NeuroImage: Clinical 8 (2015) 104–109

Contents lists available at ScienceDirect

NeuroImage: Clinical

journal homepage: www.elsevier.com/locate/ynicl

Validity of semi-quantitative scale for brain MRI in unilateral cerebral palsy due to periventricular white matter lesions: Relationship with hand sensorimotor function and structural connectivity

Simona Fiori[a,*], Andrea Guzzetta[a,b], Kerstin Pannek[c,d,e], Robert S. Ware[f,g], Giuseppe Rossi[h], Katrijn Klingels[i], Hilde Feys[i], Alan Coulthard[k], Giovanni Cioni[a,b], Stephen Rose[c], Roslyn N. Boyd[j]

[a] IRCCS Fondazione Stella Maris, Pisa, Italy
[b] University of Pisa, Pisa, Italy
[c] Australia E-Health Research Centre, Brisbane, Australia
[d] University of Queensland, School of Medicine, Brisbane, QLD, Australia
[e] Department of Computing, Imperial College London, Biomedical Image Analysis Group, London, UK
[f] School of Population Health, The University of Queensland, Brisbane, QLD, Australia
[g] Queensland Children's Medical Research Institute, The University of Queensland, Brisbane, QLD, Australia
[h] Institute of Clinical Physiology, Italian National Research Council, Pisa, Italy
[i] Department of Rehabilitation Sciences, Faculty of Kinesiology and Rehabilitation Sciences, KU Leuven, Leuven, Belgium
[j] Queesland Cerebral Palsy and Rehabilitation Research Centre, The University of Queensland, Brisbane, Australia
[k] Academic Discipline of Medical Imaging, Royal Brisbane and Women's Hospital, QLD, Australia

ARTICLE INFO

Article history:
Received 23 February 2015
Received in revised form 1 April 2015
Accepted 2 April 2015
Available online 9 April 2015

Keywords:
Brain structure
Sensorimotor function
Unilateral cerebral palsy
Magnetic resonance imaging
Diffusion
HARDI

ABSTRACT

Aim: To provide first evidence of construct validity of a semi-quantitative scale for brain structural MRI (sqMRI scale) in children with unilateral cerebral palsy (UCP) secondary to periventricular white matter (PWM) lesions, by examining the relationship with hand sensorimotor function and whole brain structural connectivity.
Methods: Cross-sectional study of 50 children with UCP due to PWM lesions using 3 T (MRI), diffusion MRI and assessment of hand sensorimotor function. We explored the relationship of lobar, hemispheric and global scores on the sqMRI scale, with fractional anisotropy (FA), as a measure of brain white matter microstructure, and with hand sensorimotor measures (Assisting Hand Assessment, AHA; Jebsen–Taylor Test for Hand Function, JTTHF; Melbourne Assessment of Unilateral Upper Limb Function, MUUL; stereognosis; 2-point discrimination).
Results: Lobar and hemispheric scores on the sqMRI scale contralateral to the clinical side of hemiplegia correlated with sensorimotor paretic hand function measures and FA of a number of brain structural connections, including connections of brain areas involved in motor control (postcentral, precentral and paracentral gyri in the parietal lobe). More severe lesions correlated with lower sensorimotor performance, with the posterior limb of internal capsule score being the strongest contributor to impaired hand function.
Conclusion: The sqMRI scale demonstrates first evidence of construct validity against impaired motor and sensory function measures and brain structural connectivity in a cohort of children with UCP due to PWM lesions. More severe lesions correlated with poorer paretic hand sensorimotor function and impaired structural connectivity in the hemisphere contralateral to the clinical side of hemiplegia. The quantitative structural MRI scoring may be a useful clinical tool for studying brain structure–function relationships but requires further validation in other populations of CP.

