Responsiveness of the ACTIVLIM-CP questionnaire measuring global activity performance in children with cerebral palsy

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ABBREVIATIONS

HABIT-ILE	Hand–arm bimanual intensive therapy including lower extremities
PEDI	Pediatric Evaluation of Disability Inventory

AIM To investigate the responsiveness of the ACTIVLIM-CP questionnaire after two evidence-based interventions for children with cerebral palsy (CP).

METHOD Seventy-five children with CP either participated in an intensive motor-skill learning intervention (hand–arm bimanual intensive therapy including lower extremities [HABIT-ILE], n=47) or received botulinum neurotoxin-A (BoNT-A) injection(s) into lower extremities combined with conventional physical therapy (n=28). All children were assessed three times: at baseline (T_0; before HABIT-ILE/the day of BoNT-A injection), at T_1 (last day of HABIT-ILE/6wks after BoNT-A injection), and at follow-up (T_2; 3–4mo after the beginning of intervention). Parents completed ACTIVLIM-CP and three other activity questionnaires. Responsiveness was analysed using group (based on intervention), subgroup (based on gross motor function level), and individual approaches.

RESULTS For the HABIT-ILE group, significant improvements in ACTIVLIM-CP were observed for the T_0–T_1 period (p<0.001) but not for the T_1–T_2 period. No significant changes were found in the BoNT-A group during assessments (p=0.84). In the subgroup analysis for the HABIT-ILE group (T_0–T_1), greater changes were demonstrated for children in Gross Motor Function Classification System levels III and IV (p<0.001, effect size=1.36). The individual approach was congruent with the group approach.

INTERPRETATION ACTIVLIM-CP demonstrated high responsiveness after HABIT-ILE, showing that this scale may be used to investigate global activity performance in clinical trials focusing on improving daily life activities.

Cerebral palsy (CP) is characterized by a disorder of movements, posture, and motor functions, which frequently reduces performance in daily life activities.[1] A child's performance in daily living is defined by the International Classification of Functioning, Disability and Health as 'what a child actually does in its usual environment'.[2] This is a latent variable, not measurable directly in the clinic, which can be inferred from the child's difficulty in performing activities perceived by individuals through questionnaires.[3] In paediatrics, parents' perceptions are commonly relied upon, as parents are better able to discriminate different levels of functioning than their children, who have a more dichotomous perception.[4] Questionnaires measuring children's performances have not been, to date, specific to children with CP (Pediatric Evaluation of Disability Inventory [PEDI],[5] Activity Scale for Kids)[6] or they were developed to separately capture activities related to either upper extremities (ABILHAND-Kids,[4] Children's Hand Use Questionnaire,[7] Children's Arm Rehabilitation Measure)[8] or lower extremities (ABILOCO-Kids)[9] but not the combination of both. As activities of daily living require the use of both upper extremities and lower extremities in a combined way (e.g. climbing a ladder, opening a fridge), the ACTIVLIM-CP questionnaire was Rasch-developed to capture the child's performance in activities of daily living involving the whole body.[10] Although its validity and reliability have been demonstrated, the responsiveness of the ACTIVLIM-CP, namely its sensitivity to change, remains unknown.

Testing responsiveness requires investigating the capacity of a tool to detect changes after intervention(s) whose efficacy has been demonstrated. A recent systematic review on the effect of therapeutic interventions in children with CP demonstrated that motor-skill learning-based interventions were efficient for improving activities of daily living.[11] In addition, although the level of evidence was only moderate, injection with botulinum neurotoxin-A (BoNT-A) combined with physiotherapy was recommended for lower extremity functioning aiming to improve walking. In

Belgium and France, this intervention represents the most current treatment for improving lower extremity functioning in children with CP.

The aim of this study was twofold. First, it investigated the responsiveness of ACTIVLIM-CP in two evidence-based therapeutic interventions: a motor-skill learning-intensive intervention targeting upper extremities and lower extremities (hand–arm bimanual intensive therapy including lower extremities [HABIT-ILE])[12] and BoNT-A injection into lower extremities combined with conventional physiotherapy.[11] Second, it determined whether the responsiveness of ACTIVLIM-CP differs according to baseline gross motor function level.

On the basis of previous observations of improvements in upper and lower extremity activities quantified with ABILHAND-Kids, ABILOCO-Kids, the PEDI self-care subscale after HABIT-ILE,[13,14] and strong correlations observed between ACTIVLIM-CP and these questionnaires,[10] we hypothesized that HABIT-ILE would have a moderate to large effect on global activity performance, as measured by ACTIVLIM-CP. Although the effect of BoNT-A injection into lower extremities is well documented to improve motor outcomes related to body functions and structures (such as spasticity), its effect on motor activities (such as walking) is still debated.[11] Therefore, we expected smaller changes in this group.

