Cognitive approach to rehabilitation in children with hyperkinetic movement disorders post-DBS

Hortensia Gimeno, MSc(OT), Richard G. Brown, PhD, Jean-Pierre Lin, PhD, Victoria Cornelius, PhD, and Helene J. Polatajko, PhD

Neurology® 2019;92:e1212-e1224. doi:10.1212/WNL.0000000000007092

Correspondence

Ms. Gimeno
hortensia.gimeno@
gstt.nhs.uk

MORE ONLINE

→ Class of Evidence

Criteria for rating therapeutic and diagnostic studies

NPub.org/coe

📺 Videos

Abstract

Objective

This proof-of-concept feasibility trial examined the potential of the Cognitive Orientation to daily Occupational Performance Approach (CO-OP) to augment deep brain stimulation (DBS) outcomes in childhood-onset hyperkinetic movement disorders (HMD) including dystonia and dyskinesia cerebral palsy.

Methods

This is a single case experimental design using multiple baseline as n-of-1 trial comprising 10 intervention sessions, with replications across participants (n = 10). Treatment focused on 3 participant-selected goals. Transfer was assessed on 2 additional untreated goals. Individuals enrolled were 6–21 years of age and had DBS in situ and sufficient manual ability. Primary outcome was functional performance change on the Performance Quality Rating Scale–Individualized (PQRS-i) measured before, during, and posttreatment, and at 3-month follow-up. Assessors of outcome were blinded to time of assessment, number of intervention session, and treatment allocation. To measure effect size, a nonoverlapping index, Tau-U, was used. Feasibility measures were captured.

Results

One participant withdrew before baseline assessment. Effect sizes of at least 0.66 were seen at both posttreatment and follow-up with all participants showing improvements in at least one trained goal in PQRS-i. Six participants improved on all 3 goals and 2 improved on 2 trained goals. Two children showed deterioration in one trained goal each. Transfer to untrained goals was observed in 3 participants for a total of 5 goals. CO-OP was feasible and acceptable to all participants.

Conclusion

A cognitive-based, task-oriented approach to support performance of personally relevant functional skills enabling participation is acceptable in childhood-onset HMD post-DBS. Further, preliminary efficacy to improve outcomes and proof of concept with CO-OP has been established in this population.

Classification of evidence

This study provides Class IV evidence that for children with HMD who had undergone DBS, CO-OP improves performance of personally relevant functional skills.

From the Complex Motor Disorders Service (H.G., J.-P.L.), Paediatric Neuroscience, Evelina London Children's Hospital, Guy's & St Thomas' NHS Foundation Trust; Department of Psychology (H.G., R.G.B.), Institute of Psychiatry, Psychology and Neurosciences, King's College London; South London and Maudsley NHS Foundation Trust (R.G.B.); School of Public Health (V.C.), Imperial Clinical Trials Unit, Imperial College London, UK; and Department of Occupational Science and Occupational Therapy (H.J.P.), University of Toronto, Canada.

Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Glossary

CO-OP = Cognitive Orientation to daily Occupational Performance Approach; **COPM** = Canadian Occupational Performance Measure; **CP** = cerebral palsy; **DBS** = deep brain stimulation; **HMD** = hyperkinetic movement disorders; **OLS** = ordinary least squares; **PQRS-I** = Performance Quality Rating Scale–individualized; **SCED** = single-case experimental design; **SCRIBE** = Single Case Reporting Guideline in Behavioural Interventions.

Rehabilitation and nonpharmacologic/surgical interventions for childhood-onset hyperkinetic movement disorders (HMD), including dystonia, are not well-established.¹ A 2016 consensus report concluded that current available treatment options for childhood dystonia provide limited benefit and urged new methodologies and interventions to be developed.²

Deep brain stimulation (DBS) is one of the most frequently reported among available pharmacologic and neurosurgical interventions. However, although effective in reducing the severity of dystonic motor symptoms (impairment) as assessed using the Burke-Fahn-Marsden Dystonia Rating Scale,³ the many reports fail to address day-to-day functional abilities important to children and their families.⁴ A recent pathway guideline for the treatment of dystonia (primarily in cerebral palsy [CP])⁵ advises on the basis of expert consensus opinion that occupational therapy, physiotherapy, and speech and language therapy should be a cornerstone of treatment interventions for dystonia. Dyskinetic CP is the largest group of childhood-onset HMD and refers to a group of disorders of posture and movement caused primarily by injury to the basal ganglia, thalamus, brainstem, or cerebellum, white matter injuries, or absence of radiologic injury.

