Investigation of optimal echo time for resting-state fMRI acquisition in Newborn infants

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Target Audience: This research will benefit researchers interested in neonatal fMRI studies.

Introduction: Functional MRI is being increasingly utilized to study the emerging functional architecture of the brain in the neonatal period. However, during early life, the brain is known to have a considerably higher water content, lower macromolecular concentration, and reduced synaptic density which results in T_2* values up to 2 times longer than those typically seen in the mature adult brain[1,2]. This factor is of particular importance for carrying out an optimized neonatal fMRI resting-state experiment, as blood oxygen level dependent (BOLD) contrast-to-noise ratio (CNR) is known to be maximal when the acquisition sequence echo time (TE) is matched to the T_2* of the tissue of interest[3]. Although there is now a growing literature of neonatal fMRI studies, none of the published studies have focused specifically on identifying the optimal TE for fMRI acquisition in this population. We hypothesized that TEs typically used for adult fMRI studies would be significantly less sensitive to BOLD contrast in neonatal subjects, and aimed to identify the optimal echo-time for performing resting-state fMRI studies in a test subject group.

Material and Methods: The study group consisted of 7 healthy neonates at term equivalent age. Written parental consent was obtained for all subjects. Data was acquired using a Philips 3T Achieva system (Best, NL) using a 32 channel reciever head coil, using a feed-and-wrap technique without sedation. In each infant, 3 dual-echo resting state echo BOLD fMRI data sets were acquired using an Echo-planar-imaging (EPI) sequence (TR = 2.998 s, flip angle 76°, in-plane resolution 2.5x2.5mm, slice thickness 3mm, 5 min. total acquisition time, TE1/TE2= 25/85,45/95,65/114ms). The data was analysed using tools as implemented in FMRIB's software library (FSL, www.fmrib.ox.ac.uk/fsl). Data was pre-processed using a standard pipeline which included removal of non-brain tissue, rigid-body motion correction, spatial smoothing (FWHM 3mm), and affine registration to a neonatal standard space template[4]. For each individual subject, ICA decomposition was first performed using MELODIC[5], and components identified (using both an automatic (FIX[6]) and manual approach) as those related to noise artifact were regressed out (denoising). Noise components were classified by a rater presented with candidate networks, but blinded to the subject/echo time,on the basis of their spatial and temporal characteristics which made them likely to be related to physiological artifacts (vascular pulsation, respiratory effects), head motion, or image distortion.

Further group level analysis was then performed on the denoised data-sets using MELODIC by temporally concatenating the individual, co- registered subject data (across all the TEs, and for each TE). The dimensionality of the ICA decomposition was limited to 20 components to reduce network fragmentation[7]. Dual regression was then used to produce subject-specific resting state networks (RSNs) maps. The maximum absolute T-statistic value was taken for each of these maps, and the average maximum T-statistic was then calculated across all components for each data set. CNR was assessed by calculating the ratio between the signal variance associated with RSN components to that of the residual noise.

Results: One data set was discarded due to excessive motion during acquisition. At longer TEs, there was a clear trend upon visual inspection towards increasing signal drop-out, particularly in the frontal and infero-temporal areas. In addition, there was also a general rise in signal loss with increasing echo times across all of the cortical tissue radiating inwards from the periphery of the brain (*Figure 1*). Despite this, group level ICA at each of the TEs detected consistent RSNs including the motor, auditory, visual, thalami, basal ganglia, and the posterior part of the default mode network. At lower TEs (25 and 45 ms), a larger amount of the variance within the ICA was proportionately explained by noise components as classified by both an automated (FIX) and manual approach (*Figure 2*). After data denoising, group ICA based CNR estimation did not identify any significant differences between TEs, although there was a trend towards a decrease at the shortest (25ms) and longest (108ms) TEs (*Figure 3*). In addition, the average maximum T-statistic across the identified RSNs were similar in all TEs, with the exception of a significant decrease at a TE of 25ms (*Figure 4*).

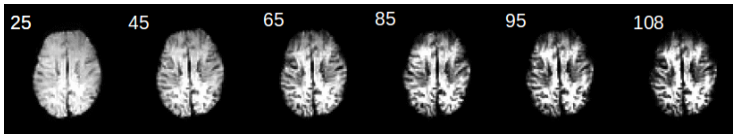

Figure 1: Example axial slices from images acquired in a single infant (PMA 41weeks) at 6 different TEs. Increasing signal drop-out can clearly be seen with longer TEs, particularly peripherally in the cortical tissue.

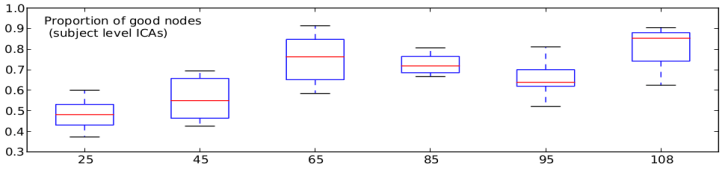

Figure 2: Total proportion of "good" (non-noise) components for each TE after manual classification.

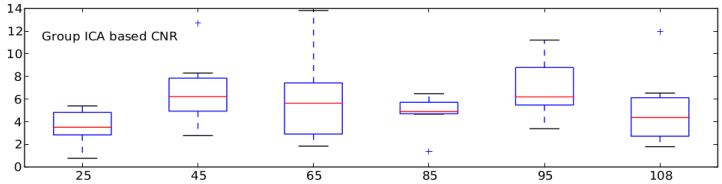

Figure 3: Average proportion of temporal variance associated to RSNs relative to noise (CNR) for each TE.

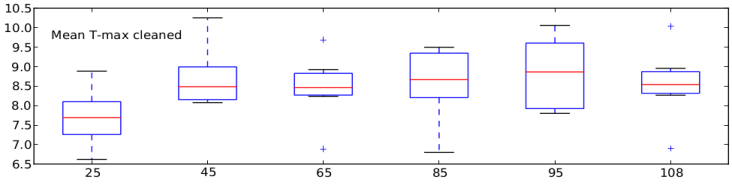

Figure 4: Average maximum T-statistic for all identified RSNs at each TE.

Discussion and Conclusions: RSNs could be reliably identified across our whole study group and at all TEs. Differences between the acquisitions were less prominent in the analysis of signal fluctuations presumed to be related to functional activity, in comparison to the structural features of the images, which were markedly affected by signal drop-out at longer TEs (65ms and above). This effect was most prominent in the peripheral cortical tissue perhaps due to the structure of the emerging cerebral vasculature during this period, which initially forms across the pial surface and then penetrates radially into the brain tissue during this stage of maturation[8]. At shorter TEs (25ms and 45ms), independent components classified as related to noise by both an automated and manual approach represented a higher proportion of the total number, perhaps related to a greater sensitivity to sources of physiological noise (in particular those related to vascular artifact).

There was a clear trend towards CNR reduction in the maximum T-statistic at a TE typically used in adult fMRI experiments, suggesting that it is sub-optimal for acquiring fMRI data in neonatal subjects. However at the higher TEs studied in this experiment, we did not identify a significant difference in either CNR or the average maximum T-statistic across the identified RSNs. Taken together, our results suggest that the selection of TE for optimal fMRI data acquisition in neonatal studies is highly dependent on the balance at a longer TE between improved CNR, decreased sensitivity to physiological sources of noise, and regional signal drop-out. This indicates that the choice should be guided by the specific aims of future resting state fMRI studies, and in particular the T2* values within the region and tissue of interest.

References:

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