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Relation between neuroradiological findings and upper limb function in hemiplegic cerebral palsy

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ABSTRACT

The relation between neuroradiological findings and upper limb function was examined in 53 children with hemiplegic cerebral palsy (CP). CT and MRI images of the children were classified into four groups (malformations, periventricular lesions, congenital cortical-subcortical lesions and postnatally acquired lesions). Additionally, each single affected neuroanatomical structure was noted. Clinical assessments included measures of activity (Melbourne Assessment of Unilateral Upper Limb Function and House Classification) and body functions (motor and sensory impairments). Comparative statistics and correlation analysis were used. Three children had a malformation, 28 a periventricular lesion, 14 a cortical-subcortical lesion and eight a postnatally acquired lesion. Children with periventricular lesions obtained the best motor functioning. Within this group, children with pure periventricular lesions performed significantly better compared to mixed lesions. The differences between congenital cortical-subcortical lesions and acquired lesions were not significant. Results further showed that middle cerebral artery infarctions and basal ganglia/thalamic lesions were significantly correlated to a worse performance. The type of lesion determined by the timing of the brain insult, and the location of the lesion distinguish children with hemiplegic CP regarding upper limb function. These insights are valuable for prognosis and may contribute to a better delineation of therapeutic interventions.

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1. Introduction

Children with hemiplegic cerebral palsy (CP) are faced with a variety of motor and sensory problems,¹ resulting in

impaired arm and hand functions and a reduced spontaneous use of the hemiplegic upper limb.² The diversity in clinical presentation is not surprising, as it can be caused by various etiological factors during either the pre-, peri- or postnatal

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period. In congenital hemiplegia, due to pre- or perinatal brain damage, three main lesion types determined by the stage of brain development at the time of the insult have been described: malformations, periventricular lesions and cortical-subcortical lesions.^{3–7} The fourth lesion type comprises all types of brain injuries acquired postnatally.⁸ Previous attempts have been made to relate the classified lesions to the severity of neurological impairment.^{7–11} While some suggest that cortical-subcortical lesions result in a more severe hemiparesis or impaired upper limb function compared to periventricular lesions,^{7–9} others could not demonstrate a relation between the different lesions types and upper limb function.^{10,11} All studies included children with congenital hemiplegia and one study also included children with a postnatally acquired hemiplegia.⁸ The majority of the studies focussed on the description of brain abnormalities and provided a global rating of the severity of upper limb dysfunction. The relation between clinical symptoms and lesion types was mainly established without statistical analysis.^{8,11} So far, none of the studies systematically assessed the different motor and sensory impairments and functional abilities of the upper limb by means of an objective and standardized evaluation protocol.

In summary, it seems that the role of the lesion type in predicting the clinical outcome has not been conclusively determined. This study investigated whether the type of brain lesion was related to motor and sensory impairments, quality of upper limb function and functional use of the arm and hand.

2. Materials and methods

2.1. Participants

All children with hemiplegic CP taken from the database of the Clinical Motion Analysis Laboratory at the University Hospital of Pellenberg (Leuven) or present in three special education schools (Dominiek Savio Institute, Gits; Windekind, Leuven; St. Gerardus Institute, Diepenbeek) were screened for entry in the study during a period of 2.7 years. Inclusion criteria were: (1) diagnosis of hemiplegic CP, congenital or acquired;¹² (2) CT or MRI available; (3) age 5–15 years; (4) sufficient cooperation to comprehend and complete the assessments. Children were excluded if they had received botulinum toxin for the upper limb within one year prior to the assessment or had undergone upper limb surgery.

The study was approved by the institutional ethical committee.

