Research in Developmental Disabilities 41–42 (2015) 86–93

Contents lists available at ScienceDirect

Research in Developmental Disabilities

Improvements in bimanual hand function after baby-CIMT in two-year old children with unilateral cerebral palsy: A retrospective study

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ARTICLE INFO

Article history:
Received 10 December 2014
Received in revised form 13 April 2015
Accepted 7 May 2015
Available online 19 June 2015

Keywords:
Constraint-induced movement therapy
Cerebral palsy
Early intervention
Hand function
Upper extremity
Hemiplegia

ABSTRACT

The common assumption that early-onset intensive intervention positively affects motor development has rarely been investigated for hand function in children with unilateral cerebral palsy (CP). This retrospective study explored the possible impact of baby constraint-induced movement therapy (baby-CIMT) on hand function at two years of age. We hypothesized that baby-CIMT in the first year of life would lead to better bimanual hand use at two years of age than would not receiving baby-CIMT. The Assisting Hand Assessment (AHA) was administered at age 21 months (SD 2.4 months) in 72 children with unilateral CP, 31 of who received baby-CIMT. When dividing the children into four functional levels based on AHA, the proportional distribution differed between the groups in favour of baby-CIMT. Logistic regression analysis indicated that children in the baby-CIMT group were more likely than were children in the no baby-CIMT group to have a high functional level, even when controlling for the effect of brain lesion type (OR 5.83, 95% CI 1.44–23.56, $p = 0.001$). However, no difference was found between groups in the odds of having a very low functional level (OR 0.31, 95% CI 0.08–1.17, $p = 0.084$). The result shows that baby-CIMT at early age can have a positive effect. Children who received baby-CIMT were six times more likely to have a high functional level at two years of age than were children in the no baby-CIMT group.

1. Introduction

There is evidence of a sensitive time window for intervention of hand motor development during the first year of life. For children with neonatal stroke and other unilateral neonatal brain damage, promotion of activity of the involved hand during this period is suggested to mitigate the effects of early brain damage more effectively than intervention at later age (Basu, 2014). In children later diagnosed with unilateral cerebral palsy (CP), asymmetric hand use is usually apparent from 3 to 5 months of age (Chen, Lo, & Heathcock, 2013; Guzzetta et al., 2010), enabling an early start of intervention. So far, intervention programmes especially addressing hand function in young infants with signs of unilateral CP are rare and evaluating their

Abbreviations: AHA, assisting hand assessment; CIMT, constraint-induced movement therapy; CP, cerebral palsy; CT, computer tomography; MCA, middle cerebral artery; MRI, magnetic resonance imaging; WMDI, white matter damage of immaturity.

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http://dx.doi.org/10.1016/j.ridd.2015.05.003
0891-4222/

effects is difficult (Lowes et al., 2013; Spittle, Orton, Anderson, Boyd, & Doyle, 2012). Retrospectively investigating a group of older children who were involved in a hand treatment programme before one year of age is a first step towards increased knowledge of the impact of early motor intervention.

The theoretical basis for early intervention of hand function is that intervention during the sensitive window of activity-dependent motor system plasticity preserves the typical pattern of development of descending motor pathways to the hands (Basu, 2014; Friel, Chakrabarty, Kuo, & Martin, 2012; Martin, Chakrabarty, & Friel, 2011; Martin, Friel, Salimi, & Chakrabarty, 2007). Ipsilateral corticospinal pathways are typically present at birth but retract during the first years of life due to competition for synaptic space from contralateral corticospinal pathways (Eyre et al., 2007). This activity-dependent reorganization does not always occur after early unilateral brain lesion, which results in an organizational pattern correlated with poorer functional outcome of hand function and bimanual hand use (Holmstrom et al., 2010). When Martin et al. (2007) synchronized constraint-induced movement therapy (CIMT)-type of activity-based training in the time period of corticospinal tract development in an animal model of CP, motor function restoration was possible. They did not find restoration if the intervention was performed at an older age (Friel et al., 2012). If similar potential is present in humans, early intervention might have a positive impact on the future development of hand function in children with unilateral CP.

