'Remind-to-move' treatment versus constraint-induced movement therapy for children with hemiplegic cerebral palsy: a randomized controlled trial

Journal:	*Developmental Medicine & Child Neurology*
Manuscript ID	DMCN-OA-16-01-0021.R2
Manuscript Type:	Original Article
Date Submitted by the Author:	n/a
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Keywords:	Remind-to-move, constraint-induced movement therapy, children, hemiplegia, cerebral palsy

'Remind-to-move' treatment versus constraint-induced movement therapy for children with hemiplegic cerebral palsy: a randomized controlled trial

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Statement:

This manuscript is the original work of the authors and has not previously been submitted for publication. No commercial party with a direct financial interest in the results of the research supporting this article has or will confer a benefit upon the authors or upon any organization with which the authors are associated.

Number of words in abstract: 198
Number of words in manuscript: 3,424
Number of tables: 3
Number of figures: 2
Number of references: 25

Manuscript submitted to *Developmental Medicine & Child Neurology* (DMCN)

TITLE

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ABSTRACT

AIM This study was conducted to evaluate 'remind-to-move' (RTM) treatment by comparing it with constraint-induced movement therapy (CIMT) and conventional rehabilitation of the upper extremity in children with hemiplegic cerebral palsy (CP).

METHOD Seventy-three children (44 males, 29 females; mean age 11y 8mo, SD 3y 1mo) – 20, 38, and 15 in Manual Ability Classification System Levels I-III, respectively – were recruited from three special schools and randomly selected for an RTM (*n*=25) or CIMT (*n*=24) programme (for 75 hours over 3 weeks) or for conventional rehabilitation (*n*=24). The Jebsen-Taylor Hand Function Test, the Bruininks-Oseretsky Test of Motor Proficiency (Subtest 3), the Caregiver Functional Use Survey, and arm movement duration captured by accelerometers were used at the baseline, post-test, and 1- and 3-month follow-ups.

RESULTS Both the RTM and CIMT treatments achieved significant gains in manual capacities and spontaneous hand use immediately after the intervention compared to conventional rehabilitation, but there were no significant differences between the two interventions.

INTERPRETATION The RTM treatment demonstrated similar therapeutic effects with CIMT in manual dexterity and functional hand use, but both interventions were superior to conventional rehabilitation. RTM is recommended as an alternative treatment for the hemiplegic upper extremity in children with CP.

(ClinicalTrials.gov Registration: NCT02645331)

(198 words)

Running Head: Remind-to-move

Keywords: Remind-to-move, constraint-induced movement therapy, children, hemiplegia, cerebral palsy

What this paper adds

- Improvement in upper-limb function shows that both the RTM treatment and the CIMT had similar effects on motor efficiency.
- Both the RTM and CIMT treatments led to more spontaneous use of the affected hand than conventional rehabilitation.

ABBREVIATIONS

BOTMP-II	Bruininks-Oseretsky Test of Motor Proficiency (2nd version)
CFUS	Caregiver Functional Use Survey
CIMT	Constraint-induced Movement Therapy
CP	Cerebral Palsy
CR	Conventional Rehabilitation
IQ	Intelligence Quotient
MACS	Manual Ability Classification System
JTHFT	Jebsen-Taylor Hand Function Test
RTM	Remind-to-move

Children with hemiplegic cerebral palsy (CP) are characterized by motor impairments mainly lateralized to one side of the body, with greater upper limb than lower limb involvement; these impairments may further limit the daily activities and school participation of children with hemiplegic CP.[1] Such children often learn strategies to manage bimanual activities with the unaffected hand only and gradually develop non-use of the more affected hand. This phenomenon, usually referred to as 'developmental disregard',[2] may lead to asymmetrical motor development and the failure of development of the more affected extremity because of a lack of spontaneous hand use in everyday life.

Constraint-induced movement therapy (CIMT) is a moderate-to-strong evidence-based intervention in children with hemiplegic CP.[2–7] CIMT involves utilizing a restraint on the unaffected hand along with forced use of the affected hand; thereby improving the unilateral capacity of the affected hand. Regarding the action mechanism of CIMT, recent evidence[8–10] suggests that the repetition of practice, immediate feedback given during treatment, and enjoyable and functional shaping activities designed to promote a child's engagement – rather than the use of a restraint that immobilizes the unaffected hand – are the key elements for causing a change of cortical activation[8,11] and sustaining improvements in upper limb functions.[6,10] Despite its benefits, CIMT has been criticized for being difficult to implement clinically because of the restraint selection, time of restraint, children's tolerance and compliance, treatment dosage, safety considerations, and the generalization of unilateral capacity to real-life activities that require the spontaneous use of both hands.

Recently, 'remind-to-move' (RTM) treatment was developed in response to the potential limitations of CIMT.[12,13] RTM treatment involves two key elements: sensory cueing on the affected arm and repetitive bimanual coordination and/or unimanual practice. A portable sensory cueing wristwatch device – which is used as an external cue worn on the affected arm instead of a restraint on the unaffected hand – is set up to emit continuous sensory cues to increase the user's attention on the affected hand and remind the user to be aware of and use the affected hand intensively. Our two preliminary studies showed that RTM treatment is useful in improving the children's arm motor-functions and functional hand use.[14,15] RTM treatment has been used for improving arm functions and treating unilateral neglect in adults who have had a stroke.[12,13] Although the beneficial effects of RTM treatment were found in our pilot studies, it was unknown if this treatment could be used interchangeably with other common interventions, such as CIMT. The purpose of this study was to determine the effects of RTM treatment on upper limb performance by comparing it with intensity-matched CIMT and conventional rehabilitation in children with hemiplegic CP. We hypothesized that the RTM group might show benefits in upper limb outcomes comparable with those in the CIMT group, and that RTM treatment could

be used as an alternative treatment for upper limb motor impairment and developmental disregard in children with hemiplegic CP.

