Antenatal Determination of Fetal Brain Activity in Response to an Acoustic Stimulus Using Functional Magnetic Resonance Imaging.

RJ Moore,*S Vadeyar, DJ Tyler, *PN Baker, *D James, *I Johnson, PA Gowland.
Magnetic Resonance Centre, School of Physics and Astronomy,*School of Human Development, City Hospital, University of Nottingham, NG7 2RD.

Introduction

The evaluation of fetal brain function is important for obstetric medicine, and neuro-developmental studies. The majority of cases of cerebral palsy originate antenatally rather than during delivery[1]. Currently there is no accurate method of assessing fetal brain activity. The only indication of brain activity used clinically is the change in fetal heart rate, associated with movements that the fetus makes in response to a stimulus. Attempts have been made to study the fetal brain directly using magnetoencephalography[2], however this technology is only available in a few centres world-wide, and this is unlikely to change soon.

This study builds on earlier pilot work[3] that showed that fMRI could provide direct evidence of fetal brain cortical activation in response to auditory stimulation. This new work aims to assess the sensitivity of this technique in a larger sample group, including a control group, and to establish methodologies for fetal fMRI.

Methods

16 healthy women with apparently normal singleton pregnancies were recruited. 12 were studied using fMRI with fetal acoustic stimulation and 4 acted as controls with maternal stimulation. Subjects were scanned during the final 3 weeks of pregnancy when the fetal head was engaged in the maternal pelvis. The local ethics committee approved this study and informed written consent was obtained. The pregnant volunteers lay in the magnet tipped on their side, to minimise pressure on the superior vena cava. Fetal Heart Rate (FHR) was monitored during imaging using a modified Doppler Ultrasound probe to identify periods of movement, to allow assessment of fetal behavioural state, and to monitor fetal well-being[4].

EPI[5] was carried out on a 0.5 T purpose built scanner. Imaging was transverse to the mother, but generally oblique to the fetus. The in-plane resolution was 5.0 mm x 5.0 mm, the slice thickness was 15 mm and the data matrix was 128 x 128. The image acquisition time was 130 ms, and the echo time to the centre of k-space was 70ms. The 6 slice volume was sampled every 3 s (T_r = 0.5 s). Scanning conformed to NRPB guidelines[6].

180 images were acquired prior to presentation of the paradigm. The stimulus used was Spanish guitar music, chosen because it has a large dynamic range in both frequency and intensity. This was played to the fetus using MR compatible headphones (Oxford), which were strapped to the maternal abdomen. 15 s of the music, interleaved with 15 s of silence, was presented 30 times. The volume of the music was adjusted to give 85 dB SPL at the surface of the maternal abdomen[5]. For the 4 controls, the same sample of music was played to the mother through the same headphones, at 70 dB SPL following a similar paradigm.

All analysis was performed blind to the experimental protocol. Fetal motion is a particular problem, especially because the fetus and mother move separately, complicating image registration. Gross fetal motion was identified in 2 ways. Several ROIs of 3 pixels were chosen spanning areas of high contrast, and the total mean signal intensity was plotted through the imaging period. Fetal motion was evidenced by large changes in signal. The FHR trace was also used to identify cycles in which the fetus was moving. If motion were detected in both plots, the cycle was removed from further analysis.

The remaining volumes were averaged to produce a mask for the fetal brain. The images were then viewed as a movie with the mask overlaid. Any cycles in which the fetus moved outside the mask were also removed. The remaining volumes were segmented using the mask to eliminate all maternal signals, and the mean pixel intensity for each slice was normalised. Each volume was interpolated to produce artificially cubic voxels. Motion correction was then carried out using AIR within Medx. The success of this process was checked by viewing the images as a movie. In several cases an artifact was observed due to the changes in susceptibility between the maternal bowel and the fetal brain. In these cases the shape of the image of the fetal brain depended upon its position relative the mother and hence the motion corrected images appeared severely distorted indicating that motion correction had failed.

Spatial filtering was performed (f.w.h.m of kernel=4.26 mm[7]). High frequency noise was removed using a Gaussian temporal filter of width 1.4 s and low frequency drift was generally removed by zeroing the 6 lowest frequency components in the Fourier domain. (If <7 cycles were left after motion correction, then the n lowest frequency components were removed, where n= number of remaining cycles –1).

The signal time course was correlated to the stimulus time course convolved with a 6 s Poisson function (model of adult HDR). Correlation coefficients were converted to z-scores and used to create SPMs. p-values were assigned to activated ROIs using Gaussian random field theory[7]. SPMs were resliced transverse to the fetal head and the position of the activation region in the brain was identified.

Results

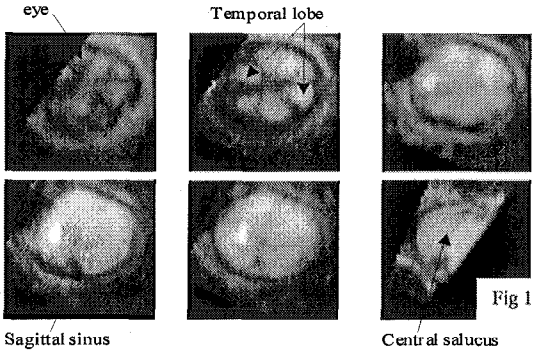
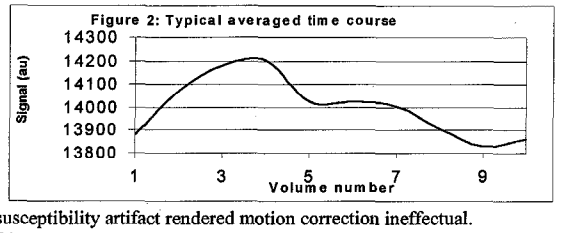


Fig 1

Fig 1.shows the activated region in one subject, Fig 2 shows the time course for the same subject. For the 12 test subjects, 2 mothers had back pain and withdrew from the study, and the data from 3 subjects could not be analysed because susceptibility artifacts rendered motion correction ineffectual. 5 of the remaining 7 subjects showed statistically significant activation ($p<0.005$), 4 in the temporal lobe and one in the frontal lobe. The signal change measured in temporal lobe activation was 2.2 +/- 0.3 %. For the 4 controls, no activation was found in 3 subjects and data from one subject could not be analysed, because a susceptibility artifact rendered motion correction ineffectual.



Discussion

Adult fMRI is usually performed at higher field. Therefore in this study, large voxels and a long experiment were used to increase S/N. However on 3/14 occasions, once images effected by large-scale movement were removed, only 5/30 cycles were left for analysis. Large voxels make identification of fetal brain anatomy difficult, hinder motion correction, and reduce activation signals by partial voluming. This is maybe one reason why, in most cases, temporal lobe activation was only detected on one side of the brain. Future work will aim at improving S/N, overcoming motion, using other stimuli, and relating the results to behavioural and anatomical data.

References

1. Pharoh P., et al, *Brit. J. Obstet.. Gynaecol.*, **102**, 356, 1994.
2. Wakai RT, et al, *Am. J. Obstet.. Gynaecol.*, **174**, 1484, 1996.
3. Hykin J, et al, *Lancet*, 1999.
4. Vadeyar S, *Proc. ISMRM*, #**364**, 1999.
5. Glover P, et al. *Brit., J., Rad.*, **68**, 1090-1094. 1995.
6. Documents of National Radiological Protection Board **2(1)**, 1991.
7. Friston KJ, et al, *Human Brain Mapping* **1**, 214, 220, 1994.

This work is funded by Tommy's Campaign.