The timing of brain lesion occurrence is reported to critically affect both the lesion characteristics and later outcome in children with CP (Krageloh-Mann & Horber, 2007). White matter damage of immaturity (WMDI) is a result of brain lesions occurring in the second trimester of pregnancy, while middle cerebral artery infarct (MCA) causes lesions closer to full-term age. These types of lesions have also been found to relate to different developmental patterns of hand function in children with unilateral CP, in favour of WMDI (Feys et al., 2010; Holmefur et al., 2013; Holmstrom et al., 2010).

The activity-dependent plasticity indicates that early activity-based intervention will have a positive impact on motor development also in the presence of an early acquired brain lesion. Based on this rationale, some years ago we developed a baby-CIMT programme adapted for young infants aged 4–12 months (Eliasson, Sjöstrand, Ek, Krumlinde-Sundholm, & Tedroff, 2014). Evidence from randomized controlled studies indicates that CIMT effectively improves hand function in children with unilateral CP over two years of age (Sakzewski, Ziviani, & Boyd, 2014). It is reasonable to assume that such training would benefit young children as well, as indicated by results from some case studies (Coker, Lebkicher, Harris, & Snape, 2009; Cope, Forst, Bibis, & Liu, 2008; Lowes et al., 2013).

This retrospective study aimed to explore the impact of a baby-CIMT programme on children's hand function at two years of age. We hypothesized that participating in baby-CIMT in the first year of life could predict better use of the affected hand in bimanual activities at two years of age than would not participating in baby-CIMT.

2. Methods

2.1. Design

The study used a retrospective explorative design including children with unilateral CP.

2.2. Participants

The study included a convenience sample of 72 children with unilateral spastic cerebral palsy that participated in previous projects at our research unit. Inclusion criteria were: (1) availability of an Assisting Hand Assessment (AHA) below 28 months of age, (2) information regarding participation in a baby-CIMT programme (3) diagnosed with unilateral CP and (4) no participation in other intensive intervention before the used AHA.

The participating children had one AHA assessment at an average age of 21 months (SD 2.4 months) (Table 1). Thirty-one children had participated in a baby-CIMT programme in their first year of life (four of these children at 13–16 months) and 41 children had not. At the time of AHA administration, all children could walk, none had any additional confirmed diagnosis

Table 1
Demographic data on participants in the baby-CIMT and no baby-CIMT groups; no significant difference between groups except for proportion of brain imaging.

	Baby-CIMT ($n = 31$)	No baby-CIMT ($n = 41$)
Gestational age (weeks), mean (SD)	37 (5.3)[a]	38 (4.1)[b]
Preterm birth (<week 37), *n* (%)	9 (29)	10 (26.3)
Female, *n* (%)	16 (52)	18 (44)
Brain imaging, *n* (%)[c]	25 (80.6)	25 (60.9)
Right hand affected, *n* (%)[d]	22 (73)	23 (58)
Age at end of baby-CIMT (months), mean (SD)	12 (2.2)	–
Age at AHA (months), mean (SD)	21 (2.4)	21 (2.4)
AHA units, median (range)	53 (0–86)	46 (7–77)

[a] Median = 39.
[b] Median = 39, $n = 38$.
[c] Pearson's chi-square 7.37, $p = .007$.
[d] Data on one participant in each group are missing.

Table 2
Information on brain lesion characteristics, where available ($n = 50$), in the baby-CIMT and no baby-CIMT groups.

	Baby-CIMT ($n = 25$)	No baby-CIMT ($n = 25$)
Neuroimaging method, *n* (%)		
MRI	20 (80.0)	11 (44.0)
CT	5 (19.2)	14 (56.0)
Basic pattern of damage, *n* (%)[a]		
Focal infarct	13 (52)	6 (24)
WMDI	6 (24)	11 (44)
Other[b]	6 (24)	8 (32)
Involvement of central nuclei, *n* (%)[c]		
None or thalamus	6 (30.0)	4 (21.1)
Basal ganglia and thalamus	14 (73.7)	15 (78.9)
Extent of white matter reduction, *n* (%)[d]		
Mild/moderate	6 (42.9)	9 (52.9)
Severe	8 (57.1)	8 (47.1)
Affected hemisphere, *n* (%)[e]		
Unilateral lesion	17 (73.9)	13 (54.2)
Bilateral lesion	6 (26.1)	11 (45.8)