METHOD

Participants

Seventy-three children with hemiplegic CP were recruited by convenience sampling from three special schools that provide special educational services for children with physical disabilities in Hong Kong and the mainland China. The eligible participants fulfilled the inclusion criteria adopted from previous studies:[10, 15] (i) being aged 5 to 16 years; (ii) having the ability to follow instructions; (iii) having the ability to grasp and release light objects, with an extension of at least 20° of the wrist and 10° of the metacarpophalangeal joints of the fingers (from full flexion of the affected hand); and (iv) having impairment of hand function at Levels I-III of the Manual Activity Classification System (MACS).[16] The exclusion criteria, which were obtained from the participating institutions, were: (i) having a severe intellectual disability as defined by the Hong Kong Wechsler Intelligence Scale for Children[17]; (ii) having visual or auditory disorder; (iii) being subject to seizures or having health problems not associated with CP; (iv) having predominant spasticity or contracture grades more than Grade 3 of the Modified Ashworth Scale in wrist and finger flexors, forearm pronators, and /or thumb adductors; and (v) having received Botulinum toxin injections and/or surgical interventions in the 6-month period prior to the study.

The study was approved by the Human Subjects Ethics Committee of The Hong Kong Polytechnic University (Reference: HSEARS20130214003) and the governing boards of the three special schools. Informed written consent forms were signed by the parents or guardians of all the participants. The trial was registered in ClinicalTrials.gov (Reference: NCT02645331).

Design and procedure

Figure 1 shows the flow chart of the recruitment. First, 256 potential participants – children diagnosed with CP – each received an individual face-to-face screening assessment to identify the eligible participants. A sample of 73 eligible participants, stratified according to the levels of MACS, was randomly allocated to three groups (to receive either RTM, CIMT, or conventional rehabilitation), using a computer generated list of random numbers and concealed envelopes; this was done by a teaching assistant who was not involved in the study. The participants were evaluated on 4 occasions: at the baseline, immediately after the intervention, and at 1- and 3-month follow-ups. The assessments, except the parental questionnaire, were performed by an

experienced occupational therapist (OT) in paediatrics, who was trained to use the assessments by the investigators, and blinded to the group allocation.

Sample size calculation

The sample size was calculated by G*Power software (Version 3.1.3, Franz Faul, University of Kiel, Germany) based on the findings of our previous pilot study on RTM,[14] a significant mean change on the Jebsen-Taylor Hand Function Test (JTHFT)[18] between pre- [mean (SD), 286(73.9)] and post-intervention [mean (SD), 201.7(64.7)] yielded 84 scores with an observed effect size of 1.214. An assumed 98% power with a 5% type I error in a one-way ANOVA meant that 23 participants were required in each group to allow detection of a significant difference in the primary outcome measure of the JTHFT across the three treatment groups. Allowing for a 10% dropout rate at follow-up, 25 participants per group were required, yielding a total of 75 participants.

Interventions

The shaping practice was similar in both RTM treatment and CIMT,[19] the difference was that the CIMT involved using a restraint to immobilize the less-affected hand whereas the RTM treatment involved reminding children to make certain predetermined movements (by a vibration cue from a wristwatch device worn on the more-affected arm) continuously at 15-minute intervals. Both the RTM treatment and the CIMT were administered during normal school hours, 5 hours per day, 5 days every week, for 3 consecutive weeks. The children in both groups received 5 hours of intensive training, which consisted of a 1-hour shaping practice session (0.5 hour/session, two sessions daily) supervised by the therapists and a 4-hour unstructured practice session supervised by the teachers or parents. The one-to-one 1-hour shaping practice session was delivered to each participant by an OT; its design was based on the training given in our previous studies;[14,15]this training included both fine-motor and gross-motor activities, general movements for range of motion and voluntary repetition of desired movements, and involved age-appropriate self-care and play activities (Table I).[10,20] During the 4-hour unstructured practice session, the children continued the typical school routine and performed the predetermined upper limb movements independently, though supervised by the teachers or parents (Table I). All the training tasks were individually tailored by the investigators and case OTs, according to the children's specific hand functions, interests, and age.[21]

The children in the RTM group were provided sensory cueing wristwatches (from PolyU Technology & Consultancy Co. Ltd, Hong Kong; US patent US-2010-0160834-A1) when they arrived at school. The wristwatch, which had a built-in accelerometer to record movement

duration, was sampled at 5Hz and with a 2-second epoch recording time. During the individual shaping practice session, children worked one-to-one with the OT, to guide the components of movement and the sequence of tasks; the children were asked to use their more affected hand to assist the functional hand to complete the bimanual shaping tasks or to perform the structured unimanual practice with the affected hand freely. During the unstructured training session, the children were encouraged to complete customized movement tasks independently once they felt the vibration cues from the wristwatch; the teachers and parents avoided providing any verbal cues to get the children to use their affected hand. The children in the CIMT group were encouraged to wear a custom-made volar-resting hand splint on their less affected hands, for 5 hours daily (but not when washing or using the toilet, writing, or playing specific physical sports), and administered during school time without interfering with performance of academic activities. The 1-hour shaping practice and the 4-hour unstructured practice sessions were similar to that of the RTM, except that the children performed the customized unilateral arm movements spontaneously. The children in the conventional rehabilitation group followed the regular routine of the conventional rehabilitation programme; this included hand splinting, muscle strengthening and stretching, using neurodevelopmental facilitation techniques, and so on, for 1 hour per day, 2 to 3 days per week, for 3 weeks.