What this paper adds

- Good responsiveness of ACTIVLIM-CP questionnaire during intensive motor-skill learning intervention.
- Higher responsiveness for children in Gross Motor Function Classification System (GMFCS) levels III and IV versus I and II after intensive intervention.
- ACTIVLIM-CP is useful to identify children improving their performance after botulinum neurotoxin-A injection.

METHOD

Participants

This study included 87 children with CP (Table I). Fifty children with CP (mean age [SD] 10y 3mo [3y 6mo]) participated in a HABIT-ILE intervention (2013–2016) at the Université catholique de Louvain (Belgium). Thirty-seven children with CP (mean age [SD] 8y 7mo [4y 3mo]) were recruited by their physician to participate in this study while receiving BoNT-A injection(s) into lower extremities as part of their usual care at the University Hospital of Brest (France, n=24) or at the Clinique Saint-Luc (Belgium, n=13). Parents of children gave their written informed consent and filled in the questionnaires. Ethical approval was provided by the review boards of the respective institutions.

Inclusion criteria were (1) a diagnosis of CP, (2) levels I to IV of the Gross Motor Function Classification System (GMFCS), and (3) fulfilled assessment time T_0 and T_1. Additional criteria for the HABIT-ILE group were age 6 to 18 years, being motivated by the intervention, no uncontrolled seizure, and no BoNT-A injection or surgery within the 6-month period preceding or the 3-month period after baseline. Children in the BoNT-A group received BoNT-A injection(s) into lower extremities to improve function. They did not receive intensive therapy within the 6-month period preceding or the 3-month period after baseline.

Interventions

HABIT-ILE group

HABIT-ILE intervention occurred over 2 weeks, ranging from 84 hours (children with bilateral CP) to 90 hours (children with unilateral CP) of therapy. HABIT-ILE includes structured bimanual activities that systematically engage postural control and lower extremity function.[12] The therapy is based on motor-skill learning principles using (1) a structured practice depending on the child's performance with repetition of movements and a progressive increase in task complexity, (2) a voluntary control of movements, and (3) verbal feedback to maintain engagement during therapy. The intervention is focused on functional goals, uses games, and is performed in a group setting with trained supervisors, including at least one interventionist per child. During the follow-up period, children received their usual conventional physiotherapy for zero to five sessions a week (mean [SD] 1.90 [1.29] sessions a week).

BoNT-A group

Children received intramuscular BoNT-A injection(s) into at least one lower-limb muscle, combined with conventional physiotherapy. Before injection(s), children were assessed by their paediatricians to determine which lower-limb muscle(s) to target, dosage by injection site, and type of BoNT-A (dosage/company and standard guidelines details are given in Appendix S1, online supporting information). Children were discharged on the day of injection (s). Children received their usual conventional physiotherapy for zero to five sessions a week (mean [SD] 2.10 [0.98] sessions a week).

Outcome measurements

Two periods were investigated: the intervention period (T_0–T_1), when change in global activity performance was expected, and the follow-up period (T_1–T_2), when global activity performance was expected to remain stable. All children were assessed three times: at baseline (T_0) (before HABIT-ILE treatment [mean {SD} 30.25d {25.32}]/the day of BoNT-A injection); at the time where changes were expected (T_1) (after 2wks of HABIT-ILE treatment [mean {SD} 16.4d {3.9}]/6wks after BoNT-A injection [mean {SD} 45.79d {12.84}]); and at follow-up (T_2) (3–4mo after the first day of HABIT-ILE treatment [mean {SD} 131.07d {36.67}]/3–4mo after the day of BoNT-A injection [mean {SD} 106.36d {27.97}]).

All children were classified using the GMFCS[15] and the Manual Ability Classification System.[16] They were all assessed with the ACTIVLIM-CP,[5] a 43-item questionnaire measuring global activity performance developed specifically for children with CP, aged 2 to 18 years. The parents were asked to provide their perception of the child's difficulty in achieving ACTIVLIM-CP activities