2.2. Procedure

A standardized protocol of clinical assessments was used to assess the level of body function and activity according to the World Health Organization's International Classification of Functioning, Disability and Health (ICF).¹³ Two senior physiotherapists performed the assessments. For reasons of uniformity, a manual with a description of the test and scoring procedures was developed. All images were independently reviewed by a neuropaediatrician, the findings were

then compared with the radiology report and discussed in case of inconsistency. The neuropaediatrician and the neuroradiologist were blind to the results of the clinical assessment. The clinical assessors were blind to the type of brain lesion. Scans taken before the age of 18 months were only accepted if the type of pathology was obvious and renewed imaging was not expected to provide further information.¹⁴

2.3. Clinical assessment

2.3.1. Activity

The Melbourne Assessment of Unilateral Upper Limb Function¹⁵ was used as the main outcome parameter. This test measures the quality of upper limb movement in 16 items involving reach, grasp, release, manipulation and gross motor functions. The Melbourne Assessment was scored by one trained physiotherapist. This measurement tool proved to be highly reliable¹⁶ and valid.¹⁷

The Classification of House¹⁸ was used to evaluate functional use of the hemiplegic upper limb during activities. The arm and hand use is ranged on a 9-level scoring system. The reliability in a previous unpublished study in 30 children with hemiplegic CP was very high (inter-rater ICC = 0.86; test-retest ICC = 0.96).

2.3.2. Body functions

Measurements of *motor impairment* included passive range of motion (PROM) and muscle tone at the shoulder, elbow, forearm, wrist and fingers, and grip strength. PROM was assessed using a goniometer. All joint movements were graded using a dichotomous score (1 = decreased PROM more than 5 degrees, 0 = normal PROM) and the total number of limited movements was calculated. Muscle tone was evaluated using the Modified Ashworth Scale (MAS).¹⁹ A sum score was calculated. Grip strength was measured with the Jamar Dynamometer in three trials. The maximum score of grip strength at the hemiplegic side was expressed as a percentage of the non-hemiplegic side. Because of the limited availability of reliability data on the measurements of motor impairment in this population, the inter-rater and test-retest reliability between the two involved assessors was evaluated in 30 children with hemiplegic CP. Results revealed high reliability coefficients (ICC between 0.85 and 0.96).

The evaluation of *sensory function* comprised four modalities: exteroceptive and proprioceptive sensibility, two-point discrimination (TPD) and stereognosis. Exteroception was evaluated by touching the palm and the distal phalanx of thumb and index and was scored normal (immediate response in three attempts), impaired (not felt in one or two attempts or a clearly delayed reaction) or absent (no attempt felt). Proprioception was evaluated by assessing the movement sense at the wrist, thumb and index. The assessor moved the different joints with small amplitude in flexion-extension and the child was instructed to say 'yes' when the movement was felt. Each location was tested three times. Proprioception was scored normal (movement immediately felt within a small amplitude in all three attempts), impaired (movement only felt within a larger amplitude) or absent (movement not felt within a large amplitude in any attempt).

TPD at the thumb and index was assessed using a Diskriminator. The minimal distance was defined as the distance at which five consecutive trials were answered correctly. The performance of the child was graded normal (ability to discriminate at 5 mm or less), impaired (ability to discriminate between 6 and 10 mm) or absent (inability to discriminate at a distance of 10 mm). Stereognosis was evaluated by tactile identification of six out of 12 familiar objects. Six objects were matched in pairs comparable in size and shape (pencil/pen, coin/button, paperclip/safety pin) and another six dissimilar objects (key, clothespin, marble, comb, spoon, ball). All 12 objects were first presented to the child and he/she was asked to look and appoint the different objects, without touching them. Vision was then occluded and the child was asked to try to identify the object. Three objects from the similar pairs and three out of the six non-similar objects were randomly selected by the assessor. If the child could not identify the object with the affected hand, the unaffected hand was tested to verify the ability to comprehend the examination. Stereognosis was scored normal (identification of all objects), impaired (recognition of some objects) or absent (no identification of any object). The inter-rater and test-retest reliability of this test battery showed moderate to high reliability coefficients for all sensory modalities.²⁰