Outcome measures

Six outcome measures that would provide results at three levels: the manual capacity of the upper extremity, hand use in real life, and hand impairment, were selected.

Primary outcomes

The JTHFT was used to measure the unimanual capacity of an impaired upper extremity by quantifying the time taken to complete a set of simulated functional tasks.[18] The JTHFT was modified by eliminating the writing task and restricting the maximum allowable time to 2 minutes for each unimanual task, giving a maximum score of 12 minutes.[22] Less time taken indicated better performance.

Subtest 3 of the Bruininks-Oseretsky Test of Motor Proficiency (2nd version; BOTMP-II) was used to measure movement efficiency with five unimanual and bimanual fine motor tasks.[23] The unimanual tasks were executed by the affected hand. A higher raw score indicated better performance. The psychometric properties of both the total scale and each subscale have been established in children with motor deficits.[23]

As in our previous study,[15] the Caregiver Functional Use Survey (CFUS)[22] was selected to quantify the spontaneous use of the affected hand in real life. It is a reliable semi-structured

interview which is used to assess parents' perceptions of how much (amount of use, AOU) and how well (quality of use, QOU) their children use the impaired hand to perform 14 bimanual daily tasks in daily situations.[22] The primary caregivers rated their children's hand use in home and school environments by scoring two subscales of the CFUS.

Secondary outcomes

The real-life functional use of the affected hand was evaluated by the ratio of the duration of movement of the affected hand to the duration of movement of the unaffected hand (these being measured by the built-in accelerometer in the wristwatch device). Each participant was asked to wear the device, with sensory signals off, on both their arms for 1 day.

Hand impairment was evaluated by the power grip strength (in lb) and the active range of motion (ROM) of the upper extremity were measured using the dynamometer and the digital goniometer of the E-LINK Evaluation System (Biometrics Ltd, Newport, United Kingdom). This system measures the standard peak outcomes and automatically calculates the average measurements of three movements and the coefficient of variation.

Statistical analysis

Intention-to-treat analysis of the data was performed using the Statistical Package for Social Science 20.0 software package (SPSS Inc., Chicago, Illinois, USA). Before analysing each variable, data distribution normality was verified by the Levene's test for homogeneity of variance. The demographic data and baseline scores of the outcome measures among the 3 groups were compared by Chi-square and one-way ANOVA respectively. A 3(group)×4(test session) ANOVA with two-way repeated measure was used to examine the time effect of each treatment and an overall group×time interaction among the three groups. In the case of a significant interaction, time and treatment effects were further analyzed by the pairwise post hoc Bonferroni Test separately at each time point. Eta-squared values (η^2) – effect size estimates – were calculated, with a large effect estimated to occur at (at least) 0.138, a moderate effect at 0.06, and a small effect at 0.01. The significance level was set at 0.05.

RESULTS

Fig. 1 shows the flow of recruitment and randomization. Seventy-three participants were randomized, with a dropout rate at 4.1% that was less than the predicted rate of 10% in the power calculation. No statistical differences were found in the baselines of the 3 groups (Table II). The children were predominantly classified as belonging to Level I (n=20) and II (n=38) of the MACS, and Level I (n=37) and Level II (n=36) of the Gross Motor Functional Classification

System (GMFCS).[24]Thirty-three participants had normal intelligence. There were two dropouts from the CIMT group in the first week of treatment, due to the fact that children did not tolerate the intervention and complain inconvenience during physical activities at school. One participant dropped out from the conventional rehabilitation group because his parents rejected the randomized group allocation. Compliance of attendance was 100% for the RTM treatment, 91.7% for the CIMT, and 95.7% for the conventional treatment. No major adverse event was reported in the above treatments. The average duration of treatment actually received daily was 4.5 (SD=0.4) out of 5 hours in the RTM group and 4.3 (SD=0.5) hours in the CIMT group. The compliance rate of treatment was 90.8% and 85.8% respectively.

Table III shows a significant time×group interaction ($F_{3.69, 129.03}$= 11.16, p<.001, η^2=0.242) of the JTFHTs over the 4 test sessions. Both RTM and CIMT led to a significant decrease in the time taken to complete the tasks immediately post-treatment, with a mean change at -63.2 and -70.4 respectively; but no significant difference was found between the 2 groups (p=0.565). Figure 2A shows a significant group difference ($F_{2, 70}$=16.47, p<0.001, η^2=0.320) revealed by the 3(group)×3(time point) ANOVA on the mean changes in the JTHFT scores from baseline to the 3 post-tests; the pairwise post hoc test showed a significant treatment effect in both the RTM and CIMT groups, compared with conventional rehabilitation (p<0.001); and the improvements were maintained for 3 months – CIMT especially demonstrated more potential long-term effects (Fig. 2A).

There was a significant group×time interaction ($F_{3.09, 108.23}$=14.74, p<0.001, η^2=0.296) of the BOTMP-II Subtest 3 among the 3 groups. There was an increase in the BOTMP-II scores (mean change, 1.98 vs. 1.35; p=0.085) immediately after the RTM and CIMT treatments. In addition, an observable group difference was noted, with a large effect size at 0.350 ($F_{2, 70}$=18.81, p<0.001) on the mean changes from baseline to the 3 post-tests (Fig. 2B). Pairwise comparisons indicate that both the RTM treatment (p<0.001) and the CIMT (p=0.001) produced better effects than the conventional rehabilitation.