[a] Pearson's chi-square 4.34, $p = 0.114$.
[b] "Other" includes children with brain lesions as follows: 2 cortical and subcortical lesions of watershed/parasagittal areas due to birth asphyxia, 1 simultaneous middle cerebral artery infarct and bilateral periventricular leucomalacia, 5 polymicrogyria, 1 closed-lip schizencephaly, 1 Sturge-Weber, 1 pons infarct, 1 sequelae of herpes encephalitis, and 2 normal findings. The children with normal findings were both in the baby-CIMT group.
[c] Baby-CIMT $n = 19$, no baby-CIMT group $n = 19$, Pearson's chi-square 0.409, $p = 0.522$. The involvement of central nuclei is defined as volume reduction; due to small sample size, it was categorized broadly into one/none or both of the structures involved.
[d] Baby-CIMT $n = 14$, no baby-CIMT group $n = 17$, Pearson's chi-square 0.313, $p = .576$ Periventricular white matter (WM) reduction in WMDI and white matter reduction in infarcts was classified as mild when based on visual assessment less than 50% of the white matter in the affected area was reduced, moderate when more than 50% of the white matter in the affected area was reduced and as severe when more than 50% of the white matter bulk of the affected hemisphere was reduced.
[e] Baby-CIMT $n = 23$, no baby-CIMT group $n = 24$, Pearson's chi-square 1.98, $p = 0.159$.

assumed to affect hand function, and any seizures were medically controlled. Most children were born full term; nine children with baby-CIMT and 10 children in the no baby-CIMT group were born preterm (<37 weeks) (Table 1). Neuroimaging information was available for 50 children (Table 2).

As infants, all children had been included in the usual physiotherapy hospital programmes which include advice on training and follow-up of motor development. In the ages of 8–12 months, the children were typically referred to local habilitation service centers. Usual care at these centers consists of psycho-social support and physical and occupational therapy, typically the occupational therapy starts somewhat later, closer to the second year. The therapies includes some training but mostly counselling and evaluation of motor function. The frequency of the different therapies are commonly once or twice per month. There has been no major changes in organization or resources of services during the period of data collection and therefore we assume that the usual care was similar for all children. This also means that baby-CIMT was an additional treatment, added to the usual care for some children.

2.3. Data extraction

The AHA-assessments included in this study had been collected between 2000 and 2012. The children had originally been recruited from the Stockholm region through their contacts with Karolinska University Hospital or habilitation service centres. The children volunteering to participate in the studies were typically recruited regardless of severity level of hand function as long as they could participate in the data collection.

Data for the no baby-CIMT group were mainly taken from other projects conducted before baby-CIMT was introduced as an early intervention programme in the Stockholm region, i.e., before 2008. For children who were included in projects after 2008, non-participation in baby-CIMT was confirmed by medical records.

Baby-CIMT was offered to children who had either previously been included in a follow-up programme after preterm birth or neonatal stroke, or been referred to the Karolinska University Hospital due to asymmetric hand function. Eligible children with observed asymmetric hand use and neurological signs of brain damage, referred to the occupational therapy department participated in the baby-CIMT programme (2008–2012). On reaching 18 months of age, children diagnosed with unilateral CP were invited to participate in ongoing projects in which AHA was used as an assessment tool and were thereby eligible for the present study.

It was confirmed that no children had been involved in other intensive training programmes before the AHA, used in this study was taken. The study was approved by the Regional Ethical Review Board of Stockholm, Sweden and was performed in accordance with the ethical principles of the Declaration of Helsinki.

2.4. Predictor variables

2.4.1. Baby-CIMT

Baby-CIMT is an activity based intervention developed from CIMT and adapted for infants by making it feasible and harmless to other aspects of development (Eliasson et al., 2014). Baby-CIMT, like CIMT for older children, is characterized by restraint of the well-functioning hand and intensive training. The preferred hand was gently restrained using a very simple restraint (e.g., a sock, ordinary glove, or soft bandage) only during the training sessions. Toys specially selected depending on the child's age, interest, and functional ability were chosen for the treatment, which was based on the concept of massed practice. Parents administered the daily treatment under weekly guidance from an occupational therapist. The training lasted 30 min each day in two six-week periods separated by six weeks.