2.4. Classification of brain lesions

Lesions were divided in four main categories: malformations, periventricular lesions (PVL-group), congenital cortical-subcortical lesions (CSC-group) and postnatally acquired brain lesions (ACQ-group).^{3–5,8} As previously reported by others,⁹ children with multiple lesions that could be referred to more than one group were classified according to the assumed most crucial lesion, based on their medical records (information on pregnancy, labour and delivery, birth weight, gestational age, events during the neonatal period and events during further development). *Malformations* (first and second trimester of gestation) comprised imaging findings consistent with either a malformation (e.g. schizencephaly) or a destructive lesion (early encephaloclastic lesion). *Periventricular lesions* (late second and early third trimester) comprised periventricular venous infarction and periventricular leukomalacia. *Congenital cortical-subcortical lesions* (late third trimester or around the age of birth) involved lesions of the gray matter structures, e.g. corticosubcortical infarctions, lesions of basal ganglia and/or thalamus. *Postnatally acquired brain lesions* reflected all non-progressive brain lesions occurring after the first 28 days of life and before the age of three (e.g. as a result of trauma or infectious diseases). Within the PVL-group, a distinction was made between ‘pure’ and ‘mixed’ lesions (i.e. additional damage of other structures). The CSC-group was subdivided into diffuse lesions (widespread), lesions affecting mainly the middle cerebral artery area and lesions affecting the basal ganglia/thalamus.

Furthermore, in order to determine the association between each of the affected neuroanatomical structures and upper limb function, the involvement of the following structures was noted for all children using a standardized checklist: periventricular structures, cortical and/or subcortical

structures, middle cerebral artery region, and basal ganglia/thalamus. Every neuroanatomical structure was scored 0 when intact and 1 when involved. This scoring was done for every child irrespective of their classification group and thus independent of the timing of the lesion. The dichotomous scoring obtained for each of the different neuroanatomical structures was then related to all clinical parameters.

Finally, it was noted whether the brain lesion occurred unilateral or bilateral.

2.5. Statistical analysis

Both parametric and nonparametric test statistics were applied depending on the type of data and data distribution. Data were tested for normality using a Shapiro–Wilk test. Differences between the main classification groups were determined via one-way analysis of variance (ANOVA) and post-hoc Gabriel tests or via the Kruskal–Wallis test with the Wilcoxon Rank Sum test as a post-hoc test. In the last case, a Bonferroni correction was applied with a *p*-value below 0.0167 considered significant. Categorical ordinal data were compared across groups with Fisher’s Exact tests.

Further statistical comparisons were made between pure and mixed periventricular lesions for which student *t*-tests, Wilcoxon Rank Sum tests and Fisher’s Exact tests were used.

Apart from the comparative statistics, correlation coefficients were calculated between affected neuroanatomical structures (dichotomous scores) and clinical measurements, using Point-biserial and Rank-biserial correlation coefficients. Correlation coefficients >0.70 were considered to indicate a high, 0.50–0.70 a good, 0.30–0.50 a fair and <0.30 a weak or no association.²¹

The level of significance was set at *p* < 0.05, unless otherwise indicated. Statistical analyses were carried out using the Statistical Analysis System software version 9.1 (SAS Institute, Inc., Cary, NC).

3. Results

3.1. Participants

Eighty-five children diagnosed with hemiplegic CP were considered for the study. Thirty-two children were excluded, due to missing brain scan (*n* = 15), incomplete clinical assessment (*n* = 11), surgery or BTX-A at the upper limb (*n* = 2) or missing etiological data (*n* = 4). The remaining 53 children (30 girls, 23 boys) participated in the study. Mean age at the time of assessment was 9 years 9 months (SD 2 years 5 months), with a range from 5 years 3 months to 14 years 2 months. Thirty-one children had a right and 22 a left hemiplegia. Thirty-three children were born at term and 20 prematurely. Twenty-two children attended special education schools and 31 followed mainstream school education.

Comparison of the study group (*n* = 53) to the 32 excluded children revealed no significant differences with respect to age, sex, hemiplegic side, congenital/acquired ratio, or functional use of the hemiplegic upper limb (House classification).

3.2. Neuroimaging data

MRI was available in 50 children. In three children only a CT was available and all had middle cerebral artery infarctions. Although MRI is known to display a greater sensitivity,²² CT is considered an adequate imaging modality for cortical-subcortical lesions in the territory of the middle cerebral artery.²³ As such, these imaging data were retained. Patients' age at the time of the scan ranged from 5 days to 15 years with a mean of 5 years 7 months (SD 4 years 6 months).

