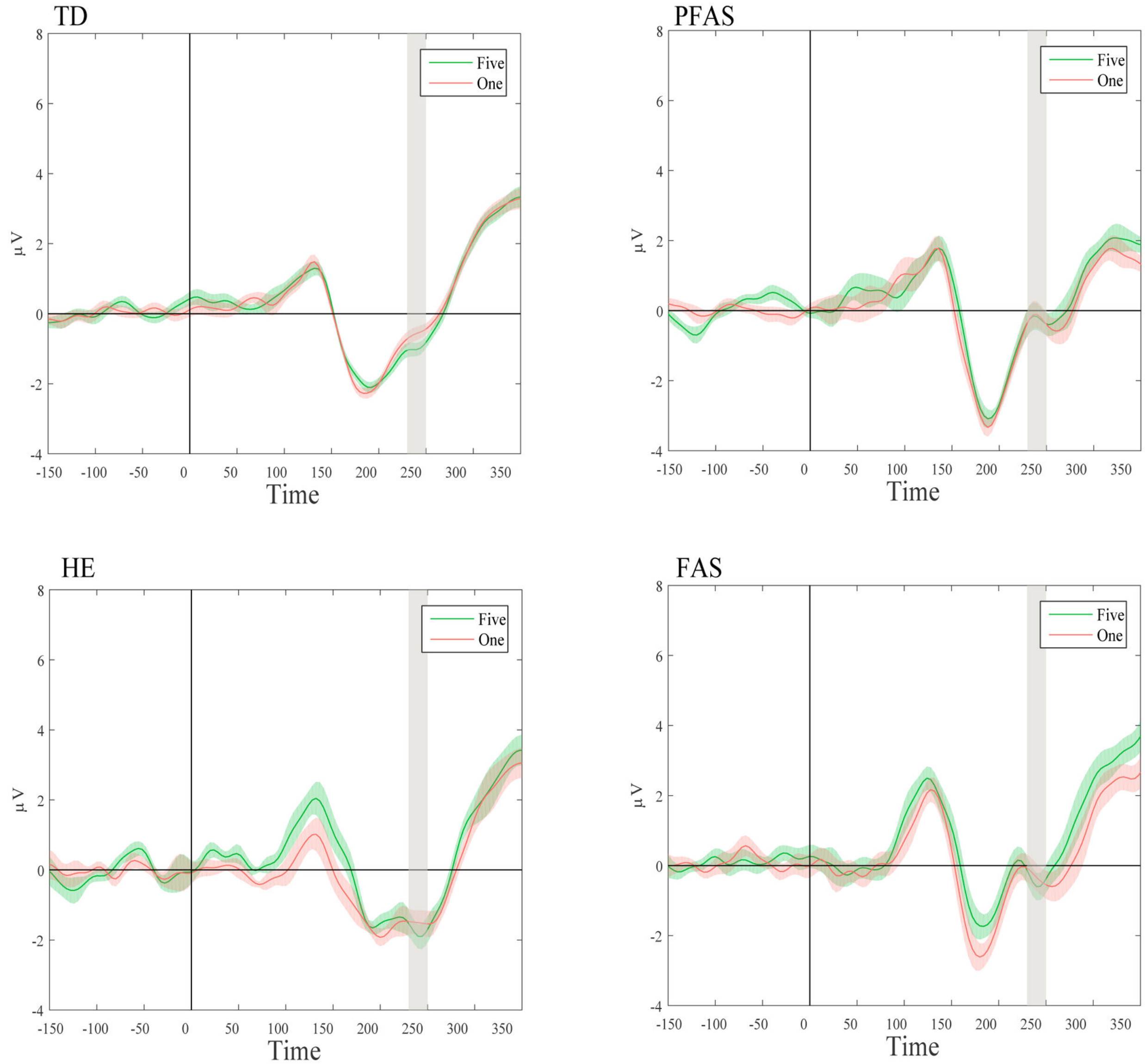

Figure 4.

Waveform of the P2p ERP component for each diagnostic group in the numerical task. The gray bar delineates the P2p time window. The green and red lines represent mean amplitude for numerical distances of 5 and 1, respectively. TD = typically developing controls, HE = heavily exposed nonsyndromal, PFAS = partial fetal alcohol syndrome, FAS = fetal alcohol syndrome.

