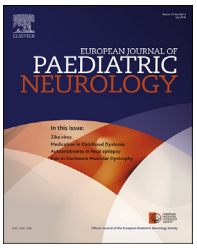
EUROPEAN JOURNAL OF PAEDIATRIC NEUROLOGY XXX (2018) 1–7

Official Journal of the European Paediatric Neurology Society



Original article

Diffusion MRI parameters of corpus callosum and corticospinal tract in neonates: Comparison between region-of-interest and whole tract averaged measurements

Sarah A. Sparrow [a], *Devasuda Anblagan* [b], *Amanda J. Drake* [c], *Emma J. Telford* [a], *Rozalia Pataky* [a], *Chinthika Piyasena* [a,c], *Scott I. Semple* [c,d], *Mark E. Bastin* [b], *James P. Boardman* [a,b,*]

[a] *MRC Centre for Reproductive Health, University of Edinburgh, 47 Little France Crescent, Edinburgh EH16 4TJ, UK*
[b] *Centre for Clinical Brain Sciences, University of Edinburgh, 47 Little France Crescent, Edinburgh EH16 4TJ, UK*
[c] *University/BHF Centre for Cardiovascular Science, University of Edinburgh, 47 Little France Crescent, Edinburgh EH16 4TJ, UK*
[d] *Clinical Research Imaging Centre, University of Edinburgh, 47 Little France Crescent, Edinburgh EH16 4TJ, UK*

ARTICLE INFO

Article history:
Received 27 July 2017
Received in revised form
28 March 2018
Accepted 11 May 2018

Keywords:
Neonatal
Diffusion
Tractography
Region-of-interest
Corticospinal
Corpus callosum

ABSTRACT

Purpose: Measures of white matter (WM) microstructure inferred from diffusion magnetic resonance imaging (dMRI) are useful for studying brain development. There is uncertainty about agreement between FA and MD values obtained from region-of-interest (ROI) versus whole tract approaches. We investigated agreement between dMRI measures using ROI and Probabilistic Neighbourhood Tractography (PNT) in genu of corpus callosum (gCC) and corticospinal tracts (CST).

Materials and Methods: 81 neonates underwent 64 direction DTI at term equivalent age. FA and MD values were extracted from a 8 mm^3 ROI placed within the gCC, right and left posterior limbs of internal capsule. PNT was used to segment gCC and CSTs to calculate whole tract-averaged FA and MD. Agreement between values obtained by each method was compared using Bland–Altman statistics and Pearson's correlation.

Results: Across the 3 tracts the mean difference in FA measured by PNT and ROI ranged between 0.13 and 0.17, and the 95% limits of agreement did not include the possibility of no difference. For MD, the mean difference in values obtained from PNT and ROI ranged between 0.101 and 0.184 $mm^2/s \times 10^{-3}$ mm^2/s: the mean difference in gCC was 0.101×10^{-3} mm^2/s with 95% limits of agreement that included the possibility of no difference, but there was significant disagreement in MD values measured in the CSTs.

Conclusion: Agreement between dMRI measures of neonatal WM microstructure calculated from ROI and whole tract averaged methods is weak. ROI approaches may not provide

Abbreviations: CST, corticospinal tract; GA, gestational age; gCC, Genu of corpus callosum; ICC, Intraclass correlation; OFC, Occipital-frontal head circumference; PLIC, posterior limb of internal capsule; PNT, probabilistic neighbourhood tractography.

* *Corresponding author*. MRC Centre for Reproductive Health, University of Edinburgh, 47 Little France Crescent, Edinburgh EH16 4TJ, UK.
E-mail address: james.boardman@ed.ac.uk (J.P. Boardman).

https://doi.org/10.1016/j.ejpn.2018.05.003

sufficient representation of tract microstructure at the level of neural systems in newborns.