Table I: Sample characteristics

	HABIT-ILE group		BoNT-A group		Comparison between groups (analysed)
	Included (n=50)	Analysed (n=47)	Included (n=37)	Analysed (n=28)	
Mean age (SD), y:mo	10:4 (3:6)	10:4 (3:6)	8:6 (4:4)	8:5 (4:5)	p=0.06[a]
Sex (females: males)	24:26	22:25	19:18	14:14	p=0.82[b]
CP type					Interaction group×CP type
Unilateral	29	28	18	14	p=0.48[b]
Bilateral	21	19	19	14	
GMFCS level					Interaction group×level
I	18	18	6	5	
II	12	9	21	18	
III	15	15	7	5	p=0.04[b]
IV	5	5	3	0	
V	0	0	0	0	
MACS level					Interaction group×level
I	6	6	15	13	
II	31	28	13	11	p=0.26[b]
III	12	12	8	3	
IV	1	1	1	1	
V	0	0	0	0	
Global activity performance (baseline)					Comparison between groups (analysed)
ACTIVLIM-CP					
Mean (SD) logits	1.55 (1.55)	1.58 (1.58)	1.96 (1.74)	2.08 (1.80)	p=0.21[a]

[a]t-test, [b]Fisher's exact test. HABIT-ILE, hand–arm bimanual intensive therapy including lower extremities; BoNT-A, botulinum neurotoxin-A; CP, cerebral palsy; GMFCS, Gross Motor Function Classification System; MACS, Manual Ability Classification System.

when completed without technical or human assistance on a three-level scale (impossible/difficult/easy). Activities that were unfamiliar or not performed in the previous 3 months were considered as missing responses (5%–7% of the data). ACTIVLIM-CP was developed with the Rasch model, allowing the total score to be transformed into a linear activity measure expressed in logits (see the conversion in the bottom panel of Fig. 1). In addition, all children were assessed with the PEDI[5] (self-care subscale, raw scores), and children older than 6 years were assessed using ABILHAND-Kids[4] (logits) and ABILOCO-Kids[9] (logits).

Sample size

Sample size calculations were performed on the basis of ABILHAND-Kids measures derived from an earlier HABIT-ILE study.[13] A mean (SD) improvement of 1.81 (1.55) logits after HABIT-ILE was reported. A minimum of 10 participants per group was required to achieve a power of 90% with alpha set at 0.05. Considering the potential drop-outs, a minimum of 12 participants was foreseen for each subgroup.

Statistical analysis

The responsiveness of ACTIVLIM-CP was investigated using group, subgroup, and individual approaches. We documented changes for the three other questionnaires using solely the group and subgroup analyses.

The group approach, based on intervention, used a statistical comparison with a one-way repeated measures analysis of variance (ANOVA) for interval-level measures showing normality and homoscedasticity, or a Friedman repeated measures ANOVA on ranks for ordinal raw scores or interval-level measures violating normality and homoscedasticity. Post hoc tests were used to identify differences between assessment times (Holm–Šidák for repeated measures ANOVA, Tukey for Friedman analysis).

The subgroup approach, based on GMFCS levels, was conducted to determine whether a subgroup would show higher responsiveness. On the basis of the hypothesis that the trunk control and walking functioning have an impact on global activity performance, two subgroups were investigated: GMFCS levels I and II versus GMFCS levels III and IV. A repeated measures ANOVA or Friedman and post hoc tests (same assumptions as for the group approach) were used to detect changes between assessments in each subgroup. In addition, both for group and for subgroup approaches, the effect size was used to characterize the amount of change between assessments. Effect size was obtained by dividing the mean change in scores by the standard deviation of the change in score and was interpreted using Cohen's benchmarks: small (0.2), moderate (0.5), or large (0.8).[17]

Finally, as some changes that have a meaning in groups may be not meaningful at an individual level, we used an individual approach with t values to track changes in each child for the intervention period. The t value was calculated as[18] $(PT_1-PT_0)/\sqrt{(SET_0^2+SET_1^2)}$, where PT_0 and PT_1 correspond to the child's performance at T_0 and T_1, and SET_0 and SET_1 are the associated standard errors of measurement. This t value indicates whether the change observed for a given child between two assessment times reflects more than fluctuation of the instrument.[18] After individual calculation of the t value, children were divided into five classes of clinical significance: significant decrease ($t \leq -1.96$), decrease ($-1.96 < t < 0$), no change ($t=0$), increase ($0 > t > 1.96$), and significant increase ($t \geq 1.96$).

