The demonstration of human fetal brain activity *in utero* using function magnetic resonance imaging.

J.Hykin, R.Moore, *K.Duncan, *P.Baker, *I.Johnson, S.Clare, R.Bowtell, P.Mansfield and P.Gowland.
Magnetic Resonance Centre, School of Physics & Astronomy, *School of Human Development, City Hospital, University of Nottingham, NG7 2RD.

Introduction

This study presents the first direct investigation of fetal brain activity *in utero* using fMRI. Human fetal brain activity is usually studied indirectly by monitoring the changes in fetal heart rate and associated fetal movements, although recently fetal MEG has been attempted[1]. fMRI offers a safe and relatively robust method of monitoring fetal brain activity. This has major implications for the study of fetal brain development, fetal learning strategies and cerebral palsy.

Methods

Subjects Five women with normal singleton pregnancies and the fetal head engaged in the maternal pelvis were recruited. Permission for the study was obtained from the local ethics committee and informed written consent was obtained from all subjects. One adult volunteer was also scanned.

Scanning All images were obtained on a 0.5T purpose built echo-planar magnetic resonance imaging scanner. Each EPI image was acquired in about 130 ms, (effective echo time= 65 ms). The slice orientation was transaxial to the mother. Initially a set of multislice images (SL = 9 mm) was acquired across the fetus. Subsequently 2 slices were selected through the fetal temporal lobes, although as the fetus would not in general be lying axially these slices were oblique in the fetus. For this reason, for fMRI SL= 15 mm. An equivalent protocol was followed for the adult volunteer but with SL=10 mm.

Activation paradigm Prior to scanning, the mother recorded a nursery rhyme on to a domestic tape recorder. The recording was replayed to the fetus so as to give 100 dB SPL at the surface of the mother's abdomen, which is known to give rise to 80 dB SLP at the fetal cochlear[2]. The stimulus was presented for 15 s on and 15 s off, repeated for 18 full cycles. Images were acquired at a rate of 4 Hz so that each slice was sampled at 2 Hz. For the adult volunteer music was used as the stimulus.

Data Analysis The image data was segmented to retain only the fetal brain and skull. The data was then normalised, in plane image re-registration was performed and a 3D 4 mm spatial filter was applied. Temporal filtering was performed using a Gaussian of width 1.4 s. The resulting pixel signals were then correlated to the expected response function. (square wave convolved with a Poisson function of width 2.8 s), and functional statistical parametric maps were constructed. The resulting functional maps were overlayed on the original multislice scans, with the slices bounding the volume scanned for fMRI highlighted to be black. The data set was then resampled to give transaxial images through the fetus, on which the region in which fMRI had been performed was bounded by a black line.

Results

Activation was seen in the temporal lobes of 4 out of 5 fetuses (in the fifth case the fetus moved so much that the fMRI data could not be analysed) but was only observed in one hemisphere in every case. This was because the temporal lobes could only be studied on one side due to the tilt of the fetal brain with respect to the axes of the scanner (as indicated by the position of the black lines in fig.1). The percentage signal changes in the fetuses ranged from 1.9-3.3%, while for the adult the value was 1.0%.

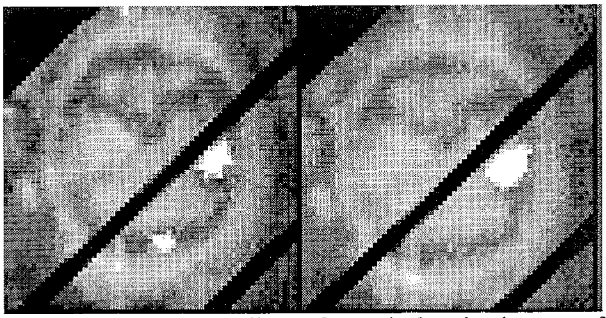

Figure 1 displays two slices of a typical activation map from one fetus. The overlayed maps have been resampled to give transverse images through the fetal brain, and the black lines indicate the limit of the oblique region through the fetal brain scanned during the fMRI experiment. BOLD signal can be seen in the temporal lobes and sagittal sinus.

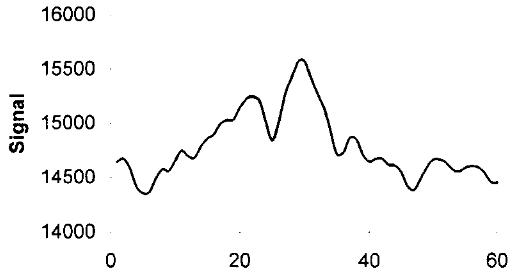

Figure 2 displays the time course of signal change in the activated temporal lobe ROI shown in fig. 1.

Discussion

A limitation of this study is that only a small proportion of the fetal brain was investigated, and in future we plan to scan a larger volume of the brain. Fetal behavioural response studies have shown that this stimulus behaves like a vibro-acoustic stimulator, inducing the F1 behavioural state. The stimulus also causes an increase in carotid artery blood flow, as measured using Doppler ultrasound. Future studies will include simultaneous monitoring of the fetal heart rate and fetal movements.

Conclusion

This paper presents the first direct assessment of fetal brain activity using fMRI. This technique has the potential to become a powerful tool in investigating brain development.

References

1. R.T.Wakai, et al, Am. J. Obstet Gynecol, 174, 5, 1484, 1996.
2. P.Glover, et al, Brit. J. Rad., 68, 1090-1094, 1995.

Acknowledgements: This work was supported by Tommy's Campaign and the MRC.