1. Introduction

Brain structural MRI can provide high-resolution images on cerebral macrostructure, thus improving our capability of investigating anatomy, morphology and volume in normal or pathological conditions. Its use has improved the understanding of the aetiology and pathogenesis of brain injury in cerebral palsy (CP) (Ashwal et al., 2004; Krageloh-Mann et al., 2007). Although essential, qualitative structural imaging approaches do not comprehensively explain the great variability in

Abbreviations: CP, cerebral palsy; MRI, magnetic resonance imaging; sqMRI, semi-quantitative MRI; PWM, periventricular white matter; AHA, Assisting Hand Assessment; MUUL, Melbourne Assessment of Unilateral Upper Limb function; JTTHF, Jebsen–Taylor test of hand function; GMFCS, Gross Motor Function Classification System; MACS, Manual Ability Classification System; FA, fractional anisotropy.

* Corresponding author. Tel.: +39 050886313; fax: +39 050886324.
E-mail address: s.fiori@fsm.unipi.it (S. Fiori).

http://dx.doi.org/10.1016/j.nicl.2015.04.005

the clinical phenotype in terms of topography and severity of the brain lesion (Yokochi et al., 1991; Aida et al., 1998; Staudt et al., 2000; Arnfield et al., 2013; Kwon et al., 2014).

Recently our team has developed a new tool for assessing brain damage in children with CP to provide a quantitative analysis of lesion severity on structural MRI, the semi-quantitative MRI (sqMRI) scale (Fiori et al., 2014). The sqMRI is comprised of a global score and a number of subscores specifically assessing the involvement of different brain regions. This modular approach was designed to capture the associations between structural damage and functional impairment within the different clinical subgroups of CP. The scale was developed by a multidisciplinary expert team to ensure good content validity and was proven to be reliable, although requiring further validation (Fiori et al., 2014). Construct validity could be established through comparison with a measure that is believed to reflect the same underlying phenomenon or by using the instrument to test specific hypotheses that support the construct of the test, e.g. that the instrument can distinguish between people with varied clinical conditions (Portney et al., 2009).

The purpose of the current study was therefore to provide first evidence for establishing the construct validity of the sqMRI scale (Portney et al., 2009) in a cohort of children with unilateral CP (UCP) due to periventricular white matter (PWM) lesions. To address this aim, we took advantage of the same cohort of children studied by Pannek et al. (2014), who explored differences in structural connectivity between UCP and typical development, and their relationships with hand function. The semi-quantitative scale was used in Pannek et al. (2014) only to describe the cohort. Here, we expand on previous findings in that we test the relationship between scores on the sqMRI scale with i) measures of impaired hand motor and sensory function and ii) measures of brain microstructure. Our first hypothesis was that sqMRI scores contralateral to the clinical side of hemiplegia correlate with clinical measures of impaired hand motor and sensory function, so that higher lesion scores would correspond to poorer hand function. Our second hypothesis was that sqMRI scores contralateral to the clinical side of hemiplegia correlate with brain MRI FA in connections/tracts, so that higher lesion scores would correspond to more severe disruption of connectivity (Scheck et al., 2012; Pannek et al., 2014).

2. Methods

2.1. Participants

Participants were the same as in Pannek et al. (2014). They were recruited as part of a cohort study of children with congenital UCP at the Queensland Cerebral Palsy and Rehabilitation Research Centre in Brisbane, Australia (Boyd et al., 2013a; Boyd et al., 2013b). Children with mild to moderate congenital spasticity motor type UCP (Gross Motor Function Classification System Score I-II, Manual Ability Classification System Score I-II), aged between 5 and 18 years were considered eligible. They were excluded if they previously had either undergone surgery in the upper limb or received BoNT-A injections within 6 weeks prior to baseline assessments (Boyd et al., 2013a; Boyd et al., 2013b). They were included if they had evidence of PWM on sMRI, no contraindication for MRI and sufficient cooperation and cognitive understanding to participate in the assessment. The University of Queensland and Children's Health Queensland ethics committees granted ethical approval. Informed parental consent was obtained for all participants.