1. Introduction

Structural and diffusion magnetic resonance imaging of the brain during the newborn period contributes to understanding the neural systems that underpin typical and atypical development. Preterm birth is closely associated with injury and/or maldevelopment of cerebral white matter,[1] and with several long-term adverse outcomes including cerebral palsy, neurocognitive impairment, social difficulties and vulnerability to psychiatric disease.[2–5]

Quantitative parameters derived from diffusion magnetic resonance imaging (dMRI) include fractional anisotropy (FA) and mean diffusivity (MD), which enable inference about the microstructural organisation of brain tissue and white matter tracts.[6] A consistent finding is that FA is decreased and MD is increased in the white matter of preterm infants at term equivalent age.[7–10] The corpus callosum (CC) and corticospinal tracts (CST) are of particular interest in the context of developing biomarkers for later neurodevelopmental outcome after preterm birth, because dMRI parameters in these tracts are influenced by gestational age, and their microstructural properties have been associated with later function.[11–13]

Two widely used methods to measure dMRI parameters in these tracts include region-of-interest (ROI) analysis and tractography, but the agreement of values obtained using these methods is uncertain; for example, ROI measures show an inconsistent correlation with values of the white matter skeleton at corresponding sites using tract-based spatial statistics.[14] ROI approaches are often used in clinical settings because they provide absolute quantification of MD and FA in selected regions without the need for substantial post-processing but they are labour intensive, prone to operator bias, and the volume and shape of the ROI can influence results.[15–17]

Probabilistic Neighbourhood Tractography (PNT) is an automatic segmentation method, which provides whole tract-averaged measures of FA and MD in major white matter fasciculi. This method, first described by Clayden et al.,[18,19] has been optimized for neonatal data.[20] It involves single seed point tractography to segment a tract of interest by modelling the length and shape variation of individual tracts compared with a pre-defined reference tract.

We aimed to compare FA and MD values measured from geometric ROIs with tract-averaged values obtained using PNT in the genu of the corpus callosum (gCC) and the CST. The secondary aim was to evaluate intra-rater variation in FA and MD values obtained by ROI placement within these tracts.

2. Materials and methods

2.1. Participants

Ethical approval was granted from the National Research Ethics Service (South East Scotland Research Ethics Committee) and informed parental consent was obtained. The study was conducted in accordance with the 18th World Medical Assembly, Helsinki 1964 and later revisions. Infants were recruited from the Neonatal Intensive Care Unit and postnatal wards between June 2012 and June 2014. The group consists of a subset of infants recruited to a longitudinal study of the effect of preterm birth on the developing brain and neurodevelopmental outcome. Preterm infants (birth weight <1500 g or gestational age <32 completed weeks) and term infants (birth after 37 weeks gestation) were recruited. All infants underwent MRI at term equivalent age (38–42 weeks' gestational age). Infants with chromosomal or congenital abnormalities and those with major parenchymal lesions including haemorrhagic parenchymal infarction and cystic periventricular leucomalacia were excluded.

2.2. Magnetic resonance imaging

A Siemens Magnetom Verio 3 T MRI clinical scanner (Siemens Healthcare GMbH, Erlangen, Germany) and 12-channel phased-array head coil were used to acquire: T1-weighted MPRAGE volume (~1 mm^3 resolution), T2-weighted STIR (~0.9 mm^3 resolution), T2-weighted FLAIR (~1 mm^3 resolution), and diffusion MRI (11 T2-and 64 diffusion encoding direction ($b = 750$ s/mm^2) single-shot spin-echo echo planar imaging (EPI) volumes with 2 mm isotropic voxels) data.

Infants were examined in natural sleep with pulse oximetry, temperature and electrocardiography data monitoring. Ear protection was used for each infant, comprising earplugs placed in the external ear and neonatal earmuffs (MiniMuffs, Natus Medical Inc., CA).

2.3. Diffusion MRI data processing

After conversion from DICOM to NIfTI-1 format, dMRI data were pre-processed using FSL tools (FMRIB, Oxford, UK; http://www.fmrib.ox.ac.uk). This included brain extraction and removal of bulk infant motion and eddy current induced artifacts by registering subsequent diffusion-weighted volumes to the first T2-weighted EPI volume for each subject. Using DTIFIT, MD and FA volumes were generated for every subject. Underlying connectivity data was provided by FSL's BedpostX/ProbTrackX algorithm run with its default parameters: 2-fiber

Please cite this article in press as: Sparrow SA, et al., Diffusion MRI parameters of corpus callosum and corticospinal tract in neonates: Comparison between region-of-interest and whole tract averaged measurements, European Journal of Paediatric Neurology (2018), https://doi.org/10.1016/j.ejpn.2018.05.003