Delays in Auditory Processing in Preschool Children with FASD Identified using MEG

J. M. Stephen[1], P. Kodituwakku[2], L. Kodituwakku[2], L. Romero[1], A. Peters[1], N. Muniswamy Sharadamma[1], B.A. Coffman[1]
[1]The Mind Research Network, Albuquerque, NM 87106 USA; [2]University of New Mexico, Albuquerque, NM 87131 USA

Introduction

Despite the known cause of fetal alcohol spectrum disorders (FASD), it remains challenging to reliably identify the children who were exposed to alcohol during pregnancy, and which children will go on to experience developmental delays due to this exposure. Despite known behavioral and cognitive deficits, behavioral measures alone do not provide sufficient sensitivity and specificity to provide a reliable differential diagnosis of FASD relative to other developmental disorders at a young age, when intervention is most likely to improve outcome (Streissguth et al., 2004; Kodituwakku, 2007). However, investigators conducting well-controlled animal studies have identified a number of physiological changes in animals exposed to alcohol across the gestational period as well as across a broad range of alcohol exposure levels. These results provide us with the motivation to use physiological measures to characterize children diagnosed with FASD relative to healthy control children. Simple sensory paradigms provide the opportunity to obtain physiological data from very young children. Animal studies show differences in auditory (Church et al. 1996) and somatosensory (Miller et al. 2006) areas in alcohol exposed animals. Additionally, sensory deficits were identified in infants with known prenatal alcohol exposure in early ERP studies (Rossig et al. 1994), but it is unclear whether these children went on to develop FASD. Therefore, identifying physiological markers in children at the age of diagnosis may provide a path to earlier identification of those children at-risk of developing an FASD.

Methods

We obtained good quality data from 10 FASD (mean age 48 months SD 10.7) and 15 healthy controls (HC; mean age 52 months SD 11.4) children aged 3-6 years for our study to investigate sensory and multisensory functioning using magnetoencephalography (MEG). The study was explained to both participants and parents and consent was obtained prior to their involvement. The children were asked to lay on the bed and MEG data collection was obtained in the supine position. A screen was placed in front of the child and a silent children's movie was played during the task described below.

The task consisted of:

- ***Condition 1***: Pure bilateral auditory tones (1000 Hz; 72 dB) presented through speakers located to the left and right of the child.
- ***Condition 2***: Tactile stimuli presented bilaterally to the left and right index fingers using a small bladder which fills with air. An air puff is generated by a device that regulates a compressed air source and is directed to the balloon through semi-rigid tubing. The pressure was set at 40 PSI for the air puff.
- ***Condition 3***: Synchronous auditory/tactile (AT) stimulation with the same stimuli as described above.
- Timing and duration of the stimuli were controlled by the Neurobehavioral Systems Presentation software.
- The duration of all stimuli was 50 ms and the interstimulus interval was 1± 0.2 s.
- The stimuli were randomized across conditions: Auditory (A), Tactile (T) and Audio/Tactile (AT)
- Approximately 120 trials were collected for each condition. The auditory condition had additional trials due to an additional P300 task component which is not reported here.
- The task took ~15 minutes to complete.

The MEG data were collected with a digitization rate of 1000 Hz with full head movement compensation. This technique allows one to track head movement during the scan and adjust the MEG data to a reference head position to reduce spatial blurring. This feature is important for studies involving children because data collection does not need to be re-started if the child moves significantly. Through this quantification, we also found that the children were quite good at remaining still during the scan (see Fig. 1). All data were preprocessed with Maxfilter to adjust head position and remove external artifacts from the data. After preprocessing, the data were averaged across trials to obtain an averaged evoked response for each condition.

Once the averaged evoked responses were obtained, source analysis was performed using the cortical-start spatio-temproal (CSST) multidipole analysis (Ranken et al. 2002, see Stephen et al. 2006, for a detailed description). This approach provides a means to perform source analysis without requiring a priori assumptions about the locations of the sources. This provides a more objective method for source analysis which is critical for proper source characterization. See Fig. 2 for an example of the output.

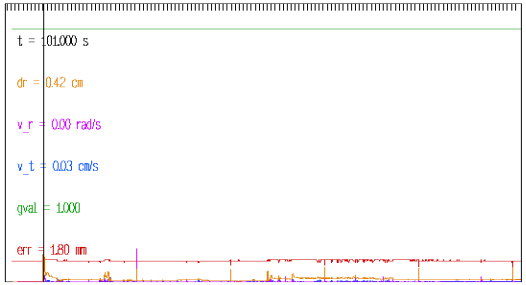

Fig. 1. Tracked movement. This figure shows the movement of a 37-month old child across the 15 minute MEG task. Maximum change in position was 0.42 cm (dr - orange line).