All children were classified into one of the four main categories (Table 1). Three children had a malformation (6%). Twenty-eight children were classified in the PVL-group (53%), whereby 19 children presented with a pure periventricular lesion and nine children had involvement of other structures (basal ganglia/thalamus and/or subcortical areas). Fourteen children were classified in the CSC-group (26%). Two children had a main lesion in the basal ganglia. Six children showed middle cerebral artery involvement and another six children presented with a diffuse (widespread) cortical-subcortical lesion. Eight children were diagnosed with an acquired hemiplegic CP (15%) and presented with a variety of affected structures. Analysis of variance revealed no significant difference in age between the four main categories.

Unilateral abnormalities were found in 31 children, while bilateral lesions were seen in 22 children. In the PVL-group, 17 of 28 children presented with a bilateral lesion. In the other groups, bilateral lesions were less frequent (three of 14 children in the CSC-group; two of eight children in the ACQ-group) or did not occur (malformations).

Table 1 – Distribution of brain lesions among the total group of hemiplegic children (n = 53).

	Frequency (n)
Malformations (n = 3; 6%)	
Cyst	2
Schizencephaly	1
PVL-group (n = 28; 53%)	
Pure	19
Mixed	9
PVL + BGT	6
PVL + SC	2
PVL + SC + BGT	1
CSC-group (n = 14; 26%)	
BGT	2
MCA	6
Diffuse	6
ACQ-group (n = 8; 15%)	
CSC + BGT	4
SC + BGT + PVL	1
SC	1
BGT	1
CSC + PVL + Malformation	1

Pure = pure lesion without involvement of other structures; Mixed = involvement of multiple neuroanatomical structures; BGT = basal ganglia/thalamic lesion; MCA = middle cerebral artery lesion; Diffuse = widespread lesion; PVL = periventricular involvement; SC = only subcortical involvement; CSC = both cortical and subcortical involvement.

3.3. Comparative statistics

3.3.1. Comparison of main classification groups

3.3.1.1. Activity. Fig. 1A gives the individual scores on the Melbourne Assessment in the four classification groups. Visual inspection shows that 15 out of the 28 children in the PVL-group obtained a score above 65 in contrast to none of the children with a malformation, two out of 14 children in the CSC-group and one of eight children in the ACQ-group. Table 2 summarizes the results of the statistical comparison between lesion groups. Malformations were not included in the analysis due to the small sample size ($n = 3$). Comparing the three main lesion groups revealed highly significant differences for the Melbourne Assessment and the House classification. For the Melbourne Assessment, post-hoc tests showed significant differences between the PVL-group and CSC-group (mean difference: 15.79%; 95% CI 5.04–26.55) and between the PVL-group and the ACQ-group (mean difference: 20.62%; 95% CI 6.58–34.65), both in favour of the children in the PVL-group. The mean difference between the CSC-group and ACQ-group was 4.82% (95% CI –13.44 to 23.08), which was not significant. For the House classification, a clear significant difference between the PVL-group and ACQ-group was demonstrated ($p = 0.0005$). There was a trend for better use of the hemiplegic hand in children in the PVL-group compared to the CSC-group ($p = 0.03$) and in children in the CSC-group compared to the ACQ-group ($p = 0.05$).

3.3.1.2. Body functions. Comparing the motor impairments between lesion groups (Table 2) revealed significant differences

Fig. 1 – Distribution of the individual scores on the Melbourne Assessment. A. Main classification groups: Malformations (n = 3), PVL-group (n = 28), CSC-group (n = 14), and ACQ-group (n = 8); B. Subdivisions within the CSC-group: main basal ganglia/thalamic lesions (BGT, n = 2), middle cerebral artery infarctions (MCA, n = 6), diffuse cortical-subcortical lesions (Diffuse, n = 6).

Table 2 – Descriptive statistics of the outcome measures in the group of periventricular ($n = 28$), cortical-subcortical ($n = 14$) and acquired lesions ($n = 8$) and the statistical comparison between groups (test statistics and p -value).

