An exploration of task based fMRI in neonates using echo-shifting to allow acquisition at longer TE without loss of temporal efficiency

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TARGET AUDIENCE This research will benefit those researchers interested in neonatal and fetal functional brain studies.

PURPOSE Optimal BOLD to noise contrast in neonatal and fetal fMRI subjects has been hard to achieve because of the much longer T2* values in developing brain tissue in comparison to those in the mature adult brain[1,2]. The conventional approach for optimizing fMRI sequences would suggest matching the echo time (TE) and the T2* values across the neonatal and fetal brain. However, use of long echo times with a conventional EPI sequence decreases the maximum temporal sampling rate. Here we apply the concept of echo shifting[3] to task based neonatal fMRI data in order to achieve an improved BOLD to noise contrast and efficient data sampling at the same time. Echo-shifted EPI (es-EPI) is a modification of a standard 2D EPI sequence which enables echo times longer than the time between consecutive excitations ($TE > TS = TR / N_{Slices}$, where N_{Slices} is the number of acquired slices and TR is the repetition time). The efficacy of the proposed method was tested with neonatal subjects using a passive sensori-motor task paradigm with direct comparison between echo shifted and matched dual-echo fMRI datasets.

METHODS Data was collected using a Philips Achieva 3T scanner with a 32 channel receiver head coil. To investigate the optimal TE for neonatal subjects, a first examination was conducted with same fMRI task sampled at different echo times (30; 45; 60; 85 ms) with one healthy neonate of 38+3 weeks. Other sequence parameters were identical in each acquisition with a TR of 2940 ms and isotropic resolution of 2 mm. Imaged-based shimming was employed[4], and shim values kept constant across all scans. The sensori-motor stimulus was elicited using a fully automated and pneumatically driven fMRI compatible robotic interface which was attached to the right wrist and hand of the infant prior to scanning[5]. Synchronized stimulation was achieved via detection of the scanner transistor to transistor logic pulse with each TR. A simple block paradigm was used, consisting of alternating periods of 0.5Hz wrist extension/flexion ("on") and rest ("off).

Baby	PMA	Dual-echo	es-EPI
1	43	Yes	Yes
2	41	No	Yes
3	41+6	Yes	No
4	33+2	Yes	No

Table 1: Post Menstrual Age (PMA) in weeks and positive/negative outcome (Yes/No) for dual-echo and es-EPI.

The second part of this study used the same paradigm to test the echo shifting approach. Three sedated babies and one preterm infant (Table 1) were scanned using es-EPI with a TR/TE 2545/75 ms, isotropic resolution of 2mm, and SENSE factor 2. As reference data, dual-echo single shot EPI was also acquired with TEs of 25 and 75 ms, with an identical TR of 2545 ms and spatial resolution of 2 mm. To achieve this, N_{Slices} was lower in the dual-echo experiments compared to the es-EPI sequences, but selected to ensure appropriate coverage of the motor cortex. The number of acquired volumes and the shimming values were the same for both experiments and the sensori-motor task was recalibrated to match the new paradigm duration.

Data from both experiments was finally analysed with tools implemented in the FMRIB software library (FSL, www.fmrib.ox.ac.uk/fsl). After removal of high motion frames, standard pre-processing steps were applied to the data followed by analysis using the General Linear Model (GLM).

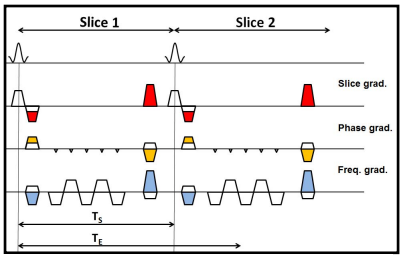

Figure 1: an Echo-Shifted EPI sequence.