Both the RTM treatment and the CIMT showed a comparable main effect in the test sessions and in the overall time×group interactions in the AOU and QOU subscales of the CFUS (Table III). Compared with conventional rehabilitation, both the RTM treatment (p_{AOU}=0.010; p_{QOU}=0.007) and the CIMT (p_{AOU}=0.034; p_{QOU}=0.014) led to a significant increase in functional hand use, but no statistical difference between the RTM treatment and the CIMT was found.

For the ratio of the duration of movement of the affected hand as captured by the built-in accelerometer in the wristwatch device, both the RTM treatment and the CIMT led to an

immediate increase in the hand use, of 16.5% (Standard Error, 1.4%) and 14.4% (Standard Error, 1.5%) respectively; and these gains were maintained up to the 3-month follow-up. No significant change was found in grip strength after the 3-week treatment.

DISCUSSION

The results of this study demonstrate that there was a greater improvement in motor efficiency and spontaneous use of the affected hand in the children in both the RTM and CIMT groups than in the children in the conventional rehabilitation group; these results are consistent with those of our two previous pilot studies.[14,15]

The CIMT is a well-known treatment with published evidence. The equivalent effects obtained by the RTM treatment may be attributed to the following reasons. Firstly, intensive shaping practice was done in both treatments, with repetitive reminders to practise movement of the affected hand (the reminders being emitted by the wristwatch device worn above the affected hand) during RTM treatment which is similar to the forced use of the affected hand in CIMT. Secondly, RTM treatment employs a user-friendly approach that promotes children's motivation and engagement in upper-limb exercise without a restraint. Attentional modulations can be divided into two types: domain-specific and domain-independent.[25] In RTM, we believed that the primary somatosensory cortex in the domain-specific attentional modulation showed the most activation when the child attended to, or when he/she was aroused by, the vibration stimulus from the wristwatch worn on the affected arm; it probably enhances awareness, voluntary movement execution, and spontaneous hand use of the affected arm.

The main effect of the RTM treatment on the unimanual capacity revealed by the JTHFT was consistent with the findings of our preliminary study,[14] whereas the effects of RTM treatment on scores achieved in the BOTMP-II were not found in one pilot study,[15] the possible explanation for this inconsistency could lie in the differences in the sample size, study design, intervention protocols, and the characteristics of the participants in the two studies. As seen in Fig. 2, the CIMT might have contributed a little more to the improvement of unilateral motor capacity in the JTFHT (Fig. 2A), while the RTM treatment demonstrated a little more benefit in improving bilateral motor skills in the BOTMP-II (Fig. 2B), but no significant differences were found between the two types of intervention. Consistent with the results of our preliminary studies,[10,15] both the RMT treatment and the CIMT were beneficial for increasing the active ROM of the more affected upper limb; however, no gains in grip strength were noted. These findings again confirm the notion that the improvement of unimanual and bimanual motor performance might be related to the restoration of motor control rather than of motor power.[15]

Regarding the spontaneous hand use captured by the accelerometer in the wristwatches and reported by the parents in CFUS, the results in both the RTM and CIMT groups indicated that the children demonstrated better hand performance than those in the CR group; these positive effects were also found in previous studies.[5,15,21] Surprisingly, an increase in movement duration of the affected hand was also noted in the conventional rehabilitation group; this interesting finding might result from the placebo effect of the wristwatch worn on the hemiplegic arm solely for the purpose of assessment (and even though the wristwatch was worn for only one day). However, the benefits of this sham effect had not been found in our previous pilot study.[14]

One potential advantage of RTM treatment is that it uses a portable wristwatch worn on the affected arm rather than a restraint on the unaffected, which was welcome by the children and parents. It could easily be incorporated into daily activities at home or in school settings. However, there was potential frustration once they became accustomed to cueing after a long wearing period.[14]

Limitations and future research

This study has several limitations. Only children with mild to moderate motor impairment in upper limb function (not those with severe impairment) were included; thus, the results cannot be generalized to all children with hemiplegic CP in special educational settings. Second, the lack of outcome measures concerning the self-care independence and health-related quality of life of the children may be another limitation. Third, this study favoured both the RTM treatment and the CIMT due to the fact that both treatments were delivered more intensively than the conventional rehabilitation; thus, it is not known whether the same results might have been produced by conventional rehabilitation of the same intensity. There were also dropouts in the CR group because the parents might not like their children left without specific intervention. The children in the sample had slightly more at Level II of the MACS, further studies should explore whether the severity of motor impairment or other factors influence response to treatment. In addition, the results of the CFUS rated by the parents could be biased as the parents were not blinded as to the types of intervention.

CONCLUSION

This was a multicentre randomized controlled trial comparing the effects of CIMT with those of the RTM treatment on upper limb outcomes in children with hemiplegic CP. The findings reveal that both treatments resulted in similar effects on their upper extremities. The RTM treatment could be used as an alternative or supplement to CIMT for targeting motor-impairment of the arm and overcoming developmental disregard in the school-aged children with hemiplegic CP.

(Words 3,424)

ACKNOWLEDGEMENTS

We sincerely thank the children and families who participated in this study. We thank Danny Lo Marcus Ng, and Shaoang Huang, as well as the occupational therapists of the Hong Kong Red Cross Princess Alexandra School, Hong Kong Red Cross John F. Kennedy Centre, and Guangzhou Rehabilitation Experimental School, for coordinating the data collection. We also thank Xijun Wei, Guohui Lin, and Yi Xie for the blinded outcome measurement. Our thanks are also extended to Raymond Chung for his advice on the statistical methods.

This work was partially supported by the General Research Fund 2012/13, University Grants Committee, Hong Kong SAR (5608/12M). The funding source had no role in conduct of the study or writing of the report.