		PVL-group	CSC-group	ACQ-group	Test statistics	p-value
Melbourne Assessment (%)	X (SD)	69.24 (16.44)	53.44 (15.84)	48.62 (19.96)	$F = 6.88$	0.003
House (0–8)	Me (IQR)	6 (5–7)	5 (3–5)	3 (2.5–4.5)	$z = 14.41$	0.001
PROM (0–12)	Me (IQR)	1 (0.0–3.0)	1 (0.5–1.5)	2.5 (0.0–5.5)	$z = 1.82$	0.403
Muscle tone (0–32)	Me (IQR)	5 (1.5–9.0)	6.7 (4.0–7.5)	10.2 (7.7–11.5)	$z = 6.46$	0.039
Grip strength (%)	Me (IQR)	51.3 (27.3–61.1)	30.0 (0.0–66.7)	7.4 (0.0–17.7)	$z = 12.83$	0.002
Exteroception						
Absent	N (%)	0 (0.0)	2 (15.4)	0 (0.0)	$Fe = 0.001$	0.008
Impaired	N (%)	0 (0.0)	1 (7.7)	2 (25.0)		
Normal	N (%)	28 (100.0)	10 (76.9)	6 (75.0)		
Proprioception						
Absent	N (%)	0 (0.0)	1 (9.1)	0 (0.0)	$Fe = 0.003$	0.073
Impaired	N (%)	7 (25.9)	6 (54.5)	1 (14.3)		
Normal	N (%)	20 (74.1)	4 (36.4)	6 (85.7)		
TPD						
Absent	N (%)	5 (18.5)	5 (55.6)	3 (37.5)	$Fe = 0.0016$	0.343
Impaired	N (%)	9 (33.3)	2 (22.2)	2 (25.0)		
Normal	N (%)	13 (48.2)	2 (22.2)	3 (37.5)		
Stereognosis						
Absent	N (%)	2 (7.4)	4 (30.8)	1 (12.5)	$Fe = 0.0006$	0.137
Impaired	N (%)	11 (40.7)	7 (53.9)	4 (50.0)		
Normal	N (%)	14 (51.9)	2 (15.4)	3 (37.5)		

X = mean; SD = standard deviation; Me = median; IQR = interquartile range; N = frequency; PROM = number of limited range of movements; TPD = two-point discrimination; F = analysis of variance; z = Kruskal–Wallis test; Fe = Fisher's Exact test.

for muscle tone and grip strength. Post-hoc tests showed significantly more grip strength ($p = 0.0002$) and a trend for lower muscle tone ($p = 0.02$) in children in the PVL-group compared to the ACQ-group. No significant differences were found between the PVL-group and CSC-group. Post-hoc comparison between the CSC-group and ACQ-group only showed a trend of lower muscle tone ($p = 0.04$) for children in the CSC-group.

All children in the PVL-group had a normal exteroception, compared to approximately 75% of the children in the other two groups ($p < 0.01$). For proprioception, TPD and stereognosis, no significant differences between groups were found.

3.3.2. Comparison within the PVL-group

3.3.2.1. Activity. Children with a pure lesion performed significantly better on the Melbourne Assessment and the House classification than children with a mixed lesion (Table 3). Children with a pure lesion obtained a very high median score of 7 on the House classification, which is the ability to perform bimanual activities with a limited spontaneous use of the hands.

3.3.2.2. Body functions. Children with a pure lesion also had significantly more grip strength compared to children with a mixed lesion. No significant differences were found for PROM and muscle tone. Seventy-two percent of the children with a pure lesion had a normal stereognosis compared to 11% of the children with mixed lesions ($p < 0.01$). No significant differences were found for proprioception or TPD.

3.3.3. Comparison within the CSC-group

Comparison between subdivisions within the CSC-group did not allow statistical comparison due to the small numbers in each group. Further data exploration was therefore limited to the Melbourne Assessment (Fig. 1B). Visual inspection revealed no clear trends between middle cerebral artery infarctions versus diffuse cortical-subcortical lesions versus main basal ganglia lesions.

3.4. Correlation analysis

Correlation analysis revealed many significant coefficients between the individual neuroanatomical lesion sites and the various clinical assessments (Table 4). Only for PROM, no significant correlations were found. Presence of a periventricular lesion, either pure or mixed, revealed a significant correlation for most measures, denoting a better outcome. Lesions in the corticosubcortical areas, the middle cerebral artery area and the basal ganglia/thalamus were significantly correlated to a worse outcome. Values of coefficients were fair.