However, there are currently no research studies investigating rehabilitation interventions in this group and the recommendations based on expert consensus are limited and should be interpreted and applied in clinical practice with caution.¹

The Cognitive Orientation to daily Occupational Performance Approach (CO-OP) is a task-orientated approach with the primary aim to improve performance in personally relevant daily activities.⁶ The strongest currently available evidence in neurologic conditions is for the use of CO-OP with stroke,^{7–12} with preliminary evidence that it is feasible and acceptable in spastic CP.^{13,14} No studies are available on CO-OP with childhood-onset HMD, or with childhood-onset HMD post DBS implant.

The primary objective of the study reported here was to explore the feasibility, acceptability, and therapeutic potential of CO-OP for children with HMD. As DBS remains the only nonlesional neurosurgical intervention addressing dystonia, the study focused on CO-OP as an adjunct to DBS. Single-case experimental design (SCED) (n-of-1 study) provided a suitable design to address such objectives, particularly in relatively rare and highly variable conditions such as childhood HMD.¹⁵ SCED is characterized by 2 components that contribute to its value

within outcome research: (1) there is an experimental manipulation of the independent variable while everything about the context except the independent variable is held constant and (2) there is a replication component demonstrating that the manipulation of the independent variable is reliably associated with dependent variable change.

The purpose of this article is to describe the results of a series of n-of-1 studies of CO-OP with replication across participants who each serve as their own baseline, to provide level 4 American Academy of Neurology evidence of efficacy.

Methods

The study evaluated CO-OP as an adjunct to DBS in children and young people with HMD. The full trial protocol is available¹⁶ and was implemented without changes. The Single Case Reporting Guideline in Behavioural Interventions (SCRIBE) guidelines were followed.¹⁵

Research question

Is there evidence for the potential efficacy of CO-OP to improve self-selected trained goals for children and young people with HMD?

Standard protocol approvals, registrations, and patient consents

The study was approved by the NHS Health Research Authority Oxford A Research Ethics Committee (14/SC/1159) and was registered with the ISRCTN Registry (ISRCTN57997252). Informed consent was obtained from all participants over 12 years of age (n = 8) and assent from younger children (n = 2). Written parent permission was obtained in all cases.

Participants

The study included children and young people with HMD who had previously undergone DBS. Participants were identified by the principal investigator (H.G.) and purposely sampled from the Complex Motor Disorders Service DBS database at Evelina London Children's Hospital, UK. Ten participants were recruited and were admitted to the study, sequentially. Following SCED methods, where 3–5 replications per variable are required, participants were selected to cover a range of HMD etiology, impairment severity, and DBS duration. To reach this number of replications across different variables, a total of 10 potential participants were approached and recruitment stopped once 10 participants were recruited. The inclusion criteria for this study are (1) diagnosis of pediatric

HMD other than neurodegenerative conditions; (2) sufficient receptive and expressive communication to follow simple instructions and engagement with treatment; (3) age 6–21 years; (4) Manual Ability Classification System levels I–IV; (5) emerging skills in self-care such as starting to want to get dressed, brushing own teeth, washing and dressing, making a sandwich, making a bed; (6) cognitive ability of 6 years of age or IQ above 70; (7) DBS electrodes in situ and without signs of infection; and (8) expression and evidence of willingness to participate. Full information about the eligibility criteria and recruitment procedure is outlined in the study protocol.¹⁶

Design

A multiple baseline n-of-1 design was used with multiple replications across individuals (n-of-1 trial with 9 replications). Outcomes were assessed several times: at baseline, during treatment, at end of treatment, and at 3-month follow-up. All participants selected 5 functional task-based goals that were important to them. Three were worked on in the CO-OP intervention sessions with the therapist (trained goals) and 2 goals were used to assess transfer (untrained goals). Participants chose which 3 goals to take forward to the intervention (trained goals) and the other 2 were untrained goals. These were not worked on in the sessions with the therapist.