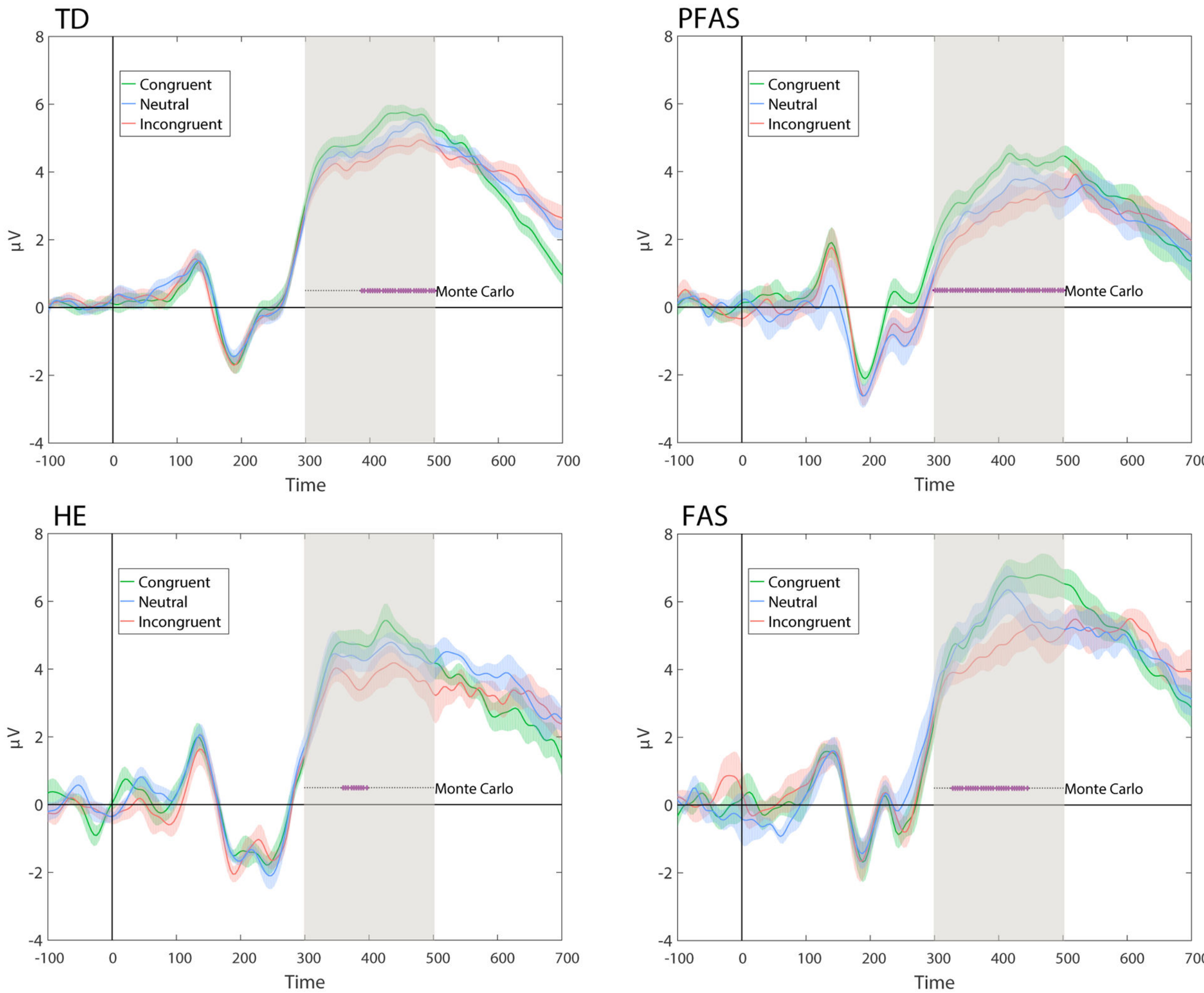

Figure 5.