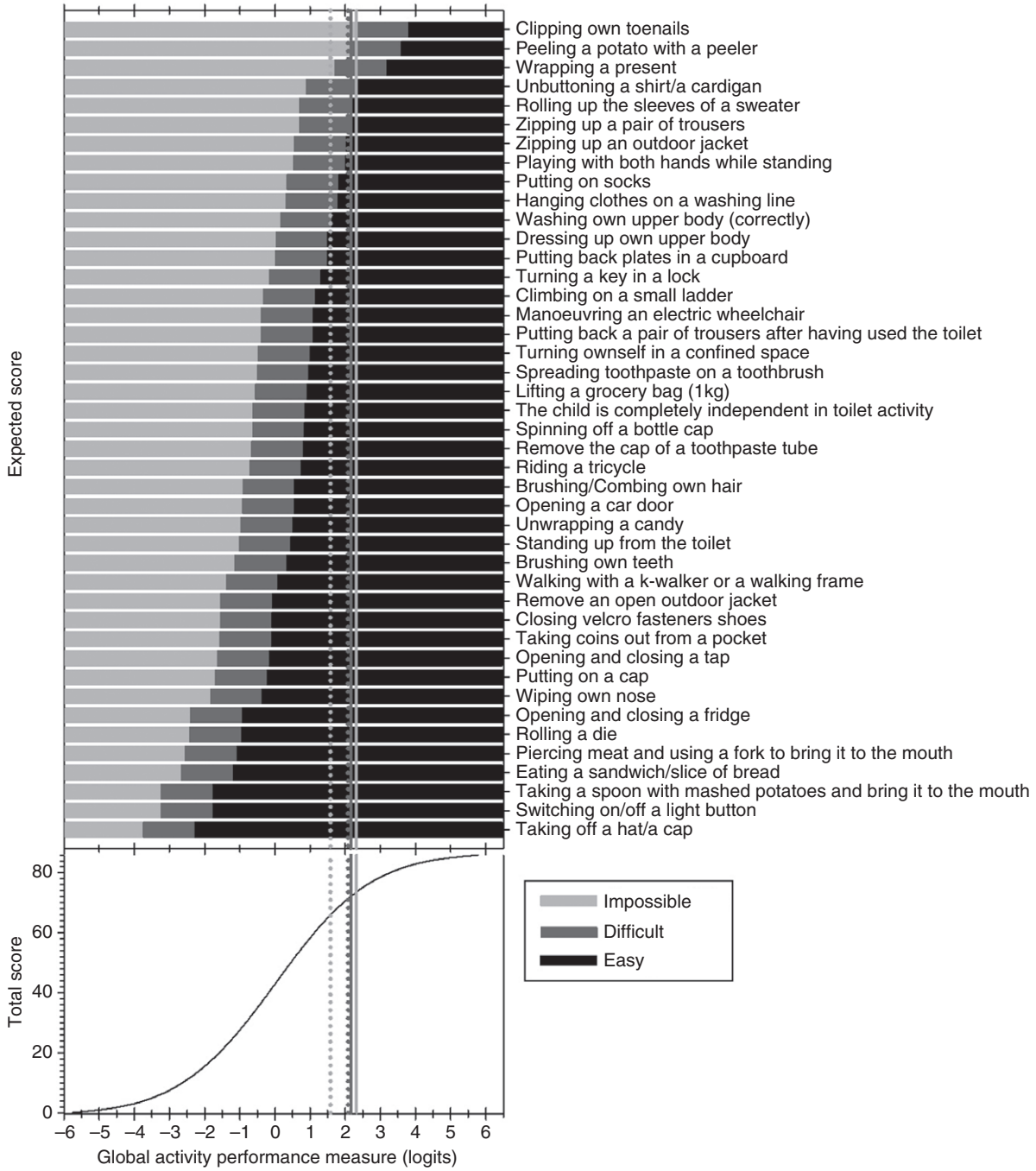

Figure 1: Top: expected response to each item related to the activities measure. The activities are sorted, from top to bottom, by decreasing difficulty. Average activity difficulty is conventionally set at 0 logits. The grey dotted line represents the ACTIVLIM-CP mean score at T_0 (1.58 logits) and the solid grey line represents the ACTIVLIM-CP mean score at T_1 (2.32 logits) for the HABIT-ILE group. For the BoNT-A group, the dark grey dotted line (mean score at T_0: 2.08 logits) and the dark grey solid line (mean score at T_1: 2.16 logits) are merged in the figure because of the very small difference. Bottom: relationship between total raw score and linear activity measure, allowing conversion from one to the other. Total score ranges from 0 to 86 because each of the 43 items could be scored as 0, 1, or 2.

Finally, correlations between changes in ACTIVLIM-CP and the other questionnaires were investigated (Pearson correlations with ABILHAND-Kids and ABILOCO-Kids; Spearman's correlations with the PEDI; results are given in Appendix S1).