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Table II: Demographics and baseline comparisons among the three groups

Characteristics	RTM (*n*=25)	CIMT (*n*=24)	CR (*n*=23)	*p* value
Demographics				
Age, mean (SD), y:mo	12:1 (3:3)	11:1 (2:7)	12:2 (3:2)	0.405[a]
Sex, male *n* (%)	15 (60.0)	15 (62.5)	14 (58.3)	0.957[b]
Side of hemiplegic hand, left, *n* (%)	11 (44.0)	12 (50)	14 (58.3)	0.603[b]
Classification				
MACS, *n* (%)				0.723[b]
Level I	5 (20.0)	7 (29.2)	8 (33.3)	--
Level II	15 (60.0)	13 (54.2)	10 (41.7)	--
Level III	5 (20.0)	4 (16.7)	6 (25.0)	--
GMFCS, n (%)				0.774[b]
Level I	14 (56.0)	12 (50)	11 (45.8)	--
Level II	11 (44.0)	12 (50)	13 (54.2)	--
Intelligence				0.960[b]
Normal	11 (44.0)	12 (50.0)	10 (41.7)	
Mild disability	12 (48.0)	10 (41.7)	11 (45.8)	
Moderate disability	2 (8.0)	2 (8.3)	3 (12.5)	
Activity Performance				
JTHFT, mean (SD), seconds	275.84 (105.18)	280.60 (107.07)	271.88 (121.30)	0.964[a]
BOTMP-II, mean (SD), scores	5.42 (1.88)	5.85 (1.99)	5.81 (2.11)	0.705[a]
CFUS scores, mean (SD)				
Amount of use	1.93 (0.42)	1.96 (0.42)	2.04 (0.43)	0.667[a]
Quality of use	1.88 (0.45)	1.93 (0.42)	1.99 (0.44)	0.684[a]
Ratio of duration of movement of affected hand (%)	40.06 (9.40)	41.22 (9.77)	43.49 (8.53)	0.425[a]
Hand Impairment				
Grip strength, mean (SD), Lb	10.74 (2.16)	10.42 (4.10)	10.74 (3.14)	0.921[a]
Active ROM, mean (SD), degrees (°)				
Shoulder flexion	131.4 (20.6)	136.0 (19.2)	133.3 (17.6)	0.699[a]
Forearm supination	45.6 (15.06)	44.5 (12.4)	46.9 (13.6)	0.836[a]
Wrist extension	44.2 (10.44)	43.0 (10.6)	44.6 (9.99)	0.866[a]

SD, standard deviation; MACS, Manual Ability Classification System; GMFCS, Gross Motor Function Classification System; RTM, remind-to-move; CIMT, constraint-induced movement therapy; CR, conventional rehabilitation; JTHFT, Jebsen-Taylor Hand Function Test; BOTMP-II, Bruininks-Oseretsky Test of Motor Proficiency (2nd version); CFUS, Caregiver Functional Use Survey.

[a]One-way ANOVA, two-tailed.

[b]Chi-square.

Table III: Means and 95% CIs of all outcomes of the four test sessions for the three groups