2.4.2. Neuroimaging

To control for possible confounding effects of the brain lesion, magnetic resonance imaging (MRI) or computer tomography (CT, $n = 5$), performed for clinical purposes, was specifically analyzed for this study. The images were visually analyzed in consensus by two experienced neuroradiologists who had no further information about child characteristics or AHA performance. MRI images were acquired using a 1.5T MRI system with protocols including T1- and T2-weighted images. The protocol for visual analysis was developed earlier (Holmstrom et al., 2010). The type of lesion in terms of the basic pattern of brain damage, lesion location, extent of white matter reduction, and involvement of the central nuclei (i.e., basal ganglia and thalamus) was defined when possible. The brain lesion characteristics are presented in Table 2. For statistical purposes, three groups of brain lesion characteristics were defined: white matter damage of immaturity (WMDI), focal infarct, and "other". Children with findings classified as "other" had various damage patterns (Table 2).

2.5. Outcome measure

2.5.1. Assisting Hand Assessment (AHA)

The AHA examines how effectively children with unilateral impairment use their affected hand in bimanual activities, the assessment can be used from 18 months of age (Krumlinde-Sundholm, Holmefur, Kottorp, & Eliasson, 2007; Holmefur, Krumlinde-Sundholm, & Eliasson, 2007). It consists of a standardized 15-min play session with pre-specified toys selected to stimulate bimanual exploration. The child sits at an adjustable table in a chair suitable for the child's age. The play session is video recorded and then scored using 22 items on a four-point scale (AHA version 4.4). The video recordings were previously analyzed by certified therapists, not aware of the aim of the present study at time of scoring. The total raw score is converted to an interval scale of AHA units ranging from 0 to 100 (Krumlinde-Sundholm, 2012).

For statistical analysis, the children were divided into four functional levels based on their AHA scores. The cutoff values were determined in a consensus discussion by an expert group and from the results of a previous study (Holmefur, Krumlinde-Sundholm, Bergstrom, & Eliasson, 2010). Clinically meaningful differences guided the decision-making process.

High functional level (63–100 AHA units): These children used both hands together in play, spontaneously holding objects in the affected hand with a stable or nearly stable grasp.

Moderate functional level (39–62 AHA units): These children often but not always used the affected hand spontaneously. They grasped toys only from the well-functioning hand. The grasp was unstable and a number of objects slipped.

Low functional level (21–38 AHA units): These children commonly used one hand only and needed help to perform bimanual play. They held only a few objects in the affected hand, objects that they had placed there.

Very low functional level (0–20 AHA units): These children consistently used one hand only and needed help to perform bimanual play. At best, they could only hold objects in the affected hand that were placed there by someone else, not initiating purposeful movements with the affected hand.

2.6. Statistics

To detect any differences in demographic data between the baby-CIMT and no baby-CIMT groups, the Mann–Whitney *U* test and Pearson's chi^2 test were used. The distribution of children with and without baby-CIMT over the four functional levels was visually determined by inspection as a first step in the prediction analysis. To investigate predictors of future hand function, two binary logistic regressions of two outcomes (high versus very low functioning) were conducted. In the analysis, these two extremes were each set against the other levels as follows: *high functioning* set against the other (i.e., moderate, low, and very low) functional levels; and *very low functioning* set against the other (i.e., high, moderate, and low) functional levels (Fig. 1 and Table 3). The two variables included as possible predictors were intervention (i.e., baby-CIMT or no baby-CIMT) and the basic pattern of brain damage (i.e., WMDI, focal infarct, and "other"). Logistic regression permits investigation of the impact of one predictor while controlling for the effect of the other predictor. Because information on brain lesion type was available for only 50 of the 72 participants (Table 4), multiple imputation of the missing brain lesion type data was conducted by means of predictive mean matching (Landerman, Land, & Pieper, 1997). The results from the logistic regression will be presented as odds ratio (OR) and 95% confidence interval. OR of 1 indicates a similar occurrence of the outcome over the predictors. OR:s > 1 indicates a higher likelihood of the outcome and OR:s < 1 indicates a smaller likelihood of the investigated predictor to have the outcome. The significance level was set to $p < 0.05$ and the data were analyzed using SPSS version 22. Multiple imputation was conducted using SOLAS version 4.0 (Statistical Solutions Inc., Saugus, MA, USA).