RESULTS

Among the 87 children initially included, 12 (HABIT-ILE: n=3; BoNT-A: n=9) were dropped from the study at T_1 because they did not fill in the ACTIVLIM-CP questionnaire (Table I). No significant difference in the

Table II: Responsiveness analysis using a group approach based on intervention

	T_0 mean (SD)	T_1 mean (SD)	T_2 mean (SD)	RM-ANOVA or Friedman Main effect	Post hoc analysis (Tukey or Holm–Šidák)		Effect size	
					T_0–T_1	T_1–T_2	T_0–T_1	T_1–T_2
HABIT-ILE group								
ACTIVLIM-CP (n=47) (logits)	1.58 (1.58)	2.32 (1.45)	2.47 (1.33)	χ^2=21.35, p<0.001[a]	S[b]	NS[b]	0.96[c]	0.06
ABILHAND-Kids (n=45) (logits)	1.55 (2.01)	2.73 (1.88)	2.83 (2.09)	F=31.30, p<0.001	S	NS	1.00[c]	0.13
PEDI (n=47) (raw score)	46.70 (11.92)	52.60 (10.47)	53.58 (10.94)	χ^2=37.66, p<0.001[a]	S[b]	NS[b]	1.16[c]	0.11
ABILOCO-Kids (n=45) (logits)	0.67 (3.93)	1.57 (3.94)	1.54 (3.81)	χ^2=13.75, p=0.001[a]	S[b]	NS[b]	0.63[d]	0.19
BoNT-A group								
ACTIVLIM-CP (n=28) (logits)	2.08 (1.80)	2.16 (1.94)	2.46 (1.79)	F=0.18, p=0.84			0.11	−0.12
ABILHAND-Kids (n=20) (logits)	3.08 (2.41)	3.30 (2.23)	3.76 (2.16)	F=0.11, p=0.90			−0.03	0.38
PEDI (n=28) (raw score)	46.89 (13.07)	47.00 (14.82)	49.22 (12.90)	χ^2=0.79, p=0.672[a]			−0.08	0.10
ABILOCO-Kids (n=20) (logits)	1.38 (1.72)	2.14 (2.49)	2.65 (2.01)	F=2.68, p=0.08			0.35[e]	0.18

[a]For Friedman analysis. [b]For Tukey post hoc test analysis. For effect size: [c]large (0.8); [d]moderate (0.5); [e]small (0.2). Results of post hoc test: S, significant; NS, not significant. *T*, testing session; RM-ANOVA, repeated measures analysis of variance; HABIT-ILE, hand–arm bimanual intensive therapy including lower extremities; PEDI, Pediatric Evaluation of Disability Inventory; BoNT-A, botulinum neurotoxin-A.

ACTIVLIM-CP scores was observed at baseline between groups (Mann–Whitney test, p=0.31).

Group approach

Table II presents the results of the group approach based on intervention. For the HABIT-ILE group, children showed a significant improvement in global activity performance in the intervention period but not in the follow-up period. On average, children showed improvements in global activity performance of 0.74 logits between T_0 and T_1. According to the item map ordering items from the most difficult to the easiest item (Fig. 1), at T_0 the children of our sample would, on average (1.58 logits), not be able to achieve the two most difficult items, be able to perform with difficulty the six following items, and easily achieve the remaining 35 items. After the HABIT-ILE intervention (T_1), they would, on average (2.32 logits), be able to perform the 43 activities, with some difficulty for the three most difficult items, and easily for the other 40 (Fig. 1). For the BoNT-A group, indices highlighted no significant improvement at both assessment periods. On average, global activity performance improved (0.08 logits) between T_0 and T_1. Theoretically, this does not represent a change in the probability of passing from the category 'difficult' to 'easy' or from 'impossible' to 'difficult' in the ACTIVLIM-CP items (Fig. 1).

For the three other questionnaires, in the HABIT-ILE group, children showed significant improvements for the intervention period but not for the follow-up period. For the intervention period, effect size showed a large effect for ABILHAND-Kids and the PEDI, and a moderate effect for ABILOCO-Kids. For the BoNT-A group, children did not show significant improvements with any questionnaire for both assessment periods. This was confirmed by effect size, with non-significant changes for ABILHAND-Kids and the PEDI but a small magnitude of change for ABILOCO-Kids (T_0–T_1).