	Pre-test (95% CI)	Immediate Post-test (95% CI)	1-Month Post-test (95% CI)	3-Month Post-test (95% CI)	Treatment Effect: Mean Changes from Baseline to Immediate Post-test		Test Sessions Effect *p* Value (Partial η^2)[a]	Time×Group Interaction *p* Value (Partial η^2)[a]
					Change in Score (95% CI)	Group Effect *p* Value[b]		
JTFHT (s)								
RTM	275.8 (231.4, 320.2)	212.6 (168.1, 257.1)	202.7 (159.2, 246.4)	200.5 (158.4, 242.6)	-63.2 (-85.0,-41.4)		*p*<0.001 (0.499)	
CIMT	280.6 (235.3, 325.9)	210.2 (165.5, 255.0)	197.5 (153.4, 241.7)	188.6 (145.7, 231.6)	-70.4 (-92.6,-48.1)	*p*<0.001	*p*<0.001 (0.569)	*p*<0.001 (0.242)
CR	271.9 (226.6, 317.2)	255.9 (210.4, 301.3)	256.1 (211.5, 300.7)	256.8 (213.9, 299.8)	-16.0 (-38.3,6.3)		*p=0.*298 (0.052)	
BOTMP-II								
RTM	5.42 (4.63, 6.21)	7.40 (6.26, 8.54)	7.44 (6.32, 8.56)	7.26 (6.15, 8.37)	1.98 (1.42, 2.54)		*p*<0.001 (0.559)	
CIMT	5.85 (5.04, 6.69)	7.21 (6.24, 8.18)	7.25 (6.30, 8.20)	7.13 (6.19, 8.06)	1.35 (0.76, 1.95)	*p*<0.001	*p*<0.001 (0.366)	*p*<0.001 (0.296)
CR	5.81 (4.99, 6.66)	5.94 (4.87, 6.91)	5.98 (4.93, 6.94)	5.85 (4.82, 6.79)	0.13 (-0.13,0.38)		*p* =0.420 (0.040)	
CFUS-AOU								
RTM	1.93 (1.76, 2.10)	2.76 (2.49, 3.03)	2.83 (2.55, 3.11)	2.81 (2.51, 3.10)	0.83 (0.57, 1.09)		*p*<0.001 (0.534)	
CIMT	1.96 (1.79, 2.14)	2.68 (2.40, 2.96)	2.69 (2.40, 2.97)	2.69 (2.39, 3.00)	0.72 (0.45, 0.98)	*p*<0.001	*p*<0.001 (0.436)	*p*<0.001 (0.222)
CR	2.04 (1.86, 2.21)	2.17 (1.89, 2.45)	2.23 (1.94, 2.52)	2.19 (1.89, 2.49)	0.13 (-0.13, 0.40)		*p* =0.237 (0.060)	
CFUS-QOU								
RTM	1.88 (1.71, 2.06)	2.71 (2.43, 2.98)	2.78 (2.49, 3.08)	2.77 (2.47, 3.07)	0.82 (0.57, 1.08)		*p*<0.001 (0.525)	
CIMT	1.93 (1.75, 2.11)	2.67 (2.39, 2.95)	2.68 (2.38, 2.98)	2.70 (2.39, 3.00)	0.74 (0.48, 1.00)	*p*<0.001	*p*<0.001 (0.458)	*p*<0.001 (0.231)
CR	1.99 (1.81, 2.17)	2.09 (1.81, 2.37)	2.18 (1.88, 2.48)	2.12 (1.81, 2.42)	0.09 (-0.17, 0.36)		*p*=0.178 (0.069)	
Real-life hand use (%)								
RTM	40.1 (36.4, 43.8)	56.6 (52.2, 60.9)	59.3 (55.0, 63.6)	59.9 (55.5, 64.4)	16.5 (12.6, 20.4)		*p*<0.001 (0.675)	
CIMT	41.2 (37.5, 45.0)	55.7 (51.3, 60.1)	57.2 (52.8, 61.6)	57.1 (52.6, 61.7)	14.4 (10.5, 18.4)	*p*<0.001	*p*<0.001 (0.596)	*p*<0.001 (0.326)
CR	43.5 (39.7, 47.3)	46.8 (42.4, 51.2)	47.7 (43.3, 52.2)	49.0 (44.4, 53.5)	3.3 (-0.7, 7.3)		*p*=.0028 (0.125)	
Grip strength								
RTM	10.7 (9.5, 12.0)	11.2 (9.8, 12.6)	11.3 (9.8,12.8)	11.4 (9.9,12.8)	0.44 (-0.26, 1.13)		*p* =0.148 (0.081)	
CIMT	10.4 (9.1, 11.7)	10.9 (9.5, 12.3)	11.0 (9.5, 12.5)	10.9 (9.4, 12.3)	0.49 (0.02, 0.96)	*p*=0.669	*p* =0.052 (0.124)	*p*=.0656 (0.016)
CR	10.7 (9.4, 12.0)	10.9 (9.5, 12.4)	10.9 (9.4, 12.4)	11.1 (9.7, 12.6)	0.19 (-0.08, 0.46)		*p* =0.112 (0.095)	
Active ROM, degrees (°)								
Shoulder flexion								
RTM	144.5 (137.1, 151.8)	150.9 (143.6,158.2)	150.4 (143.1, 157.7)	149.5 (139.3, 156.9)	10.7 (7.2, 14.2)		*p*<0.001 (0.416)	
CIMT	146.9 (139.3, 154.5)	151.2 (143.6,158.7)	150.1 (139, 158.5)	151.3 (142.6,159)	8.0 (5.9, 10.2)	*p*=0.005	*p*=0.001 (0.276)	*p*=0.003 (0.106)
CR	147.0 (139.2, 154.8)	148.2 (140.4, 155)	147.3 (139.5,155)	146.2 (138.8,155.2)	4.2 (1.6, 6.8)		*p*=0.489 (0.033)	
Forearm supination								
RTM	46.2 (40.8, 51.5)	52.1 (46.7, 57.5)	51.8 (46.1, 57.4)	52.2 (45.9, 58.5)	3.6 (2.6, 4.5)		*p*<0.001 (0.459)	
CIMT	44.5 (38.9, 50.1)	48.2 (42.6, 53.8)	48.1 (42.2, 54.0)	48.2 (41.7, 54.7)	3.0 (2.2, 3.8)	*p*=0.017	*p* =0.001 (0.277)	*p*=0.001 (0.131)
CR	46.3 (40.6, 52.0)	47.3 (41.5, 53.0)	46.0 (40, 52)	47 (40.3, 53.7)	1.7 (0.8, 2.7)		*p* =0.311 (0.051)	
Wrist extension								
RTM	44.2 (40.2, 48.3)	50.8 (46.0, 55.6)	51.3 (46.5, 56.2)	51.5 (46.1, 57.0)	6.6 (4.1, 9.1)		*p*<0.001 (0.451)	
CIMT	43.0 (38.3, 47.3)	47.8 (42.8, 54.7)	49.8 (44.8, 54.7)	49.4 (43.8, 54.9)	4.7 (3.1, 6.3)	*p*=0.015	*p*<0.001 (0.486)	*p*=0.010 (0.098)
CR	44.6 (40.4, 48.8)	47.1 (42.2, 52.1)	47.0 (42.1, 52.0)	46.7 (41.2, 52.3)	2.5 (0.8, 4.2)		*p*=0.334 (0.041)	

CI, confidence interval; CIMT, constraint-induced movement therapy; RTM, remind-to-move; CR, conventional rehabilitation; JTHFT, Jebsen-Taylor Hand Function Test; BOTMP-II, Bruininks-Oseretsky Test of Motor Proficiency (2nd version); CFUS, Caregiver Functional Use Survey; AOU, amount of use; QOU, quality of use; ROM, range of motion; η^2, effect size.
[a]3(group)x4(test sessions) ANOVA with repeated measure.
[b]One-way ANOVA.