Waveform of the P300 component for each diagnostic group in the numerical task. The green, red, and blue lines line represent mean amplitude for the congruent, incongruent, and neutral conditions, respectively. The gray bars delineate the time window taken for the Monte Carlo bootstrapping testing. The purple lines mark the timepoints during which the Monte Carlo analysis (congruent vs incongruent) was significant. TD = typically developing controls, HE = heavily exposed nonsyndromal, PFAS = partial fetal alcohol syndrome, FAS = fetal alcohol syndrome.

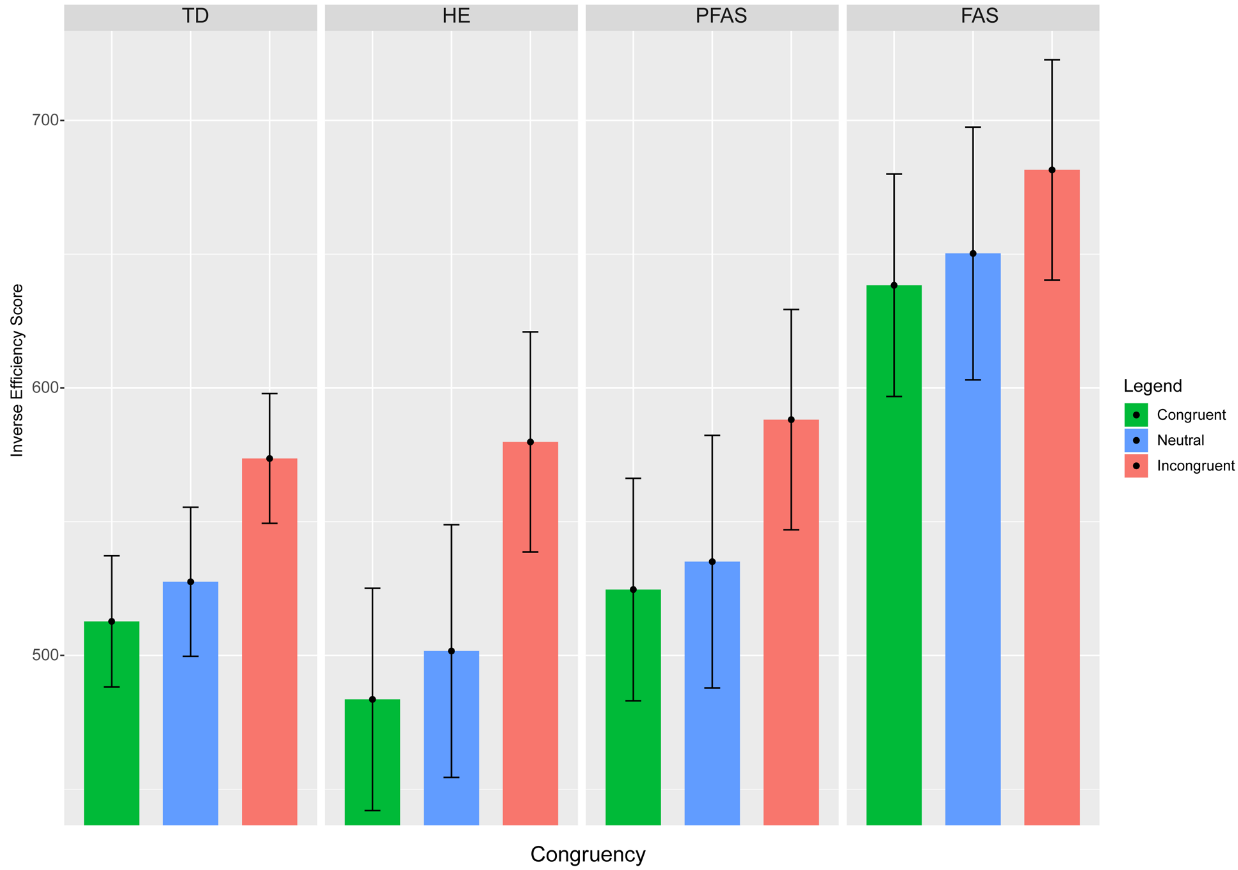

Figure 6.

