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Review

# The need for improved brain lesion segmentation techniques for children with cerebral palsy: A review

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ABSTRACT

Cerebral palsy (CP) describes a group of permanent disorders of posture and movement caused by disturbances in the developing brain. Accurate diagnosis and prognosis, in terms of motor type and severity, is difficult to obtain due to the heterogeneous appearance of brain injury and large anatomical distortions commonly observed in children with CP. There is a need to optimise treatment strategies for individual patients in order to lead to lifelong improvements in function and capabilities. Magnetic resonance imaging (MRI) is critical to non-invasively visualizing brain lesions, and is currently used to assist the diagnosis and qualitative classification in CP patients. Although such qualitative approaches under-utilise available data, the quantification of MRIs is not automated and therefore not widely performed in clinical assessment. Automated brain lesion segmentation techniques are necessary to provide valid and reproducible quantifications of injury. Such techniques have been used to study other neurological disorders, however the technical challenges unique to CP mean that existing algorithms require modification to be sufficiently reliable, and therefore have not been widely applied to MRIs of children with CP. In this paper, we present a review of a subset of available brain injury segmentation approaches that could be applied to CP, including the detection of cortical malformations, white and grey matter lesions and ventricular enlargement. Following a discussion of strengths and weaknesses, we suggest areas of future research in applying segmentation techniques to the MRI of children with CP. Specifically, we identify atlas-based priors to be ineffective in regions of substantial malformations, instead propose relying on adaptive, spatially consistent algorithms, with fast initialisation mechanisms to provide additional robustness to injury. We also identify several cortical shape parameters that could be used to identify cortical injury, and shape modelling approaches to identify anatomical injury. The benefits of automatic segmentation in CP is important as it has the potential to elucidate the underlying relationship between image derived features and patient outcome, enabling better tailoring of therapy to individual patients.


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## 1. Introduction

Cerebral palsy (CP) is the most prevalent cause of physical disability in children, occurring in approximately 2 per 1000 live births worldwide (Stanley et al., 2000). It describes a heterogeneous group of permanent disorders of posture and movement caused by non-progressive disturbances in the brain during fetal or perinatal development (Rosenbaum et al., 2007). Depending on the timing of these disturbances, a range of injuries may occur, including brain maldevelopments, lesions in the white matter (WM) and grey matter (GM) as primary lesions, and the enlargement of the lateral ventricles as secondary insults, resulting in motor impairments as well as potential cognitive, linguistic, behavioural, and sensory problems (Himmelmann and Uvebrant, 2011). Current diagnosis of CP is based on clinical observations and qualitative assessment of motor development (Krigger, 2006) using several functional scales, allowing for treatment strategies to be tailored to individual patients with the aim of increasing the efficacy of rehabilitation. Determining the most appropriate treatment for individual cases remains challenging due to difficulties in obtaining consistent diagnoses, and the variable influence of neuroplasticity (Belsky and Pluess, 2009; Chapman et al., 2003), which introduces complexity when predicting functional impairments (Accardo et al., 2004). Standardising clinical assessment could improve the consistency of diagnoses, help elucidate the relationship between cerebral structure and functional outcome and assist the optimisation of treatment strategies for individual patients.