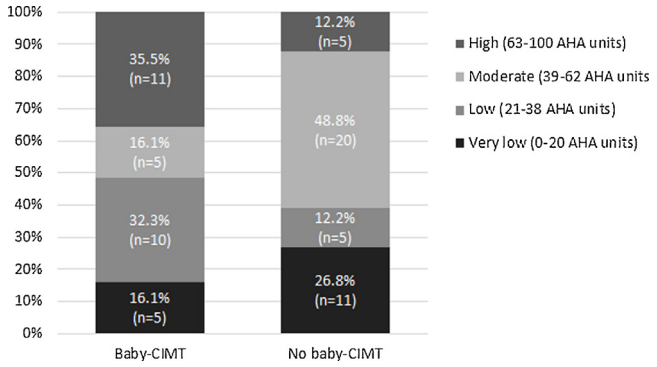

Fig. 1. Proportional distribution over the four AHA levels for children with and without baby-CIMT, in per cent.

Table 3
Dichotomization of the outcome for the logistic regression.

a) *High functioning*			b) *Very low functioning*		
	High	63-100 AHA units	High	63-100 AHA units	
		Versus	Moderate	39-62 AHA units	other
other	Moderate	39-62 AHA units	Low	21-38 AHA units	
other	Low	21-38 AHA units		**Versus**	
other	Very low	0-20 AHA units	Very low	0-20 AHA units	

(a) Functional levels moderate, low and very low are grouped as other and set against high functional level.
(b) Functional level very low is kept and set against high, moderate and low functional levels which are grouped together as other.

3. Results

Children with and without baby-CIMT were equivalent in gestational age (Mann–Whitney *U* test $p = 0.794$), gender (Pearson's chi$^2 = 0.421$, $p = 0.516$), affected side (Pearson's chi$^2 = 1.909$, $p = 0.167$), and age at the AHA (Mann–Whitney *U* test $p = 0.683$). Children with and without baby-CIMT had similar median values on the AHA and the variation in ability was large within both groups with no significant difference in variation between groups (Mann–Whitney *U* test $p = 0.189$, Table 1). The children were differently distributed among the four functional levels between the baby-CIMT and no baby-CIMT groups (Fig. 1 and Table 4). More children with baby-CIMT had a high functional level ($n = 11$, 35.5%) than did children with no baby-CIMT ($n = 5$, 12.2%). Fewer children with baby-CIMT had a very low functional level (Table 4), though the proportion (16.1%) was not significantly lower than in the no baby-CIMT group (26.8%) (Fig. 1).

The analysis of available neuroimaging data (baby-CIMT $n = 25$, 80.6%, no baby-CIMT $n = 25$, 60.9%; Table 1) indicated a similar distribution of the basic patterns of brain damage in the two groups (Pearson's chi$^2 = 4.34$, $p = .114$). The baby-CIMT and no baby-CIMT groups were also found to be equivalent in other brain lesion characteristics ($p > 0.05$, Table 2). Bilateral lesions were found in both groups, despite clinical symptoms that were clearly unilateral (Table 2).

3.1. Prediction of high functioning

Participation in baby-CIMT was found to be a significant predictor of having a high functional level regardless of the underlying basic pattern of brain damage (i.e., controlling for the different distributions of brain lesion types in the baby-CIMT and no baby-CIMT groups) (OR 5.83, 95% CI 1.44–23.56, $p = 0.001$; Table 5—*High Functioning*). Children in the baby-CIMT group were 5.83 times more likely to be high functioning than were children in the no baby-CIMT group. There was no significant difference in the odds of high functioning between the two basic patterns of brain damage (i.e., focal infarct and WMDI) when controlling for intervention (OR 2.96, 95% CI 0.42–21.06, $p = .277$; Table 5—*High functioning*). Subjects with brain lesions classified as "other" had higher odds of being high functioning than did those with focal infarct (OR 8.15, 95% CI 1.11–59.79, $p = .039$), although this finding should be interpreted with caution due to the large variation in brain lesion types within the "other" group (Table 2).