Figure 1 shows the RF and gradient profiles for two consecutive slices of an es-EPI sequence; the coloured components indicate the gradients that achieve echo shifting, whereas the black lines represent a normal 2D EPI sequence; the signal coming from the 1st slice is crushed and is only refocused after the second RF pulse. This second pulse acts on a different slice and its signal is again crushed and then read out after the subsequent excitation (third slice). The dephasing gradients introduce a phase accumulation of 2π along each pixel in the read, phase encoding and slice directions and the effective TE achieved is $TE = TS + TE_{nom}$, where TE_{nom} is the nominal echo time of the corresponding standard EPI sequence. The signal suppression in the es-EPI sequence was tested on a phantom by changing the polarity of the spoiler gradients just preceding each RF pulse and comparing the residual dephased signal to an equivalent sequence with the RF turned off.

RESULTS No residual signal was visible when we unbalanced the echo shifting spoiler gradients and the noise pattern was comparable with the measurement performed with no RF. Figure 2 reports the average signal change over the top quartile of the activated voxels for the first fMRI experiment with TEs of 30 ms and 85 ms (left plot), 45 ms and 60 ms (center plot) and BOLD to noise ratio (right plot) calculated as the standard deviation of the BOLD time series divided by the standard deviation of the noise. It can be seen that higher TEs achieve both an increase task-related signal change and BOLD to noise ratio.

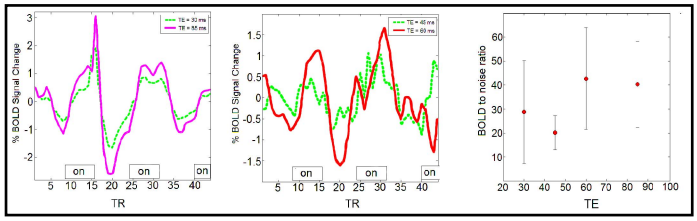

Figure 2: Percentage of average signal change over the activated clusters for the first fMRI experiment. Left: TEs of 30 (green) and 85 ms (purple). Center: TEs of 45 (green) and 60 ms (red). Right: BOLD to noise ratio.

Subject 1 produced useful data with both sequences, whereas subjects 2, 3 and 4 moved significantly either in the dual-echo or es-EPI experiments. Figure 3 presents transverse, coronal and sagittal views of es-EPI (first row) and dual-echo data (second and third rows) for subject 1. Tissue contrast is very different between the 2 echoes, with the contrast between CSF, white and gray matter clearly more visible at 75 ms. Overlaid on the EPI images, are the activation clusters of the top quartile of activated voxels obtained by the GLM analysis. Activated clusters are in the left contralateral primary somatosensory cortex. The signal time courses were also extracted, averaged across subjects for each type of data, and converted into percent signal change. Standard deviation of the signal variation for es-EPI data, first and second echoes were 1.03%, 0.4% and 0.72%, respectively.

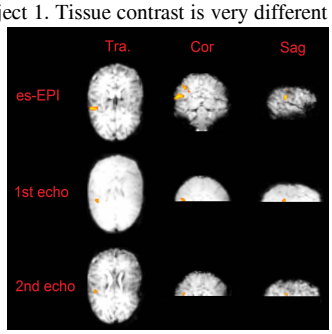

Figure 3: Transverse, coronal and sagittal views of the activated clusters for es-EPI data (first row) and dual-echo experiments (second and third row).

CONCLUSIONS This study investigates the possibility of elongating TE via the use of es-EPI to match the longer T2* of developing brain tissue for neonatal fMRI experiments without sacrificing sampling rate. These task activation experiments are extremely challenging, particularly as there is a need to perform two task activation runs and motion is not predictable. Nonetheless, three examples were obtained for dual-echo and two for es-EPI consistent with the proposition that echo shifting does allow access to longer echo times without loss of data quality when comparing the late echo in a dual-echo sequence. Despite the T2* being longer in immature brains, the issue of signal dropout at air-tissue interfaces at longer TE remains. This is an aspect that warrants further exploration. Spatial distortion is the same for all the data obtained as the readout structure is identical. This preliminary data suggests that echo shifting is a viable approach. The methodology could be particularly suitable for fetal fMRI studies, where signal dropout is less significant as air/tissue boundaries are absent in the womb. Echo shifting is completely compatible with multi-band methods [6] and the combination can provide high sampling rates at long echo times.

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