Non-invasive medical imaging crucially contributes to the diagnostic procedure and the aetiological elucidation of CP. This allows clinicians to qualitatively assess a number of injury types including brain malformations, WM and GM lesions and ventricular enlargement based on known classification systems (Krägeloh-Mann and Horber, 2007), which is utilised to predict functional impairment and adjust treatment strategies accordingly. Medical imaging is crucial in improving individualisation of treatment (Bax et al., 2006; Ment et al., 2009), as well as increasing consistency in the diagnosis of CP. Several imaging technologies are used to assess CP (Accardo et al., 2004), including cranial ultrasonography, magnetic resonance imaging (MRI), and computed tomography in specific cases. Of these techniques, MRI is favoured as it does not expose patients to ionizing radiation, and has a sufficient resolution and soft tissue contrast to identify subtle GM and WM lesions (Hoon and Vasconcellos Faria, 2010). Although alternate modalities including functional and diffusion MRI can provide complementary information on brain structure and function (Heeger and Ress, 2002; Madden et al., 2009), structural MRI remains most widely used in clinical practice, as it detects injury in approximately 85% of patients (Krägeloh-Mann and Horber, 2007). Qualitative MR findings are a strong predictor of the pathogenesis of CP (De Vries et al., 2011; Palmer, 2004) that can be used to assess neurodevelopmental risk (Ashwal et al., 2004; Mathur and Inder, 2009), and predict neurological deficits (Hoon and Vasconcellos Faria, 2010; Krägeloh-Mann and Horber, 2007).

Utilizing medical imaging in a *quantitative* manner is likely to be more revealing than the broad qualitative classifications of injury currently used in the assessment of CP. Quantitative assessment has the potential to assist diagnosis (Bax et al., 2005), and also elucidate the underlying physiological relationship between the extent of brain injury and function (Arnfield et al., 2013; Krägeloh-Mann and Horber, 2007). This will assist in developing image-derived biomarkers predictive of functional outcomes, which has an important role in tailoring patient specific treatment strategies. The link between imaging findings and functional outcomes is an important area of investigation in the CP setting (Arnfield et al., 2013), but is hampered by the current need for time intensive manual or semi-automated assessment, which automated approaches can alleviate.

Extensive automated quantitative image analysis methods exist to analyse structural MRI data, which have been applied to numerous diseases, including Alzheimer's Disease (AD) (Ferrarini et al., 2008), Schizophrenia (White et al., 2003), and Multiple Sclerosis (MS) (Van Leemput et al., 2001). To the best of our knowledge, very few of these have been validated specifically on CP patients. The development of automated image segmentation techniques for CP would reduce the need for manual delineation of injuries, giving a finer assessment of injury by including characterization of the location and extent of lesions. Furthermore the ability to measure the extent of anatomical injury and repeatability could enable correlations between injury and motor function impairment across very large cohorts, as has been performed for AD (Adaszewski et al., 2013; Villemagne et al., 2013).

The dearth of techniques applied to CP is due to the number of technical challenges present in this setting. Firstly, all three types of injury; including primary maldevelopments and focal WM and GM lesions, and the secondary enlargement of the ventricles, have different appearances, however all injury types need to be considered during assessment (Krägeloh-Mann and Horber, 2007; Sööt et al., 2008), necessitating the use of multiple segmentation techniques. The heterogeneity in lesion appearance within each class is also an important factor. For instance, injury may appear as subtle malformations, requiring algorithms highly sensitive to changes to cortical shape and robust to partial volume effects, or as excessive ventricular enlargement extending to the cortex, invalidating structural *a priori* assumptions on the brain, which are challenging for atlas based techniques to resolve (Northam et al., 2011). The severity of injury is a significant challenge in the CP setting, requiring the exclusion of up to a quarter of data as the commonly used segmentation approaches remain error prone, and require substantial manual intervention. Segmentations obtained from three approaches commonly used in neurological settings are illustrated in Fig. 1. As shown, all the segmentation results degrade as the extent of malformations increases, with even the best method showing substantial mislabelled regions even for moderate malformations. Finally, as the MR images of CP patients may be taken between birth to 18 years of age, specific challenges relating to reduced contrast between WM and GM due to reduced myelination and higher levels of noise in neonates (Mewes et al., 2006; Prastawa et al., 2005), and the temporal development of complex structures, particularly the cortical surface (Dubois et al., 2008a), need to be considered. New methods tailored to CP are required to meet these challenges.

The remainder of the paper is organised as follows. In Section 2, a background on the broad classifications of CP related lesions and their appearance in MR images is given. In Section 3, we