Subgroup approach

For the HABIT-ILE group, in the intervention period, children's global activity performance significantly improved in the subgroup GMFCS levels III and IV while a tendency for improvement was observed in the subgroup GMFCS levels I and II (Table III). This was confirmed by effect size, which was characterized as moderate in the subgroup GMFCS levels I and II and large in the subgroup GMFCS levels III and IV. For the BoNT-A group, no significant difference in ACTIVLIM-CP scores during assessments was observed for either subgroup. This observation is congruent with the small effect size in the subgroup GMFCS levels I and II and no significant effect size for the subgroup GMFCS levels III and IV for the intervention period. During follow-up, only the subgroup GMFCS levels III and IV presented a significant effect size.

For the three other questionnaires, in the HABIT-ILE group, both subgroups showed significant improvements during the intervention period. Effect size was described as large with ABILHAND-Kids in both subgroups; large with the PEDI for the subgroup GMFCS levels I and II and moderate for the subgroup GMFCS levels III and IV; and small with the ABILOCO-Kids in both subgroups. For the BoNT-A group, no significant changes during assessments were highlighted with the three other questionnaires for either subgroup. This lack of significant change was confirmed in both subgroups by a non-significant effect size for ABILHAND-Kids and the PEDI, and a small effect size for ABILOCO-Kids, during the intervention period. During follow-up, only the subgroup GMFCS levels III and IV presented a significant effect size for ABILHAND-Kids and ABILOCO-Kids.

Individual approach

For the HABIT-ILE group, 39% of the children showed significant increase ($t \leq -1.96$), 41% showed increase ($0 > t > 1.96$), 4% did not change (t=0), 16% tended to

Table III: Responsiveness analysis using a subgroup approach based on Gross Motor Function Classification System (GMFCS) levels

	T_0 Mean (SD)	T_1 Mean (SD)	T_2 Mean (SD)	RM-ANOVA or Friedman Main effect	Post hoc analysis (Tukey or Holm–Šidák)		Effect size	
					T_0–T_1	T_1–T_2	T_0–T_1	T_1–T_2
HABIT-ILE group								
GMFCS levels I and II								
ACTIVLIM-CP (n=27) (logits)	2.34 (1.36)	2.94 (1.11)	2.94 (1.10)	χ^2=5.18, p=0.07[a]	S[b]	NS[b]	0.73[d]	0
ABILHAND-Kids (n=26) (logits)	2.15 (1.80)	3.11 (1.71)	3.30 (1.88)	χ^2=21.25, p<0.001[a]	S[b]	NS[b]	0.86[c]	0.19
PEDI (n=27) (raw score)	51.80 (8.09)	56.5 (6.20)	57.3 (6.21)	χ^2=19.57, p<0.001[a]	S[b]	NS[b]	1.33[c]	0.02
ABILOCO-Kids (n=26) (logits)	3.43 (1.73)	4.19 (1.57)	4.06 (1.65)	F=8.93, p<0.001	S	NS	0.47[e]	0.15
GMFCS levels III and IV								
ACTIVLIM-CP (n=20) (logits)	0.55 (1.24)	1.48 (1.44)	1.77 (1.36)	F=30.03, p<0.001	S	NS	1.36[c]	0.15
ABILHAND-Kids (n=19) (logits)	0.42 (1.92)	1.81 (2.22)	2.01 (2.17)	F=16.88, p<0.001	S	NS	1.07[c]	−0.04
PEDI (n=20) (raw score)	39.75 (12.88)	47.30 (12.70)	48.26 (13.87)	χ^2=18.01, p<0.001[a]	S[b]	NS[b]	0.59[d]	0
ABILOCO-Kids (n=19) (logits)	−3.28 (2.36)	−2.40 (3.08)	−1.96 (3.03)	χ^2=6.71, p=0.035[a]	NS[b]	NS[b]	0.37[e]	0.09
BoNT-A group								
GMFCS levels I and II								
ACTIVLIM-CP (n=24) (logits)	2.09 (1.74)	2.22(1.96)	2.42 (1.81)	F=0.52, p=0.60			0.22[e]	−0.21
ABILHAND-Kids (n=16) (logits)	3.48 (2.13)	3.41 (2.05)	3.98(1.93)	F=0.09, p=0.91			−0.06	0.34[e]
PEDI (n=24) (raw score)	47.74 (12.98)	47.13 (14.92)	49.15 (13.43)	χ^2=0.79, p=0.67[a]			−0.10	0.14
ABILOCO-Kids (n=16) (logits)	2.13 (1.06)	2.63 (2.31)	2.84 (2.01)	F=0.94, p=0.40			0.29[e]	−0.08
GMFCS levels III and IV								
ACTIVLIM-CP (n=5) (logits)	2.07 (2.29)	1.84 (2.03)	2.69 (1.99)	F=0.34, p=0.72			−0.32	0.88[c]
ABILHAND-Kids (n=5) (logits)	1.91 (2.99)	1.93 (3.38)	2.84 (3.32)	F=0.06, p=0.94			−0.02	0.57[d]
PEDI (n=5) (raw score)	46.16 (14.19)	46.40 (16.04)	49.67 (10.79)	χ^2=0.80, p=0.94[a]			0.06	−0.10
ABILOCO-Kids (n=5) (logits)	−1.70 (1.68)	−1.05 (3.72)	1.81 (2.18)	F=2.11, p=0.20			0.21[e]	1.63[c]