Behavioral results on the physical task. Values are IES measurements for each of the groups in each of the conditions. IES = inverse efficiency score, which assesses reaction time and errors (mean reaction time/(1 - mean proportion of errors)). Higher IES score indicates slower reaction time and more errors. TD = typically developing controls, HE = heavily exposed nonsyndromal, PFAS = partial fetal alcohol syndrome, FAS = fetal alcohol syndrome.

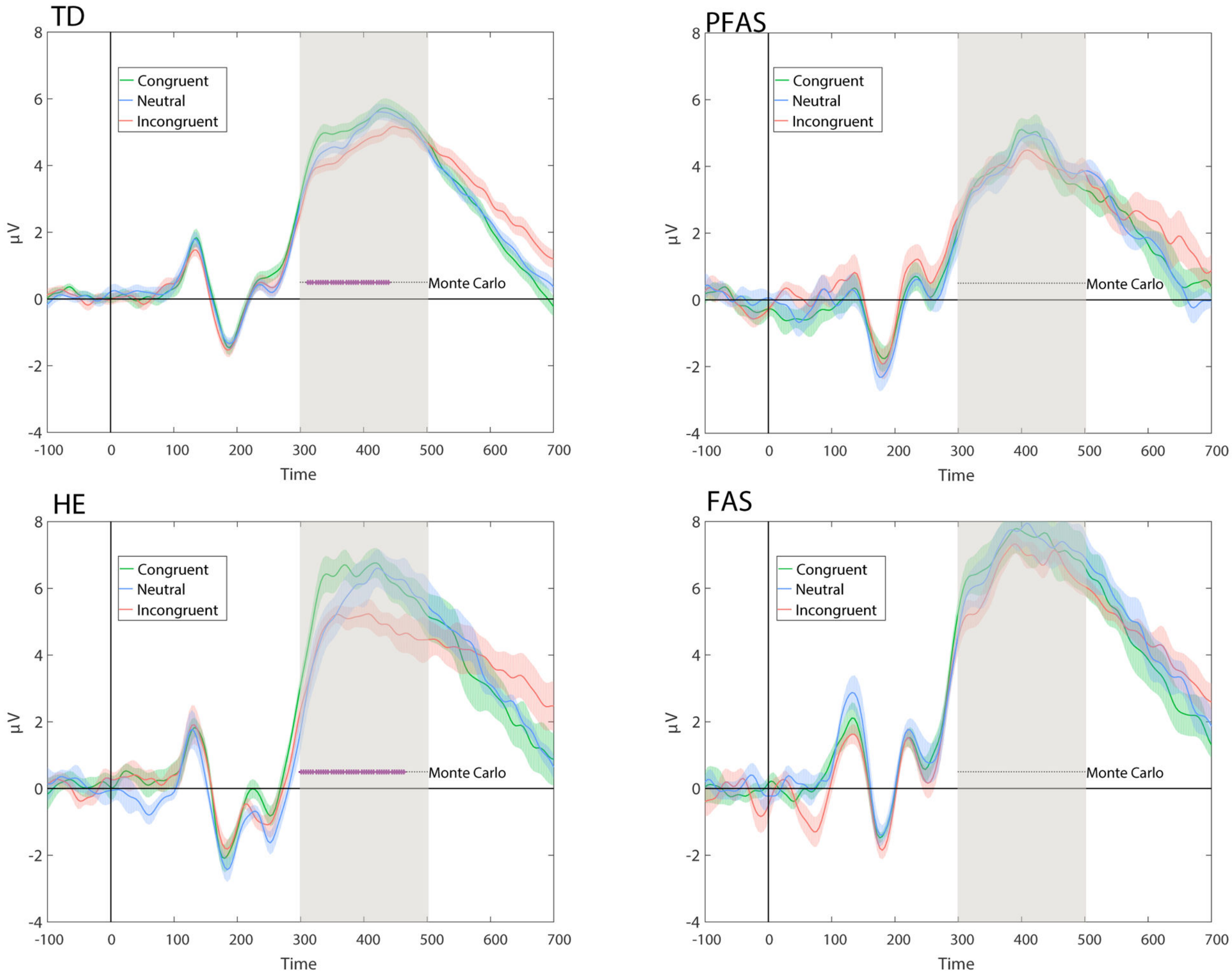

Figure 7.