Figure 1: Flow diagram of the recruitment and randomization procedure

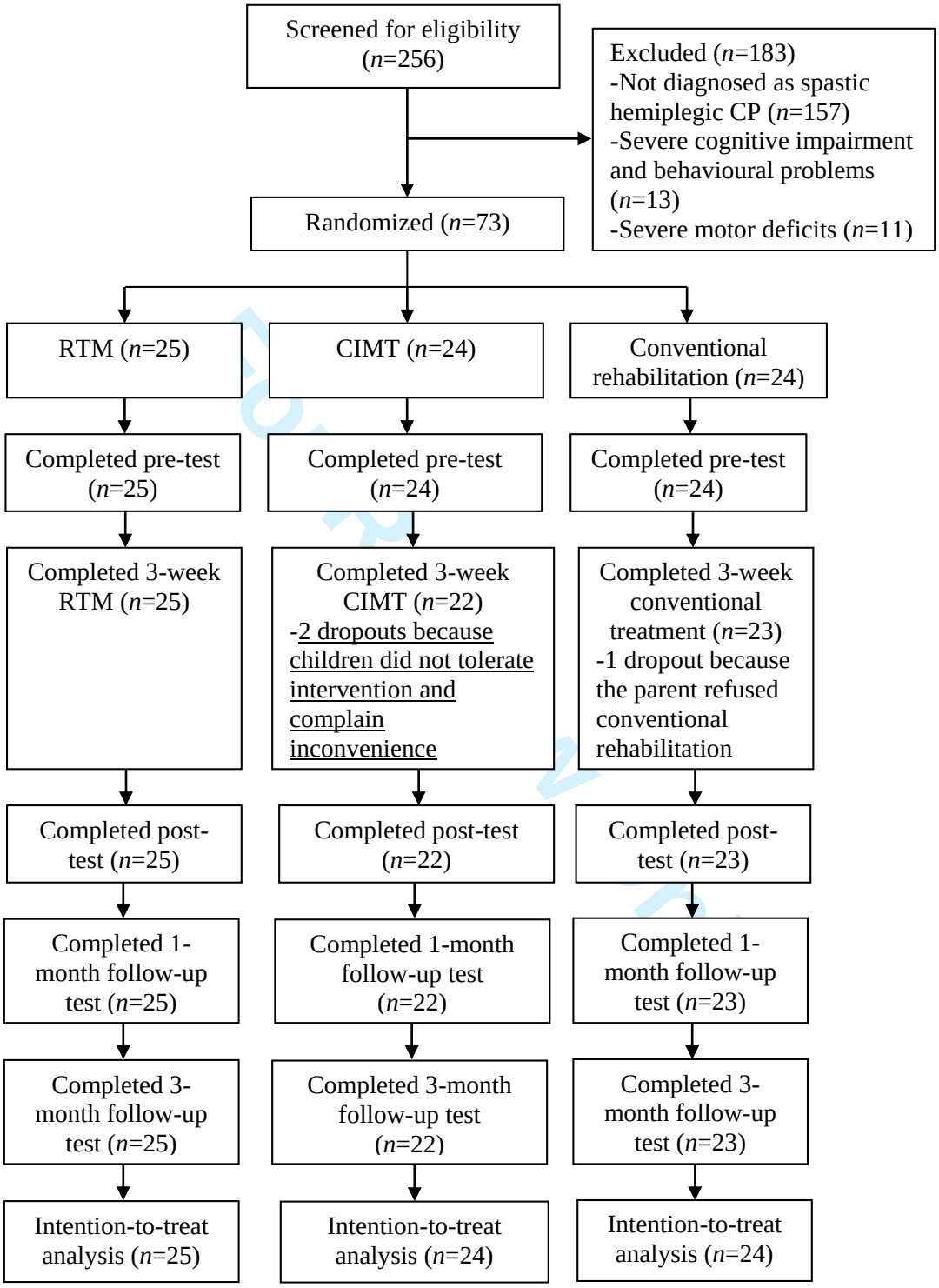

Figure 2: Mean changes from baseline in JTHFT and BOTMP-II Subtest 3 scores

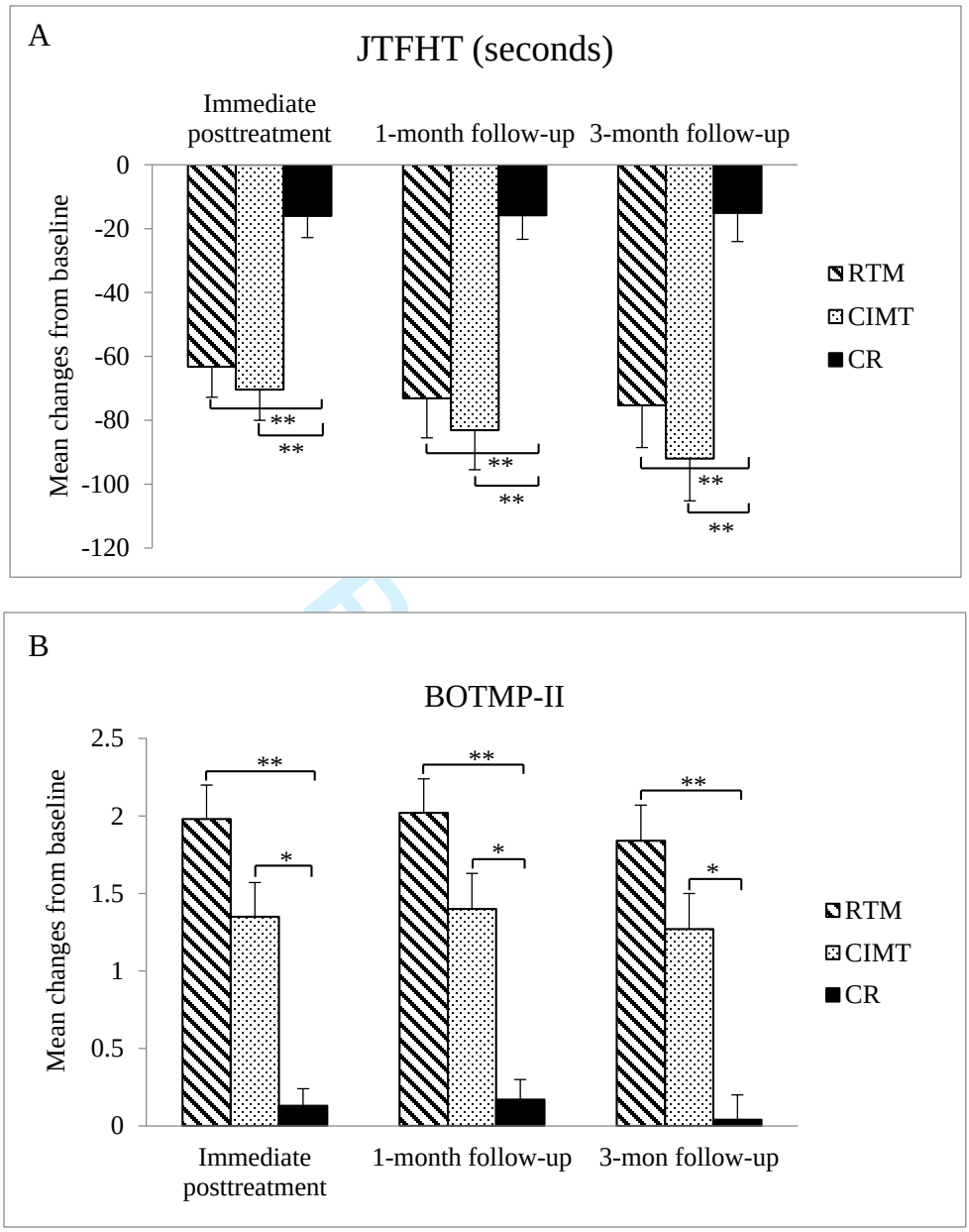

Figure 2A Mean changes and error bars in the time taken to complete six unimanual tasks of the Jebsen-Taylor Hand Function Test (JTFHT), from baseline to immediately after the intervention and in the 1- and 3-month follow-ups. Less time taken indicates better performance.

Figure 2B Mean changes and error bars in the scores for the manual dexterity subtest of BOTMP-II, from baseline to immediately after the intervention and in the 1- and 3-month follow-ups. Higher scores represent better performance.

Abbreviations: RTM, remind-to-move treatment; CIMT, constraint-induced movement therapy; CR, conventional rehabilitation.

*p<0.05; **p<0.001

Table I: Training activities for the RTM and CIMT programmes (online)

Activities	Predetermined upper limb movements
Card games (e.g. playing cards games, turning cards etc.)	- Precision grasp[1] - Wrist stabilization & supination[1] - Maintaining grasp cards for 1-2 minutes[1] - Bilateral coordination[2]
Beads stringing	- Thumb opposition[1] - Pincer grasp[1] - Wrist stabilization, extension & supination[1] - Eye-hand coordination[1] - Bilateral coordination[2] - In-hand manipulation (e.g. translation) [1]
Puzzles	- Precision grasp[1] - Release accuracy[3] - In-hand manipulation[3] - Eye-hand coordination[1] - Bilateral coordination[2]
Lego construction	- Precision grasp[1] - Wrist extension & stabilization[1] - Eye-hand coordination[1] - Release accuracy[3] - In-hand manipulation[3] - Bilateral coordination[2]