[a]For Friedman analysis. [b]For Tukey post hoc test analysis. For effect size: [c]large (0.8) [d]moderate (0.5); [e]small (0.2). Results of post hoc test: S, significant; NS, not significant. *T*, testing session; RM-ANOVA, repeated measures analysis of variance; HABIT-ILE, hand–arm bimanual intensive therapy including lower extremities; PEDI, Pediatric Evaluation of Disability Inventory; BoNT-A, botulinum neurotoxin-A.

decrease ($-1.96<t<0$), and no child showed significant decrease ($t\leq-1.96$). For the BoNT-A group, no child showed significant increase ($t\leq-1.96$), 54% showed increase ($0>t>1.96$), 3% showed no change ($t=0$), 32% showed a tendency towards decrease ($-1.96<t<0$), and 11% showed significant decrease ($t\leq-1.96$).

DISCUSSION

This study investigated the responsiveness of the ACTIVLIM-CP using two evidence-based interventions. ACTIVLIM-CP showed good sensitivity to change after HABIT-ILE intervention, while no significant change was observed after BoNT-A injection(s) into lower extremities combined with conventional physiotherapy. After HABIT-ILE intervention, larger changes were detected in children classified in GMFCS levels III and IV.

At the group level, ACTIVLIM-CP demonstrated high responsiveness after HABIT-ILE intervention. The amount of change observed in this study with the ABILHAND-Kids, PEDI, and the ABILOCO-Kids was similar to previous observations.[13,14] The amount of change detected with ACTIVLIM-CP was equivalent to the amount of change observed with ABILHAND-Kids, a criterion standard upper extremity questionnaire shown to be highly responsive after HABIT intervention.[19] The PEDI self-care subscale revealed significant changes as well. ACTIVLIM-CP and ABILHAND-Kids were developed with the Rasch model, which allows transformation of the raw score into a linear measure and thus permits quantitative comparison whereas the PEDI questionnaire uses the raw score. We did not use the PEDI-CAT Rasch-developed version of the questionnaire because it was not developed specifically with a sample of children with CP,[20] although it was shown that difficulties with most manual activities were diagnosis dependent.[21] The raw score of the PEDI questionnaire used in this study is a nonlinear unit of measure that could mischaracterize the real changes observed; therefore the effect size should be carefully considered. Changes observed with the ACTIVLIM-CP were greater in magnitude than those observed with ABILOCO-Kids. This could be explained by the target used in HABIT-ILE, which is based on bimanual training combined with postural/lower extremity engagement to improve function in daily life activities but does not directly target locomotion activities. Alternatively, this could reflect a lower capacity of ABILOCO-Kids to detect changes. Further studies are required to investigate the responsiveness of ABILOCO-Kids.

After BoNT-A injection into lower extremities combined with conventional physiotherapy, no changes were detected with the ACTIVLIM-CP or other questionnaires. A possible explanation could be the primary effect of BoNT-A injection, which reduces muscular overactivity and thus relates to 'body functions and structures'. Regarding activity level, the efficiency of BoNT-A injection into upper extremities in association with a motor-skill learning, time-limited, goal-directed, and context-focused intervention has been demonstrated.[11] Although evidence-based guidelines

for BoNT-A injection into lower extremities remain to be established, some studies that provided goal-oriented physiotherapy programmes have demonstrated effectiveness in improving daily life activities.[22,23] Efficiency at the activity level seems to be conditioned by the rehabilitation strategies used, including the dosage of intervention and the components of the practice. In the present study, physiotherapy was delivered at a low-level intensity and mostly based on neurodevelopmental approaches, which have been described as not efficient at the activity level.[11] Thus, we hypothesize that the combination of BoNT-A injection into lower extremities with conventional physiotherapy had insufficient effect in the domain of activity to allow activity questionnaires, including the ACTIVLIM-CP, to be sensitive to change. Another possible explanation for the absence of change could be that BoNT-A injection, in this study, targeted only the lower extremities, while the ACTIVLIM-CP is a more global measure. However, this explanation is unlikely, because of the absence of significant change as measured by ABILOCO-Kids, a questionnaire that focuses on lower extremity activity. These results suggest that the ACTIVLIM-CP is a responsive tool to be used after goal-directed motor-skill learning intervention. Although questionnaires of functional activities should not be taken as a primary outcome if the treatment targets 'body functions and structures', it may be interesting to use them to study the impact of functions and structures on activities and participation.