Waveform of the P300 component for each diagnostic group in the physical task. The green, red, and blue lines represent mean amplitude for the congruent, incongruent, and neutral conditions, respectively. The gray bars delineate the time window taken for the Monte Carlo bootstrapping testing. The purple line marks the timepoints during which the Monte Carlo (congruent vs incongruent) was significant. TD = typically developing controls, HE = heavily exposed nonsyndromal, PFAS = partial fetal alcohol syndrome, FAS = fetal alcohol syndrome.

Table 1.

Sample characteristics (N = 47)

	TD (n = 23)	HE (n = 8)	PFAS (n = 8)	FAS (n = 8)	F or χ^2	η_p^2 [90% CI]	*Post-hoc* differences
Maternal characteristics							
Age at delivery (years)	26.4 (4.5)	24.1 (5.5)	24.4 (4.2)	34.1 (5.0)	8.24***	0.37 [0.15, 0.51]	FAS < TD, HE, PFAS
Education (years)	9.9 (1.6)	9.4 (2.8)	7.4 (2.0)	8.1 (1.8)	4.11*	0.22 [0.03, 0.37]	TD > FAS, PFAS; HE > PFAS
Socioeconomic status[a]	24.6 (8.6)	20.9 (7.6)	13.2 (4.8)	16.3 (6.7)	5.41****	0.27 [0.07, 0.42]	TD > FAS, PFAS
Prenatal exposure							
Alcohol							
AA/day (oz)	0.0 (0.0)	1.0 (0.7)	1.0 (0.6)	2.0 (2.3)	8.30***	0.37 [0.16, 0.51]	TD < HE, PFAS, FAS
AA/drinking occasion (oz)	0.1 (0.2)	4.6 (4.6)	3.4 (1.2)	5.1 (1.6)	18.72***	0.57 [0.38, 0.68]	TD < HE, PFAS, FAS
Frequency (days/week)	0.003 (0.01)	1.9 (1.0)	2.0 (0.7)	2.2 (1.9)	19.28***	0.57 [0.39, 0.68]	TD < HE, PFAS, FAS
Cigarettes/day	1.6 (4.3)	5.8 (7.1)	10.1 (7.5)	6.7 (6.5)	4.82**	0.25 [0.05, 0.40]	TD < PFAS, FAS
Adolescent characteristics							
Age at EEG assessment (years)	16.3 (0.7)	16.2 (0.6)	16.6 (0.8)	16.4 (0.8)	0.63		
Sex (% male)	52.2	50.0	50.0	37.5	0.52		
Education (years)	10.1 (0.9)s	8.8 (1.4)	8.8 (1.3)	8.4 (1.8)	5.81**	0.29 [0.08, 0.44]	TD > HE, PFAS, FAS
WISC-IV IQ[b]	84.8 (13.3)	83.9 (11.1)	68.9 (9.8)	67.9 (10.3)	6.43**	0.31 [0.10, 0.46]	TD > PFAS, FAS; HE > PFAS, FAS
WIAT[c]							
Mathematical reasoning	78.4 (18.5)	77.6 (16.0)	67.3 (15.7)	62.3 (12.2)	2.55+	0.15 [0.00 0.29]	TD, HE > FAS
Numerical operations	74.4 (18.5)	77.3 (16.5)	62.3 (12.2)	57.5 (16.5)	2.99*	0.17 [0.00, 0.31]	TD, HE > FAS

Values are mean (standard deviation), except for sex, which is % male. *Post hoc* comparisons indicate group differences significant at $p < 0.05$. This table includes all participants who provided usable data from at least one of the tasks. TD = typically developing controls, HE = heavily exposed nonsyndromal, PFAS = partial fetal alcohol syndrome, FAS = fetal alcohol syndrome, CI = confidence interval, AA = absolute alcohol.

[a] Hollingshead Four Factor Index of Social Status (2011)

[b] Wechsler Intelligence Scale for Children, 4th Ed., administered at 10.3±0.9 years.

[c] Wechsler Individual Achievement Test, administered at 16.3±0.8 years.

† $p < 0.10$,

* $p < 0.05$

** $p < 0.01$

*** $p < 0.001$

Table 2.

