Corticospinal tract integrity and motor function following neonatal stroke: a case study

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Abstract

Background: New MRI techniques enable visualisation of corticospinal tracts and cortical motor activity. The objective of this case study was to describe the magnetic resonance evidence of corticospinal pathway reorganisation following neonatal stroke.

Case presentation: An 11 year old boy with a neonatal right middle cerebral artery territory ischaemic stroke was studied. Functional MRI was undertaken with a whole hand squeezing task, comparing areas of cortical activation between hands. White matter tracts, seeded from the area of peak activation in the cortex, were visualised using a diffusion weighted imaging probabilistic tractography method. Standardised evaluations of unilateral and bilateral motor function were undertaken. Clinically, the child presented with a left hemiparesis. Functional MRI demonstrated that movement of the hemiparetic hand resulted in activation in the ipsi-lesional (right) hemisphere only. Diffusion tractography revealed pathways in the right (lesioned) hemisphere tracked perilesionally to the cortical area identified by functional MRI.

Conclusion: Our case demonstrates that neonatal stroke is associated with maintenance of organization of corticospinal pathways sufficient to maintain some degree of hand function in the affected hemisphere. Functional MRI and diffusion weighted imaging tractography may inform our understanding of recovery, organisation and reorganisation and have the potential to monitor responses to intervention following neonatal stroke.

Keywords: Stroke, Children, Plasticity, Functional imaging, Motor outcome

Background

Neonatal arterial ischaemic stroke (AIS) is an important cause of cerebral palsy. The middle cerebral artery is the most common vascular territory affected. Functional consequences are diverse, and may emerge over time. Hemiparesis is less common in neonatal onset stroke when compared with childhood onset [1]. It has been postulated that the developmental stage of the brain at the time of injury may influence recovery from brain injury in children. A number of mechanisms may be responsible for cerebral recovery including formation of new synaptic connections, change of function of neurons in response to injury, and utilisation of pathways contralateral to the injury site [2].

Magnetic resonance imaging (MRI) techniques enable visualisation of corticospinal tracts (using diffusion-weighted imaging (DWI)) and cortical motor activity (using functional MRI (fMRI)). This information has the potential to be used to explore mechanisms of recovery and reorganisation and to measure response to interventions aimed at improving outcome. The aim of this study was to investigate whether there was evidence of relocation of cortical motor activity and reorganisation of motor pathways in a school-aged child who had a unilateral perinatal AIS affecting the motor cortex with residual hemiparesis.

Case presentation

Method

The subject, an 11 year old boy, sustained an AIS affecting the right middle cerebral artery territory diagnosed radiologically during the perinatal period. Perinatal MR imaging had previously been obtained on a 1.5-Tesla General Electric LX Echospeed system (version 9.0). Transverse T1 fast spin echo (TR/TE 1400/10, ETL 2, BW +/- 20 kHz, FOV 20 cm, slice thickness 3.5 mm;
The subject presented with a MACS level 2 and GMFCS level 2 left hemiparesis, and a PSOM score of 1. He was able to achieve an inferior pincer grip but not reliably, with his left (affected) hand. The left arm and hand were used to assist in bilateral activities by holding with a restricted repertoire of movements. Consistent with this functional picture, his AHA score was 65 % and BOT2 total composite standard score was 33 (below average). On structural MRI, the site of the brain injury was identified in the right perisylvian region with cystic leukoencephalomalacia involving posterior right frontal, right parietal pre- and post-central gyri and superior temporal lobe. Comparison of cortical activation between left and right hemispheres using fMRI demonstrated that movement of the affected left hand resulted in activation in the ipsi-lesional hemisphere only, anterior to the lesion within the motor cortex. In comparison, movement of the right hand resulted in expected activation of the motor cortex. DWT revealed pathways in the right (lesioned) hemisphere tracked perilesionally to the cortical area identified by fMRI. The right hand motor task resulted in expected and more robust motor cortical activation with the expected contralateral hemisphere and corticospinal tracts when compared to left (see Figures 1, 2). DWT was seeded from areas of maximal fMRI activation to the pons (Figure 3). Sampling of FA values sequentially along the corticospinal tracts

![Figure 1 Motor fMRI Findings. Coronal view. fMRI activation in R cortical region with left (affected) hand motor task. (R side of brain appears on L side of image).](http://www.biomedcentral.com/1471-2377/12/53)
(Figures 4, 5) shows reduced FA in the ipsilesional tracts when compared to the contralesional side.