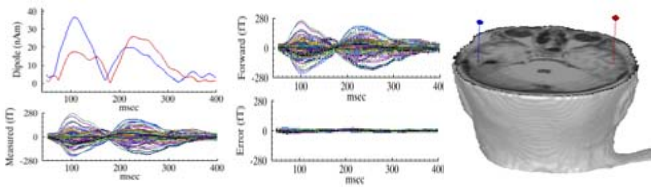

Fig. 2. Dipole modeling example. The output of CSST for the auditory condition (L. (blue) and R. (red) STG) are shown along with the source timecourses ('Dipole'). The 'Measured' and 'Forward' waveforms represent the original and modeled data, respectively. The 'Error' represents the difference between the original and the modeled data.

Results

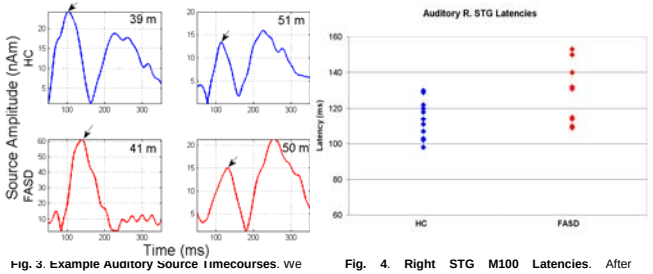

Fig. 3. Example Auditory Source Timecourses. We identified the superior temporal gyrus (STG) sources pertaining to primary auditory cortex activation for each child obtained with CSST source modeling. As seen in the above examples, we obtained good quality STG timecourses in both HC and FASD children. For each child we identified the latency of the M100 responses for statistical comparison (see arrows in each plot).

Fig. 4. Right STG M100 Latencies. After identification of each of the STG sources and the M100 latencies we performed a 2-way t-test to identify any differences in latencies between HC and FASD children.

Example auditory source timecourses are shown in Fig. 3. We found a significant difference in right STG M100 latencies (see arrows in Fig. 3) with FASD children (128 ms) showing longer M100 latencies than HC children (114 ms). The distribution of latencies for both groups is shown in Fig. 4. Although some children with FASD had latencies within the normal range, there was a significant group difference in latencies for R. STG ($t = 2.2$; $p = 0.04$). A similar pattern was identified for L. STG, but the difference did not reach statistical significance at the $p = 0.05$ level.

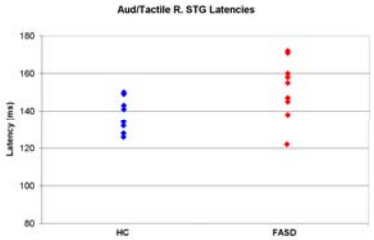

Fig. 5. R. STG M100 Latencies for AT condition. Similar differences in M100 latencies were identified in the AT condition. The initial findings suggested that the AT latency difference was more pronounced in the multisensory condition. Our current results show the same 14 ms delay between conditions.

We found a significant difference in the M100 latency in response to the AT condition ($t = 2.2$; $p = 0.04$). The latencies were shifted relative to the auditory condition due to an imposed auditory delay in the AT condition to ensure truly synchronous audio/tactile stimulation. The same 14 ms delay was identified in the AT condition as the A condition (FASD – 152 ms; HC – 138 ms). This replication of the initial auditory delays suggests that the tactile stimulus does not cause facilitation of the R. STG M100 in the AT condition, and likely represents the unisensory auditory delay.

Discussion & Conclusions

We identified auditory M100 latency delays in young FASD children relative to the age- and gender-matched HC children (age difference $p = 0.4$, gender difference $p = 1.0$). These delays were identified in both the auditory alone and the synchronous auditory/tactile conditions. The consistency of the delays across conditions acts as a partial replication of the unisensory delays. In addition, it suggests that the AT condition does not facilitate M100 latencies. Other differences are yet to be explored.

Larger variance in the FASD latencies are apparent in Figs. 4 and 5. This is not surprising given the expected variance in alcohol exposure and genetic factors that lead to differential effects of alcohol exposure across children (Christoffel and Salafsky, 1975). However, it is not clear from our current results that the M100 latencies map directly to the subtypes of the FASD diagnosis. That is, when grouping the FASD children by subtypes, there was not a direct correlation with M100 latencies. These results are consistent with some literature suggesting that cognitive deficits may not be directly linked to FASD subtype (Streissguth et al. 2004).

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Acknowledgements

Supported by: P20 AA017068 (D. Savage); MRN Internal Award DE- FG02-08ER64581(J. Stephen); and NCRR #1P20RR021938-01 (V. Calhoun)

Contact info: Julia Stephen, Ph.D. - jstephen@mrn.org