Behavioral and ERP numerical task outcomes by diagnostic group

	TD (*n* = 23)	HE (*n* = 8)	PFAS (*n* = 8)	FAS (*n* = 8)
IES -- Overall	787.3 (195.4)	656.6 (127.4)	873.4 (236.0)	866.1 (266.0)
Congruent	687.4 (171.7)	592.1 (96.2)	746.7 (125.0)	749.0 (159.8)
Neutral	757.5 (181.2)	631.2 (81.4)	819.7 (193.4)	847.3 (217.5)
Incongruent	857.0 (197.8)	746.5 (146.5)	1002.5 (326.9)	1002.1 (339.7)
Distance 1	827.7 (200.2)	708.5 (134.6)	976.4 (263.7)	946.6 (303.4)
Distance 5	706.9 (171.7)	604.7 (97.5)	770.5 (148.8)	785.7 (198.8)
P2p amplitude (μV)				
Distance 1	−0.6 (3.0)	−1.7 (3.1)	−0.2 (18)	0.8 (2.5)
Distance 5	−0.9 (2.9)	−1.4 (3.3)	−0.3 (19)	−0.9 (2.4)
P300 amplitude (μV)				
Congruent	5.1 (2.2)	4.2 (2.3)	3.8 (2.4)	5.4 (4.6)
Neutral	4.5 (2.5)	3.5 (17)	3.3 (2.2)	5.0 (4.4)
Incongruent	4.3 (2.2)	3.2 (2.2)	2.6 (2.3)	4.2 (4.1)
Distance 1	4.6 (2.3)	3.3 (19)	3.1 (2.1)	4.2 (4.3)
Distance 5	4.7 (2.3)	3.9 (2.2)	3.4 (2.6)	5.5 (4.2)

Values are mean (standard deviation). TD = typically developing controls; HE = heavily exposed nonsyndromal; PFAS = partial fetal alcohol syndrome; FAS = fetal alcohol syndrome; IES = inverse efficiency score, in which a higher score indicates slower speed and poorer accuracy.

Table 3.

Behavioral effects on the numerical task within each of the diagnostic groups

	TD (n = 23)	**HE (n = 8)**	**PFAS (n = 8)**	**FAS (n = 8)**
Size congruity effect	$t(39) = -6.52$	$t(39) = -2.86$	$t(39) = -4.57$	$t(39) = -4.70$
	(p<0.0001)	(p<0.005)	(p<0.0001)	(p<0.0001)
	$\eta_p^2 = 0.52$	$\eta_p^2 = 0.17$	$\eta_p^2 = 0.34$	$\eta_p^2 = 0.36$
	CI [0.34, 0.65]	CI [0.03, 0.35]	CI [0.16, 0.51]	CI [0.17, 0.52]
Interference	$t(39) = -5.44$	$t(39) = -3.08$	$t(39) = -4.19$	$t(39) = -3.92$
	(p<0.0001)	(p<0.005)	(p<0.0005)	(p<0.0005)
	$\eta_p^2 = 0.43$	$\eta_p^2 = 0.19$	$\eta_p^2 = 0.31$	$\eta_p^2 = 0.28$
	CI [0.24, 0.58]	CI [0.04, 0.37]	CI [0.12, 0.48]	CI [0.10, 0.45]
Facilitation	$t(39) = -6.20$	$t(39) = -1.53$	$t(39) = -3.72$	$t(39) = -4.48$
	(p<0.0001)	(p=0.067)	(p<0.001)	(p<0.0005)
	$\eta_p^2 = 0.49$	$\eta_p^2 = 0.05$	$\eta_p^2 = 0.26$	$\eta_p^2 = 0.34$
	CI [0.31, 0.63]	CI [0.0, 0.21]	CI [0.09, 0.44]	CI [0.15, 0.50]
Numerical distance effect	$t(39) = 8.18$	$t(39) = 3.31$	$t(39) = 6.17$	$t(39) = 4.87$
	(p<0.0001)	(p<0.005)	(p<0.0001)	(p<0.0001)
	$\eta_p^2 = 0.63$	$\eta_p^2 = 0.21$	$\eta_p^2 = 0.49$	$\eta_p^2 = 0.37$
	CI [0.47, 0.73]	CI [0.06, 0.40]	CI [0.30, 0.63]	CI [0.18, 0.54]