4. Discussion

This study evaluated the relation between neuroradiological findings and upper limb function in children with hemiplegic CP. The majority of the children presented with congenital lesions (85%). These could be attributed to the three main categories: malformations, PVL-group and CSC-group, whereby the PVL-group was the largest group. This is in

Table 3 – Descriptive statistics of the outcome measures in the group of pure ($n = 19$) and mixed ($n = 9$) periventricular lesions and the statistical comparison between groups (test statistics and p -value).

		Pure PVL-group	Mixed PVL-group	Test statistics	p -Value
Melbourne Assessment (%)	X (SD)	74.32 (14.97)	58.51 (14.74)	$t = -2.62$	0.014
House (0–8)	Me (IQR)	7 (5–7)	5 (4–6)	$z = -2.14$	0.033
PROM (0–12)	Me (IQR)	1 (0–3)	1 (1–2)	$z = 0.24$	0.811
Muscle tone (0–32)	Me (IQR)	3.7 (1–7.5)	7 (5.5–9)	$z = 1.67$	0.094
Grip strength (%)	Me (IQR)	53.3 (33.3–75.0)	40.0 (15.4–52.6)	$z = -1.99$	0.046
Exteroception					
Absent	N (%)	0 (0.0)	0 (0.0)	–	–
Impaired	N (%)	0 (0.0)	0 (0.0)		
Normal	N (%)	19 (100.0)	9 (100.0)		
Proprioception					
Absent	N (%)	0 (0.0)	0 (0.0)	$Fe = 0.29$	0.653
Impaired	N (%)	4 (22.2)	3 (33.3)		
Normal	N (%)	14 (77.8)	6 (66.7)		
TPD					
Absent	N (%)	2 (11.1)	3 (33.3)	$Fe = 0.021$	0.151
Impaired	N (%)	5 (27.8)	4 (44.4)		
Normal	N (%)	11 (61.1)	2 (22.2)		
Stereognosis					
Absent	N (%)	0 (0.0)	2 (22.2)	$Fe = 0.001$	0.004
Impaired	N (%)	5 (27.8)	6 (66.7)		
Normal	N (%)	13 (72.2)	1 (11.1)		

X = mean; SD = standard deviation; Me = median; IQR = interquartile range; N = frequency; PROM = number of limited range of movements; TPD = two-point discrimination; PVL-group = group of periventricular lesions; t = t -test; z = Wilcoxon Rank Sum test; Fe = Fisher's Exact test.

accordance to several other studies.^{8–10,23,24} Remarkably, a great number of children with periventricular damage also had basal ganglia/thalamic involvement. Recently, it has been recognized that deep gray matter volume, including thalamus and basal ganglia, is reduced among preterm born children at term-equivalent age, and that this is most prominent among children with periventricular leukomalacia or haemorrhagic infarction.^{25–27} On the other hand, it has been described by several authors that PVL lesions can also occur in term born.^{6,24} This is supposed to be caused by silent intra-uterine brain damage. Additional basal ganglia/thalamic involvement

in these children might be caused by complications during the end of pregnancy or labour.

Also, bilateral lesions were frequently seen. Particularly in the PVL-group many children presented with bilateral lesions, despite the fact that all children had a clear clinical presentation of hemiplegia without functional disabilities at the non-hemiplegic side. A similar large proportion of bilateral lesions in hemiplegic children with periventricular lesions was reported by others.^{5,8,11}

A prominent finding was the significantly better motor performance of children in the PVL-group compared to both

Table 4 – Correlation coefficients between the neuroanatomical structures and the outcome.^a

	pvl ($n = 34$)	csc ($n = 14$)	mca ($n = 8$)	bgt ($n = 23$)
Melbourne Assessment	$r_{pb} = 0.46^{***}$	$r_{pb} = -0.50^{***}$	$r_{pb} = -0.43^{**}$	$r_{pb} = -0.54^{***}$
House	$r_{pb} = 0.50^{***}$	$r_{pb} = -0.47^{***}$	$r_{pb} = -0.43^{**}$	$r_{pb} = -0.51^{***}$
PROM	–	–	–	–
Muscle tone	–	$r_{pb} = 0.39^{**}$	$r_{pb} = 0.32^*$	$r_{pb} = 0.35^*$
Grip strength	$r_{pb} = 0.40^{**}$	$r_{pb} = -0.31^*$	$r_{pb} = -0.34^*$	$r_{pb} = -0.35^*$
Exteroception	$r_{rb} = 0.47^{***}$	$r_{rb} = -0.33^*$	$r_{rb} = -0.36^{**}$	–
Proprioception	–	–	$r_{rb} = -0.28^*$	–
TPD	$r_{rb} = 0.40^{**}$	$r_{rb} = -0.31^*$	$r_{rb} = -0.36^*$	$r_{rb} = -0.40^{**}$
Stereognosis	$r_{rb} = 0.41^{**}$	$r_{rb} = -0.37^{**}$	$r_{rb} = -0.36^{**}$	$r_{rb} = -0.45^{**}$

