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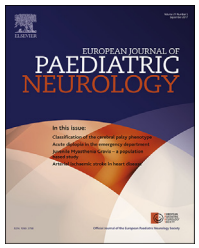

Original article

How does the interaction of presumed timing, location and extent of the underlying brain lesion relate to upper limb function in children with unilateral cerebral palsy?

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ABSTRACT

Background: Upper limb (UL) function in children with unilateral cerebral palsy (CP) vary largely depending on presumed timing, location and extent of brain lesions. These factors might exhibit a complex interaction and the combined prognostic value warrants further investigation. This study aimed to map lesion location and extent and assessed whether these differ according to presumed lesion timing and to determine the impact of structural brain damage on UL function within different lesion timing groups.

Materials and methods: Seventy-three children with unilateral CP (mean age 10 years 2 months) were classified according to lesion timing: malformations (N = 2), periventricular white matter (PWM, N = 42) and cortical and deep grey matter (CDGM, N = 29) lesions. Neuroanatomical damage was scored using a semi-quantitative MRI scale. UL function was assessed at body function and activity level.

Results: CDGM lesions were more pronounced compared to PWM lesions ($p = 0.0003$). Neuroanatomical scores were correlated with a higher degree to UL function in the CDGM group ($r_s = -0.39$ to $r_s = -0.84$) compared to the PWM group ($r_{rb} = -0.42$ to $r_s = -0.61$). Regression analysis found lesion location and extent to explain 75% and 65% ($p < 0.02$)

Abbreviation: sqMRI scale, semi-quantitative MRI scale.

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respectively, of the variance in AHA performance in the CDGM group, but only 24% and 12% ($p < 0.03$) in the PWM group.

Conclusions: In the CDGM group, lesion location and extent seems to impact more on UL function compared to the PWM group. In children with PWM lesions, other factors like corticospinal tract (re)organization and structural connectivity may play an additional role.

1. Introduction

Cerebral palsy (CP) is the most frequent cause of childhood disability in which a brain lesion causes motor and sensory dysfunction.[1] In children with unilateral CP, upper limb (UL) impairments such as spasticity, muscle weakness and sensory deficits result in activity limitations which are expressed in difficulties with grasping, releasing and manipulating objects.[2,3] The heterogeneity of these impairments and activity limitations is large,[3,4] and may strongly depend on the anatomical characterization of the underlying brain lesion, i.e. presumed timing, location and extent.[5–14]

Brain lesions in children with unilateral CP are often classified into three broad categories according to presumed lesion timing: cortical malformations (first and second trimester of pregnancy), periventricular white matter (PWM) lesions (from late second till early third trimester) and cortical and deep grey matter (CDGM) lesions (around term age).[1] Children with PWM lesions have higher chances of developing a better UL function than children with CDGM lesions.[5–12] Nevertheless, there is a large heterogeneity in severity of UL dysfunction within each of these groups.[7] A second possible neural correlate of UL function is lesion location.[7,9,10,12,13] Previous studies indicated that the UL is most impaired in case of damage of subcortical structures, such as the basal ganglia,[7,9,12] thalamus[7,9,12] or the posterior limb of the internal capsule (PLIC).[10,13] A third factor suggested to influence UL function is lesion extent. Three studies found that the severity of lesion extent was related with a more impaired UL.[8,9,13] Another study, however, could not demonstrate that the degree of white matter loss contributed to the explanation of the variability in hand function.[14]

Although some evidence exists for the role of presumed timing, location and extent, these factors might exhibit a complex interaction and their combined prognostic value has not yet been investigated. Furthermore, the use of qualitative brain lesion classifications hinders the detailed mapping of lesions in children with CP. Recently, a visual semi-quantitative scale was developed specifically for children with CP providing an in-depth assessment of structural brain damage (location and extent) on MRI (sqMRI scale).[13,15] The structure-function relationship has been investigated in unilateral CP with PWM lesions using this scale, but only limited in children with CDGM lesions.[13,16] Furthermore, there is a paucity of data on the difference in location and extent of brain lesions between different timing groups and on the combined impact of the three mentioned neurological factors on UL function assessed on the level of body function and activity.

The first objective of this study was to map brain lesion locations and extent in children with unilateral CP using the sqMRI scale by Fiori et al.,[15] and to assess whether this differs between different timing groups. A second objective was to determine the relation between lesion location and extent and UL function for the different timing groups. The insights of these results might contribute to a better prediction of UL outcomes for the child and to a more individualized treatment planning.

2. Materials and methods

2.1. Participants

Participants were recruited via the CP-care program of the University Hospitals Leuven. Children with a predominant spastic type of congenital unilateral CP were included if they were aged between 4 and 15 years, able to comprehend test instructions and had a brain MRI scan available. This scan included at least fluid-attenuated inversion recovery sequences, taken after the age of 3 years as described by Fiori et al.,[15] to be able to score the brain lesion with the sqMRI scale. Children were excluded if they had a history of UL surgery or Botulinum toxin-A injections during the last six months prior to testing. The protocol was approved by the Ethical Committee of the University Hospitals Leuven and informed consent was obtained from the parents.

2.2. Procedure

Clinical assessments were performed at the Clinical Motion Analysis Laboratory of the University Hospitals Leuven using a standardized test protocol.[17] Children were assessed by three physiotherapists routinely involved in the clinical evaluation of children with CP. Each MRI was scored using the sqMRI scale[13,15] by one paediatric neurologist (EO) who was blinded to the clinical outcome. In case a child had multiple MRI scans available, the scan closest to the clinical assessment was chosen. In 22 children, the scan was performed at least one year before the UL clinical assessment, in 28 in the same year and in 23 children, the scan was taken at least one year after the UL clinical assessment. However, all children were included as structural brain damage is not expected to change after the age of three when the myelination process is completed.[18] All children were also classified according to their presumed lesion timing.[1] In case children had multiple lesions that could be assigned to more than one group; they were classified according to their