Art of cards making (e.g. cutting papers, sticking stickers, finger painting etc.)	- Stabilization[2] - Scissors grasping[3] - Fingers isolation[3] - Wrist extension & supination[1] - Precision grasp[1] - Eye-hand coordination[1] - Bilateral coordination[2] - Tools use (scissors) [2]
Board games	- Wrist extension & stabilization[1] - Precision grasp[1] - Bilateral coordination[2] - Eye-hand coordination[1] - Pincer grasp[3] - In-hand manipulation[3]
Gross motor (e.g. pushing matte board, shoulder hanging pulley, throwing and catching basketball etc.)	- Shoulder flexion, abduction & rotation[1] - Elbow extension[1] - Forearm supination[1] - Wrist extension & stabilization[1] - Bilateral coordination[2]
Functional tasks (e.g. dressing, grooming, buttoning and zipping, tying shoe laces, opening a lock etc.)	- Stabilization[1] - Wrist extension & supination[1] - Precision grasp[1] - Eye-hand coordination [1] - In-hand manipulation[3] - Bilateral coordination[2] - Fingers isolation[3] - In-hand manipulation[3]

[1]RTM or CIMT programmes; [2]RTM programme alone; [3] CIMT programme alone; RTM, remind-to-move; CIMT, constraint-induced movement therapy

Figure legends

Figure 1: Flow diagram of the recruitment and randomization procedure

Figure 2: Mean changes from baseline in JTHFT and BOTMP-II Subtest 3 scores

Figure 2A Mean changes and error bars in the time taken to complete six unimanual tasks of the Jebsen-Taylor Hand Function Test (JTFHT), from baseline to immediately after the intervention and in the 1- and 3-month post-test JTHFTs. Less time taken indicates better performance.
Figure 2B Mean changes and error bars in the scores for the manual dexterity subtest of BOTMP-II, from baseline to immediately after the intervention and in the 1- and 3-month post-tests. Higher scores represent better performance.
Abbreviations: RTM, remind-to-move treatment; CIMT, constraint-induced movement therapy; CR, conventional rehabilitation.
*$p<0.05$; **$p<0.001$