pvl = periventricular involvement; csc = both cortical and subcortical involvement; mca = middle cerebral artery involvement; bgt = basal ganglia/thalamic involvement. r_{pb} = point-biserial correlation coefficient; r_{rb} = rank-biserial correlation coefficient. $^*p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$; – not significant.

a This table is based on 53 children. As some children have involvement of multiple neuroanatomical structures, the sum of all lesions does not concur with the number of children.

the CSC-group and ACQ-group. Children in the PVL-group displayed a moderate to good upper limb function and use of the hemiplegic hand. Better upper limb function among hemiplegic children with periventricular lesions was also reported by others.^{7–9} However, in these studies the evaluation of hand function was limited to a simple grading of the severity using 3- to 4-point ordinal scales. Results in our study additionally showed that children in the PVL-group had more grip strength and a tendency for lower muscle tone compared to children in the ACQ-group.

Comparison of the CSC-group and ACQ-group showed no significant differences. Still, inspection of the descriptive statistics showed marked clinical differences, with a less spontaneous use of the hand and a higher muscle tone in the children with an acquired hemiplegia. *p*-Values ranged between 0.04 and 0.05, but were not considered significant because of the applied Bonferroni correction. The small number of children in each group may account for the lack of significance.

The better upper limb function in children in the PVL-group versus the CSC-group and the clear trend for a better performance of the latter group compared to the ACQ-group, emphasize the influence of the timing of the brain insult in relation to hand motor abilities. Recent studies using functional MRI support the hypothesis that the maturational stage of the nervous system is of particular importance to influence the reorganization potential of the brain.^{7,28} Staudt et al.⁷ demonstrated more reorganization possibilities in children with congenital brain lesions in the first and second trimester versus the early third trimester versus the late third trimester. They suggested a significant correlation between the gestational age at the time of the insult and the efficacy by which the reorganization with ipsilateral corticospinal tracts takes place. This might contribute to the better hand function in children in the PVL-group found in our study. Another finding was the significantly more impaired upper limb function in children with brain lesions due to a postnatal event. Our clinical impression of the acquired hemiplegic CP showing a high muscle tone and limited muscle strength distally similar to many stroke patients was also mentioned in one other study.⁸ The compensatory capabilities of the immature nervous system following focal brain injury are reported to be superior to those of the adult brain. This observation, known as the Kennard principle, is based on a study of recovery following experimental lesions of the motor cortex in monkeys.²⁹ However, it seems that those superior compensatory capabilities for the motor system decline already substantially towards the end of pregnancy.^{7,30}

In the group of *malformations*, all three children appeared to have a moderately impaired upper limb function. Some authors^{8,9} also found moderate motor impairments, while others⁷ suggested a better outcome in this patient group. Firm conclusions are limited as there were few children in this group.

Whereas the comparison of the three main classification groups assessed the influence of the timing of the lesion, the correlation analysis allowed us to gain further insight in the relation between the affected neuroanatomical structures, or lesion location, and upper limb function. This analysis showed some further interesting findings. Significant correlations denoted a more disabled upper limb function and more motor and sensory impairments in children with *middle*

cerebral artery infarctions. None of these children had a normal stereognosis or TPD. Another result was that *basal ganglia/thalamic involvement* significantly correlated to a worse motor performance. This significant association was reported in one previous study.³¹ Also a significantly larger number of these children displayed an impaired or absent TPD or stereognosis compared to children without involvement of the basal ganglia/thalamus. Since almost all sensory information that reaches the cortex is first processed by the relay station in the thalamic nuclei and the major output of the basal ganglia passes through the thalamus, the more frequent occurrence of sensory deficits in children with basal ganglia/thalamic lesions can be understood.