Size congruity effect = difference in inverse efficiency score (IES) between congruent and incongruent conditions. Interference = difference in IES between the neutral and incongruent conditions. Facilitation = difference in IES between neutral and congruent conditions. Numerical distance effect = difference in IES between conditions with a numerical distance of 1 between the two digits, compared to 5. TD = typically developing controls, HE = heavily exposed nonsyndromal, PFAS = partial fetal alcohol syndrome, FAS = fetal alcohol syndrome, CI = 90% confidence interval.

Table 4.

Behavioral and ERP physical task outcomes by diagnostic group

	TD (*n* = 23)	HE (*n* = 8)	PFAS (*n* = 8)	FAS (*n* = 8)
IES -- Overall	537.9 (102.7)	521.7 (102.8)	549.0 (61.6)	656.0 (209.0)
Congruent	512.7 (97.4)	483.6 (98.5)	555.9 (113.3)	638.4 (206.6)
Neutral	527.5 (99.5)	501.7 (100.1)	571.6 (119.4)	650.3 (256.5)
Incongruent	573.6 (105.5)	579.8 (95.3)	609.5 (98.2)	681.5 (186.5)
P300 amplitude (μV)				
Congruent	5.2 (1.9)	6.4 (3.3)	4.3 (1.6)	7.2 (5.7)
Neutral	4.9 (2.4)	5.7 (2.2)	4.2 (1.8)	7.2 (5.8)
Incongruent	4.5 (2.2)	5.0 (2.8)	4.0 (1.4)	6.6 (6.2)

Values are mean (standard deviation). TD = typically developing controls; HE = heavily exposed nonsyndromal; PFAS = partial fetal alcohol syndrome; FAS = fetal alcohol syndrome; IES = inverse efficiency score, in which a higher score indicates slower speed and poorer accuracy.

Table 5.

Behavioral effects on the physical task within each of the diagnostic groups

	TD (n = 23)	**HE (n = 8)**	**PFAS (n = 8)**	**FAS (n = 8)**
Size congruity effect	$t(43) = -7.56$	$t(43) = -7.04$	$t(43) = -4.65$	$t(43) = -3.15$
	(p<0.0001)	(p<0.0001)	(p<0.0001)	(p<0.005)
	$\eta_p^2 = 0.57$	$\eta_p^2 = 0.54$	$\eta_p^2 = 0.33$	$\eta_p^2 = 0.19$
	CI [0.40, 0.68]	CI [0.36, 0.66]	CI [0.15, 0.49]	CI [0.04, 0.36]
Interference	$t(43) = -4.47$	$t(43) = -4.76$	$t(43) = -3.04$	$t(43) = -1.78$
	(p<0.0001)	(p<0.0001)	(p<0.005)	(p<0.05)
	$\eta_p^2 = 0.32$	$\eta_p^2 = 0.32$	$\eta_p^2 = 0.18$	$\eta_p^2 = 0.07$
	CI [0.32, 0.48]	CI [0.16, 0.50]	CI [0.04, 0.34]	CI [0.0, 0.22]
Facilitation	$t(43) = -2.33$	$t(43) = -1.70$	$t(43) = -0.97$	$t(43) = -1.11$
	(p<0.05)	(p<0.05)	(p=0.167)	(p=0.135)
	$\eta_p^2 = 0.11$	$\eta_p^2 = 0.06$	$\eta_p^2 = 0.02$	$\eta_p^2 = 0.03$
	CI [0.01, 0.26]	CI [0.06, 0.21]	CI [0.00, 0.14]	CI [0.0, 0.15]

Size congruity effect = difference in inverse efficiency score (IES) between congruent and incongruent conditions. Interference = difference in IES between the neutral and incongruent conditions. Facilitation = difference in IES between neutral and congruent conditions. TD = typically developing controls, HE = heavily exposed nonsyndromal, PFAS = partial fetal alcohol syndrome, FAS = fetal alcohol syndrome, CI = 90% confidence interval.