3.2. Prediction of very low functioning

Whether or not a child had participated in baby-CIMT was not a significant predictor of very low functioning (OR 0.31, 95% CI 0.08–1.17, $p = 0.084$; Table 5—*Very low functioning*) when controlling for brain lesion type. When comparing the basic pattern of brain damage (i.e., WMDI vs. focal infarct), the odds were lower for children with WMDI regardless of whether or

Table 4
Distribution over functional levels and observed basic pattern of brain damage for the baby-CIMT and no baby-CIMT groups, shown as number of participants.

	Baby-CIMT					No baby-CIMT				
	Focal infarct	WMDI	Other	Missing	Total	Focal infarct	WMDI	Other	Missing	Total
High	2	2	3	4	11	0	0	0	5	5
Moderate	3	2	0	0	5	1	9	2	8	20
Low	5	2	1	2	10	1	0	2	2	5
Very low	3	0	2	0	5	4	2	4	1	11
Total	13	6	6	6	31	6	11	8	16	41

Table 5
Results of the two separate logistic regression analyses: *high functioning* shows the analysis of high vs. other functional levels, *very low functioning* shows the analysis of very low vs. other functional levels.

	High functioning			Very low functioning		
	OR	95% CI	*p*-Value	OR	95% CI	*p*-Value
Intervention[a]						
No baby-CIMT	1.00	–	–	1.00	–	–
Baby-CIMT	5.83	1.44–23.56	0.014*	0.31	0.08–1.17	0.084
Brain lesion type[b,c]						
Focal infarct	1.00	–	–	1.00	–	–
WMDI	2.96	0.42–21.06	0.277	0.13	0.02–0.90	0.038*
Others	8.15	1.11–59.79	0.039*	0.76	0.17–3.34	0.713

[a] No baby-CIMT group ($n = 41$) were set as the reference variable.
[b] Imputed values instead of missing values were used.
[c] Focal infarct was chosen as the reference variable in dummy coding the basic pattern of damage.
* Significance level, $p < 0.05$.

not they had participated in baby-CIMT (OR 0.13, 95% CI 0.02–0.90, $p = 0.038$). This indicates that children with WMDI were less likely to have very low function at two years of age than were children with focal infarct. No significant difference was found between children with lesions classified as "other" and with focal infarcts (OR 0.76, 95% CI 0.17–3.34, $p = 0.038$; Table 5—*Very low functioning*).

4. Discussion

The present findings show that using baby-CIMT, in addition to usual care, during the first year of life increases the odds of having better use of the affected hand in bimanual activities at two years of age. The likelihood of having a high-functioning involved hand was six times higher in the baby-CIMT group, regardless of the basic pattern of brain damage. It was not as clear whether baby-CIMT prevents children from having a very low functional level, since the *p*-value of 0.084 can only suggest a possible intervention effect in favour of baby-CIMT.

Compared to earlier attempts to demonstrate that early intervention affects motor development, the baby-CIMT programme is promising. No early intervention programme has yet demonstrated a long-lasting effect on motor development, in either preterm children (Spittle et al., 2012) or children at high risk of developmental disorders (Hielkema et al., 2011). As suggested by Hadders-Algra (2011), this might be because the previous programmes apply a broad developmental perspective and include various more or less defined treatment elements administrated to a heterogeneous group of children, i.e., including children who would not later fulfill the diagnostic criteria of CP (Hadders-Algra, 2011). The different dosage of treatment in this study, (usual care or usual care + baby-CIMT) makes it still difficult to know if it was the treatment elements or different dosage which mainly contributed to the results. However, baby-CIMT differs from previous approaches in that it involves specific, high-intensity hand training and targets only the specific limitations of children with unilateral CP. There have been concerns about the effects of baby-CIMT on the non-involved hand; however, it should be emphasized that the non-involved hand was restrained only during training, for 30 min per day. There have also been concerns about a minimal cognitive level required for taking advantage of CIMT in older children. By adjusting CIMT to baby-CIMT it is shown that even children at early age, with immature cognitive level can benefit from the programme.