**Conclusion**

The DWT results described in this case show that the region identified by fMRI as supporting hemiparetic hand use has the necessary white matter connections to perform this function. The underlying white matter may not be sufficiently preserved to allow a full recovery of function, but partial recovery is evident. The reduced FA within the ipsilesional cortico-spinal tract compared to the contralesional side may be explained by a number of factors. These include absence of myelin; compromised axonal membranes; reduced axonal density; and increased extra-cellular water [12]. In this case however, it is unlikely given the child’s medical history that the observed FA changes are due to demyelination or compromised axonal membranes. Given the nature of the brain insult, it may however be expected that there would be loss of axonal density, and corresponding
increase in extra-cellular water, due to loss of some projections to/from the site of injury.

Our findings suggest that chronic functional motor deficits following neonatal AIS may be associated with limited preservation of organisation to ipsilesional regions of the cortex, and there was reduced pathway density in regions of the tracts distal to the site of injury. The underlying mechanisms for these processes remain unknown. Wallerian degeneration of the descending corticospinal tracts has been associated with poor motor outcome in both acute and chronic paediatric stroke [13,14].

In this case, despite unilateral damage to the motor cortex, the child developed useful functional ability of the impaired upper limb, as a non-dominant limb. DWT suggests intact perilesional motor pathways were associated with the use of the child's impaired hand. fMRI and DWI of structures associated with motor outcome may improve our ability to predict outcome following paediatric stroke. In paediatric clinical practice a number of approaches have shown potential to improve motor function including transcranial magnetic stimulation [15], modified constraint induced movement therapy, and bimanual training [16]. It is possible that activity-dependent synaptic plasticity and reorganisation of motor and sensory maps is influenced by lesion, age and intervention characteristics. Prospective magnetic resonance studies imaging motor tracts longitudinally in relation to functional recovery may assist in identifying targets for motor rehabilitation intervention. Future studies are indicated to explore the impact of intervention on axonal density in the corticospinal tracts and functional outcome.

Summary
DWT enables visualisation and quantification of white matter tracts and can inform our understanding of mechanisms of recovery in early acquired damage to the developing brain. Further studies are needed to explore the relationship between white matter tracts (as characterised using DWT) and the degree of motor recovery. This has the potential to underpin rehabilitation interventions aimed at improving motor function following stroke in infancy.

Consent
Written informed consent was obtained from the patient's parents for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Series Editor of this journal.

Abbreviations
MRI: Magnetic resonance imaging; fMRI: Functional MRI; DWT: Diffusion weighted tractography; DWI: Diffusion-weighted imaging, AIS, Arterial ischaemic stroke (AIS, BOT2, Bruininks-Oseretsky Test of Motor Proficiency 2; AHA: Assisting Hand Assessment v4.1, PSOM, Pediatric Stroke Outcome Measure, MACS, Manual Ability Classification System; GMFCS: Gross Motor Functional Classification System (Expanded & Revised).

Competing interests
The authors declare they have no competing interests.

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Authors’ contributions
AG conceived of the study, undertook the clinical examinations, participated in the imaging data acquisition and drafted the manuscript; RH conceived of the study, and data interpretation and helped draft the manuscript; AW participated in the study design and Chris Adamson and Jian Chen for assistance with data analysis. This study was funded by a Murdoch Childrens Research Institute Critical Care & Neurosciences Theme small project grant. JDT is grateful to the National Health and Medical Research Council (NHMRC) of Australia, Austin Health, and the Victorian Government’s Operational Infrastructure Support Program for their support.

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