In the HABIT-ILE group, when children were considered by the GMFCS subgroups, larger changes in global activity performance were observed for those in GMFCS levels III and IV (children with bilateral CP) than those in GMFCS levels I and II (mostly children with unilateral CP). This could be explained by a greater potential for improvement in children with significant motor impairment (GMFCS levels III–IV). This hypothesis would be validated if all questionnaires showed systematically larger improvements in these children. According to previous studies,[13,14] the mean change as measured with ABILHAND-Kids (manual ability) was smaller in children with bilateral CP (1.00 logits) than in those with unilateral CP (1.91 logit). Conversely, children with bilateral CP had mean change of 2.20 logits with ABILOCO-Kids, while children with unilateral CP had mean change of 1.11 logits. This suggests that children with bilateral CP do not improve globally more than children with unilateral CP but present more improvements in lower extremities and fewer in upper extremities. The trunk control needed to perform ACTIVLIM-CP items could be an alternative explanation of higher changes detected after HABIT-ILE for children in GMFCS levels III and IV. ACTIVLIM-CP items are all characterized by trunk engagement, under either static conditions (including sitting or standing without steps [67%]) or dynamic conditions (when the child must lean their trunk >45°, with/without steps [33%]).[10] Trunk control is a key component in daily life activities: upper extremities, lower extremities, and combination activities.[24] Although all children with CP may encounter deficits in postural adjustment compared with typically developing peers, children with bilateral CP were observed to have more difficulty with trunk control.[25] Because ACTIVLIM-CP showed the highest effect size in the subgroup of children in GMFCS levels III and IV, we therefore hypothesize that trunk control, which is practised in the HABIT-ILE intervention, improves more in these children, as reflected in the corresponding component of the ACTIVLIM-CP, which is sensitive to change.

Changes observed at the individual level were congruent with results detected in the group approach. After HABIT-ILE intervention, most of the children showed either significant increase or increase; no child showed a significant decrease. Some of these children showed a decrease in performance; but their t values ranged from -0.004 to -0.60, which is closer to 0 (no change) than -1.96 (decrease), with only one outlier ($t=-1.26$). In contrast, after BoNT-A intervention, no children showed a significant increase, more than half of the children showed a non-significant increase, and some showed either decrease or significant decrease. With the group approach after BoNT-A injection, most children did not show improvement on the ACTIVLIM-CP (or on the three other questionnaires). On the contrary, it is interesting to note that, at the individual level, some children showed an increase in their global activity performance. Future research should investigate the characteristics of such children to better target those who are likely to functionally improve after that intervention.

Limitations and perspectives

As the lack of changes observed with ACTIVLIM-CP after BoNT-A injection(s) into lower extremities might be related to the associated conventional physiotherapy, it would be interesting to investigate changes in daily life activities when injection(s) are followed by intensive goal-oriented motor-skill learning programmes.

In the BoNT-A group, the results of children in GMFCS levels III and IV should be interpreted cautiously because of the low number of children included. Although no significant improvement was observed for any of the questionnaires used in this study after BoNT-A intervention, the low number of children with CP in GMFCS levels III and IV is a limitation, particularly because ACTIVLIM-CP responsiveness differed between gross motor functional levels in the HABIT-ILE group. Complementary investigations should be performed after BoNT-A injection in children with CP in GMFCS levels III and IV.

CONCLUSION

The ACTIVLIM-CP questionnaire demonstrated high responsiveness after HABIT-ILE, showing the utility of this scale for investigating global activity performance in clinical trials. Children in GMFCS levels III and IV exhibited larger changes in global activity performance than those in GMFCS levels I and II after HABIT-ILE intervention. After BoNT-A injection, no change was detected with

ACTIVLIM-CP or with any of the three other questionnaires. This suggests the interest of using ACTIVLIM-CP for measuring changes after intensive interventions and for investigating characteristics of children transferring changes due to BoNT-A injection into daily life activities, potentially allowing optimization of the indications of this treatment in the future.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Appendix S1: Protocol of botulinum neurotoxin-A injection for each child and correlations between ACTIVLIM-CP and other questionnaire changes.

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