As earlier descriptive studies clearly indicate that the type, location, and timing of the brain lesion strongly influence and can be used as predictors of development (Boardman et al., 2005; Holmefur et al., 2013; Holmstrom et al., 2010; O'Shea et al., 2008), one can expect brain damage to exert a stronger effect in the present study. Interestingly, baby-CIMT seems promising independent of brain lesion, at least in high-functioning children. However, brain lesion type was still an important factor predicting bimanual hand function in the low-function group, in which children with WMDI were less likely to be very low functioning. In this study we only investigated the type of brain lesion related to lesion timing, but the results are probably

also influenced by other brain lesion characteristics, such as lesion size, that we could not take into account in the statistical model. The impact of brain lesion on intervention outcome is rarely considered. One study demonstrates that one block of CIMT at age 2–3 years can predict better longitudinal development of bimanual hand use, but this treatment effect diminishes when controlling for brain lesion and baseline ability (Eliasson & Holmefur, 2014); in other studies of older children, the results are inconclusive (Islam et al., 2014; Kuhnke et al., 2008).

The present retrospective cohort design including only one measure of the children's hand function could be seen as a weakness, because it does not establish a causal effect to the extent of an experimental design. However, an experimental design requires assessments that can be used both before and after intervention and there are few assessment options available for children with unilateral CP at two years of age (Greaves, Imms, Dodd, & Krumlinde-Sundholm, 2010). The choice of design enabled us to study a possible effect of early intervention, which has so far been very difficult to do using prospective designs. In prospective designs, the lack of sensitive assessments specifically measuring hand function in infants with unilateral CP is an obstacle (Krumlinde-Sundholm et al., 2015). The assessments available are normative tests of developmental milestones or neurological examinations in which the child is expected to use the preferred hand. None of these tests can validly capture or measure the specific hand function characteristics of children with signs of unilateral CP. By using a retrospective design, we were able to use an assessment tool developed and evaluated for children with unilateral CP. Another advantage of this design is that only children with a confirmed diagnosis were included. Including young infants in research studies before their diagnosis is confirmed has inherent problems. Early signs of CP do not necessary lead to a confirmed diagnosis; for example, in a previous intervention study in infants, only 50% of children had a confirmed diagnosis of CP at later age (Blauw-Hospers, de Graaf-Peters, Dirks, Bos, & Hadders-Algra, 2007).

Convenience sampling of children included in the present study could be another source of bias. On the other hand, data on children in the no baby-CIMT group were collected mainly before baby-CIMT was an available therapeutic option and could be seen as a strength, as it ensures the usual care concept. To enable statistical analysis, the children were divided into functional levels. We used findings from a previous study (Holmefur et al., 2010) and clinical reasoning to define additional levels ahead of further analysis. Due to the small sample size, we could only control for three groups of brain lesion in the statistical model. The WMDI and focal infarct groups are clearly defined, while the third group, "other," is very heterogeneous and therefore difficult to interpret (Table 2). The complexity of brain lesions needs further exploration. Even more importantly for this study would have been a measure of the development of the corticospinal tract since this brain structure is expected to be targeted by the investigated intervention. To avoid overestimating the predictive value of baby-CIMT, we conducted multiple imputation of the variable basic pattern of damage, allowing us to include all children in the logistic regression model (Baneshi & Talei, 2011; van der Heijden, Donders, Stijnen, & Moons, 2006).

5. Conclusions

Taking into account the limitations of this study, the findings show that neurorehabilitation at early age can be effective and that baby-CIMT was an applicable model of intervention. Whether it is more effective than later intervention or other models for intervention has to be investigated further. Future studies monitoring early motor development in relation to different brain lesion types, training dosages, and training frequencies along with instrument development for this group is also needed.

Conflict of interest statement

Authors Holmefur and Eliasson are both shareholders in the company Handfast AB (Inc.) which supplies training courses and test material for the Assisting Hand Assessment which is the main outcome measure in this study. This company is partly owned and supported by the Karolinska Innovations AB (Inc.). The company has not been involved in or funded any part of the study. For other authors, Nordstrand and Kits, no conflict of interest is present.

Acknowledgements

We would like to thank the statistician, Jan Kowalski, for his excellent advice. This study was financially supported by Stiftelsen Frimurarna Barnhuset i Stockholm (2012), Stiftelsen Majblomman (2013), Hjärnfonden (2013), Swedish Research Council (grant nos. 521-211-2655 and 521-2011-456), Karolinska Institutet Faculty Funds (KID), and Strategic Research Program in Care Sciences at Karolinska Institutet.

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