2.2. MRI acquisition

MRI data were acquired at study enrolment, prior to commencing any of the COMBIT or Mitii protocol of rehabilitative intervention (Boyd et al., 2013a; Boyd et al., 2013b) using a 3 T Siemens Tim Trio scanner (Siemens, Erlangen, Germany). A high-resolution structural image was acquired using a 0.9 mm isotropic 3D T1 Magnetisation Prepared Rapid Gradient Echo (MPRAGE) sequence. An axial T2-weighted Fluid Attenuated Inversion Recovery (FLAIR) image was acquired for lesion classification of structural images. FLAIR images were selected over FSE T2 due to its sensitiveness to gliotic white matter lesions (Bastianello et al., 1997) and to match reliability parameters of the semi-quantitative scale (Fiori et al., 2014). Diffusion weighted images were acquired along 64 uniformly distributed diffusion encoding directions ($b = 3000$ s/mm^2) along with one $b = 0$ image, using a twice-refocussed single-shot echo-planar-imaging sequence to reduce eddy current distortions. An acceleration factor of 2 was employed to reduce susceptibility distortions. A gradient-echo based field map was additionally acquired to assist in the correction of image distortions as described by Pannek et al. (2014).

2.3. Structural image analysis

An MRI-trained child neurologist (SF) assessed all structural images. Each MRI was scored accordingly to the sqMRI scale (Fiori et al., 2014). Briefly, each periventricular, middle and cortico/subcortical layer of the frontal, parietal, temporal and occipital lobes was scored and summarised into a lobar score (LS) ranging from 0 to 3 for each lobe (i.e. a score from 0 to 1 for each of the 3 layers). All lobar scores on each (of the right and left) side were summed to result in the hemispheric score (HS) (range: 0–12). The basal-ganglia-and-brainstem (caudate, lenticular, posterior limb of internal capsule, thalamus and brainstem) corpus callosum and cerebellum scores were also determined. For each side, the hemispheric summary score (HSS) was calculated as the result of the hemispheric and basal-ganglia-and-brainstem scores (range: 0–17). The sum of all the scores of the scale resulted in a global score (GS) (range: 0–40). For all scores, the higher is the score the bigger is the lesion. Good reliability has been confirmed between independent raters for the sqMRI scale (Fiori et al., 2014).

2.4. Clinical testing

The use of the impaired hand as an assisting hand in bimanual tasks was assessed using the school kids version of the Assisting Hand Assessment (AHA) (Krumlinde-Sundholm et al., 2003). Unimanual capacity of the impaired hand was assessed using the Melbourne Assessment of Unilateral Upper Limb Function (MUUL) (Johnson et al., 1994). For both AHA and MUUL, a higher score indicates better function. Speed and dexterity of the impaired upper limb were assessed using the Jebsen–Taylor Test of Hand Function (JTTHF) (Jebsen et al., 1969) where a lower score indicates faster speed. Sensory function was assessed using the stereognosis and 2-point-discrimination (2PD) tests for the impaired hand (Auld et al., 2012). For stereognosis, the number of correct responses out of a possible maximum of nine was recorded (Auld et al., 2012). 2PD was assessed using the Disk-Criminator (MacKinnon et al., 1985; Zalesky et al., 2010) as the smallest separation (in mm) between the two points that could be perceived on at least 7 of 10 trials (Zalesky et al., 2010).

2.5. Diffusion data preprocessing and connectome generation

Cortical reconstruction, volumetric segmentation, and diffusion processing for the generation of connectomes were executed (Pannek et al., 2014). In brief, freesurfer (http://surfer.nmr.mgh.harvard.edu, version 5.0) was used to parcellate the brain into 68 cortical regions, left and right thalami (2 regions), left and right cerebellum (2 regions), and brain stem (1 region). Posterior limb of internal capsule (PLIC) was not included in the connectome because it is not a region where connections should terminate. A total of 73 regions were thus included in the connectome construction.

Following extensive preprocessing of diffusion data to correct for head motion, image distortions and artefacts (Pannek et al., 2014), MRtrix