

Accelerated development in the visual areas of preterm infants? A voxel-based morphometry study on diffusion tensor MR imaging

M. Gimenez^{1,2}, M. J. Miranda³, P. A. Born³, Z. Nagy⁴, T. Jernigan^{3,5}, E. Rostrup³

¹University of Barcelona, Barcelona, Spain, ²Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Hospital Clínic, Barcelona, Spain, ³Danish Research Centre for Magnetic Resonance, Copenhagen University Hospital, Copenhagen, Denmark, ⁴Karolinska Institute, Stockholm, Sweden, ⁵Laboratory of Cognitive Imaging (LOCI), La Jolla, CA, United States

Background: Premature birth has been related to delayed brain maturation (1). However, some studies suggest that stimulation in the extrauterine environment stimulates development, and delayed maturation may therefore be associated with concomitant risk factors, rather than preterm birth itself. The possibility of a more rapid maturation of certain brain areas has not been directly demonstrated. Maturation processes underlying the preterm brain development have been investigated by different Magnetic Resonance (MR) techniques, such as diffusion tensor imaging (DTI). DTI is a method that enables the possibility of studying structural maturation of white matter (WM) tracts.

Objective: The present study was undertaken to compare brain maturation by a voxel-based morphometry (VBM) approach in fractional anisotropy (FA) and in apparent diffusion coefficient (ADC) images in a sample of preterm newborns compared to a control group. Both groups were MR scanned at similar postmenstrual ages (38-46w). Moreover, we wanted to test the effect of the postnatal age (PNA) period in brain maturation at the first weeks of life.

Participants & Methods: The sample consisted of 27 healthy preterm newborns (mean gestational age: 31w) and 10 full-term newborns (mean gestational age: 39w). All infants were clinically stable throughout the neonatal period and had no evidence of major abnormalities by brain ultrasound scans. Diffusion weighted EPI images were acquired on a Siemens Magnetom Trio 3T scanner (b-value 1000 mm²/s, 6 directions). FA and ADC images were calculated based on the diffusion tensor. For the VBM technique we used the SPM2 programme, and the VBM applied to images was based on the optimized method proposed by Good et al. (2). As T2W neonate templates from several subjects are not available, the first step was to create a T2 template from 5 preterms and 5 control infants (these infants were scanned as a part of the preterm cohort, but did not have usable DTI). The T2W and DTI parametric images were adjusted to a standard orientation. We compared the FA and ADC images using the two *t*-test comparison (contrasts: control infants > preterm infants; preterm infants > control infants).

Results: When compared with the full-term group, the healthy preterm infants at corrected full-term age showed an increase in FA in areas related to visual function. The *t*-test group comparison between preterm and control infants showed an FA increase in the preterm group at the medial temporal region at the level of the sagittal stratum (see Figure 1). Correlation analysis demonstrated a positive relationship between FA values and PNA in the preterm group in the same areas (see Figure 2). No significant group differences or correlations were found for ADC.

Conclusion: This new VBM approach to FA images can provide a new insight into the quantification of maturation in different WM brain regions, with a voxel-by-voxel approach. Our study suggests that brain development in preterm newborns is stimulated by early experience. The differences observed in the sagittal stratum in the preterm group compared to controls are interesting since they seem to involve visual-related brain areas. A previous study focused on the effects of early postnatal experience on brain development has demonstrated a modification of certain cerebral structures in preterm infants, apparently as a response subject to an individualized developmental care program compared to a control group (3). Related to visual areas, face perception is an especially prominent stimulus from the earliest post-natal period. A recent investigation focused on 6-month-old infants showed an effect of early experiences in the ability of face processing, which is an especially prominent stimulus from the earliest post-natal period (4). We therefore speculate that visual stimulation, possibly face perception, could enhance brain maturation regionally. Our findings may lead to new investigations evaluating the adaptive mechanisms of the immature developing brain at early stages.