Further comparisons *within the PVL-group* also demonstrated that children with a pure lesion had a very good motor outcome compared to mixed lesions. In our sample, about 80% of the mixed PVL-group had basal ganglia/thalamic involvement, which was significantly correlated to a worse motor performance. Comparison between *subdivisions within the CSC-group* revealed no clear differences in upper limb function. Other authors have reported on mixed lesions, though without evaluating clinical impairments.^{5,24}

Results for sensory modalities were less consistent than for motor outcome. In our study, no differences in sensory function were found between main groups, except for exteroception. Still, we found a negative correlation for TPD and stereognosis with cortical-subcortical involvement or middle cerebral artery infarctions. Other studies reported significantly worse TPD⁹ and stereognosis^{9,10} in children with cortical-subcortical lesions. Sensory impairments in the latter group can be expected due to the possible involvement of cortical or subcortical structures (e.g. somatosensory cortex, ascending sensory pathways). On the other hand, some authors showed by diffusion tensor MRI that apart from corticospinal tract damage, children with a periventricular lesion also had involvement of thalamocortical pathways.^{32,33} Interestingly, recent imaging studies suggest that motor and sensory reorganization may be mediated by different forms of neuroplasticity.^{30,34} Interhemispheric reorganization differences may account for the different levels of sensory and motor outcomes. Further study is necessary for a better understanding of the sensory reorganization in relation to its clinical presentation.

Some critical reflections are appropriate. First, the study is not population-based and results may therefore be limited by selection bias. However, children were recruited consecutively from a hospital setting and special education schools, providing a fairly representative study sample. The relative contribution of the different lesion groups was very similar to previous studies.^{8–10,23,24} Also, no significant differences were found between included and excluded children with respect to demographic characteristics and functional use of the arm. Second, the cross-sectional nature of the study with the wide range in age is a limitation. Still, no significant difference was found between age and performance on the Melbourne Assessment. Finally, only few children were included in some lesion groups, especially within the group of *malformation* and also for the *acquired lesions*. Therefore, conclusions about the effect of very early or late timing of the brain lesion should be interpreted with

caution. Despite these criticisms, this was, to our knowledge, the first study that related lesion type to upper limb function in hemiplegic CP using an extensive clinical investigation based on standardized assessments. In contrast to previous studies, the diversity of the affected structures was taken into account by means of correlation analysis for each of the affected structures and by comparing pure versus mixed lesions. Other strengths were the consistency in radiological interpretation, the performance of the clinical examination by trained assessors who were involved in a reliability study and the use of blinded assessors, reducing the potential for bias.

The present study gave valuable insights into the relation between the neuroradiological findings and upper limb function in children with hemiplegic CP. The timing of the lesion seems to be important with regard to the prognosis of their hand motor abilities. Besides timing of the brain insult, the location of the lesion also seems to play a role. This was revealed by the correlation analysis for each of the neuro-anatomical structures. Still, part of the variance in upper limb function is not yet explained as shown by the large variability within the classification groups and the magnitude of the correlation coefficients. This may partially be explained by the different possibilities of reorganization of the infantile brain, as demonstrated in some studies in children with hemiplegic CP.^{30,34} In addition, structural properties and the extent of the lesion may also play a role.³¹ Several new techniques in magnetic resonance are emerging in clinical care and research. Diffusion weighted imaging and magnetic resonance spectroscopy highlight the metabolic state of the different brain structures, diffusion tensor imaging gives the possibility to visualize individual white matter tracts (e.g. corticospinal tract) and functional MRI has the potential to show a relationship between neuronal activity and function. Further studies using advanced brain evaluation techniques in combination with thorough clinical evaluation, might give insight in this complex issue. Additionally, other factors such as amount of therapy, cognitive capabilities and socio-economic aspects could offer a further explanation for the observed variability. The importance of these factors has not yet been studied. Research aiming at the longitudinal follow-up of upper limb function in the different classification groups and the contribution of the abovementioned factors to upper limb function could bring further clarification. These insights are important with regard to prognosis and may contribute to a better delineation of therapeutic interventions in the future.

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