Figure 1. Sections of images illustrating an increase in FA values mainly in the sagittal stratum region (including mainly the inferior fronto-occipital fasciculi, the optic radiation, inferior longitudinal fasciculus and the lateral geniculate nucleus), bilaterally, in the preterm infant group compared to controls. a) axial sections with representative slices at 1 slice-interval. b) sagittal view of the right cluster with representative slices at 2 slice-interval. Differences are overlaid on the anatomic T2 mean of the sample. The color bar represents the T scores. Results were displayed at voxel uncorrected *p* threshold of < 0.001. Statistical Parametric Maps (SPMs) with left as right.

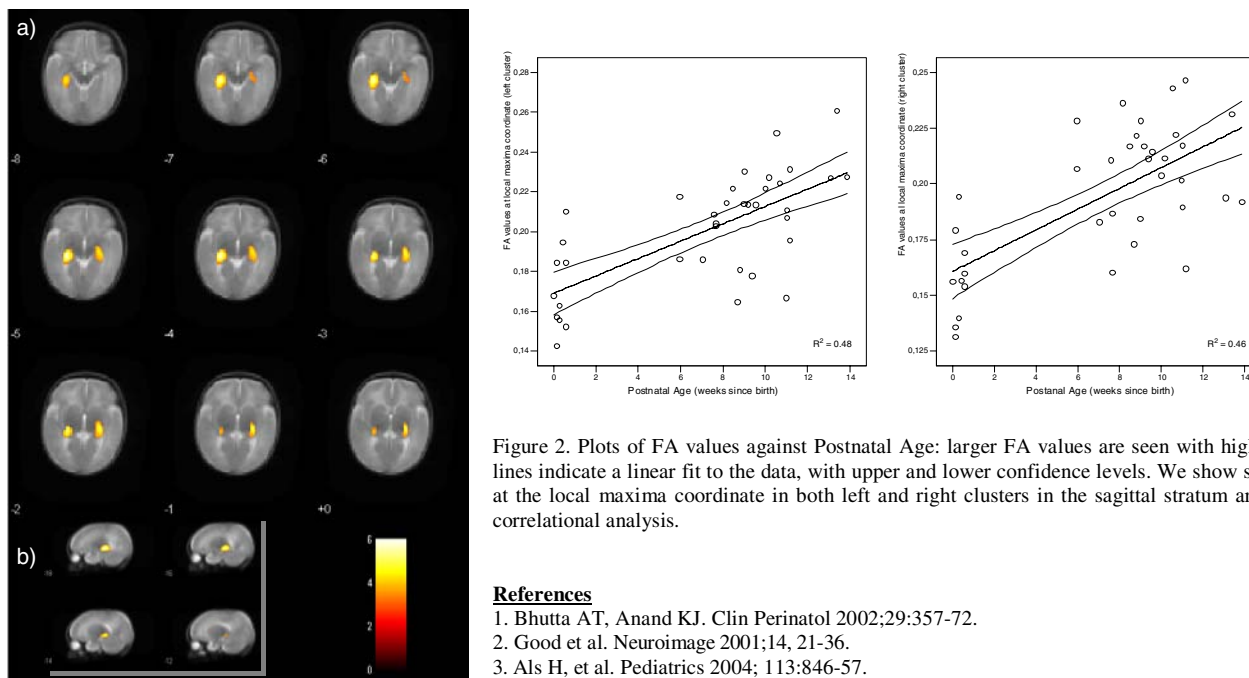


Figure 2. Plots of FA values against Postnatal Age: larger FA values are seen with higher postnatal age. The lines indicate a linear fit to the data, with upper and lower confidence levels. We show significant relationship at the local maxima coordinate in both left and right clusters in the sagittal stratum area, obtained from the correlational analysis.

References

1. Bhutta AT, Anand KJ. Clin Perinatol 2002;29:357-72.
2. Good et al. Neuroimage 2001;14, 21-36.
3. Als H, et al. Pediatrics 2004; 113:846-57.
4. Pascalis O, et al. Proc Natl Acad Sci USA 2005; 102:5297-300.