Intervention

CO-OP is based on current theories of motor learning, which suggest that a person's ability to perform movement-based activities is a complex interaction of the person, the environment, and the task to be performed. The intervention comprised a maximum of ten 1-hour treatment sessions. CO-OP is based on a number of therapeutic principles including client-centered practice, a focus on person-chosen functional goals, the use of a meta-cognitive problem-solving strategy, guided discovery, and domain-specific strategies.

Prior to treatment, participants identified 5 goals with the aid of the Canadian Occupational Performance Measure (COPM).¹⁷ The total number of intervention sessions, the targeted goals for each session, and the rate of treatment (i.e., once or twice a week) was negotiated between the treating therapist and the participant. For further information about the intervention, see the study protocol.¹⁶ Treatment followed the CO-OP format published by the CO-OP developers.⁶

All of the intervention sessions were delivered in the participant's home by investigator H.G., an occupational therapist with 16 years experience at the start of the study, 8 years exclusively working with children and young people with HMD including using CO-OP. She was trained in the CO-OP approach through a 2-day workshop and 2 subsequent courses run by one of the CO-OP developers (investigator H.J.P.), who also supported her in the application of the Approach throughout the study and monitored treatment fidelity and adherence to the CO-OP protocol from video recordings.

Participants were not specifically instructed to practice the task at home. As per CO-OP protocol, homework was set up

by the occupational therapists. This may or may not have included practicing of the problem-solving strategies or the task itself.

Primary outcome

The primary outcome measure was the observer-rated Performance Quality Rating Scale–individualized (PQRS-i).¹⁸ This is a 10-point scale, with 1 representing client “can't do the task at all” and 10 representing client “does the task very well.” Performance criteria were operationalized a priori for each goal. Two trained independent assessors rated performance blinded to the sequential order of the video recording. Inter-rater reliability (intraclass correlation) was 0.947. Performance on each task was rated from a minimum of 3 video recordings at each of baseline, posttest, and follow-up performances. For evaluation during the treatment sessions, a sample of 18 recordings were used. For details on how the performance video clips for intervention were selected, refer to the study protocol.¹⁶

Analysis

Following SCRIBE guidelines, outcomes were analyzed using a set of parallel and complementary approaches: (1) visual analysis and description, (2) a range of quantitative statistical analyses, and (3) clinical significance of goal improvement.

- (1) Visual analysis: Visual graph analysis was used to evaluate changes in means, levels, trends, variability, latency, and consistency.^{19–21} PQRS-i data for all goals were graphed using Prism (GraphPad Software, La Jolla, CA) with separate data points in each phase (baseline, intervention, post, and 3-month follow-up). Repetitions within the same day of assessment are represented by interconnected points.
- (2) Quantitative statistical analysis of performance change: To guide the selection of quantitative methods, autocorrelations were calculated to examine serial dependency for the multiple assessments at baseline. Serial dependency was statistically calculated using lag-1 autocorrelation with the Durbin-Watson Test. An autocorrelation value of 2 indicates no autocorrelation; autocorrelation 0 to <2, positive; autocorrelation >2 to 4, negative with possible trend to baseline. Approximately two-thirds of goals showed autocorrelations. Based on these data, 3 different statistical analyses were employed as recommended by SCRIBE guidelines where autocorrelation is present: (a) difference in individual means and 95% confidence interval for overall change pre and post, and pre and 3-month follow-up (*t* test); (b) a regression approach initially fitting a naive linear regression model using ordinary least squares (OLS) for reference only. A generalized least squares approach to regression model was then fitted^{22,23}; and (c) effect size calculated using the nonoverlap index of Kendall Tau combining nonoverlap between phases with baseline trend control (Tau-U).²⁴ Change in PQRS-i over time was evaluated at the level of the individual for each of the 5 self-selected goals in turn.

- (3) Clinically significant change: A change of at least 2 points on the PQRS-i was used to indicate clinical significance in order to match other similar scales such as the COPM.²⁵ Difference between mean scores from pre and post and post to follow-up was calculated for each individual for each goal.

Data availability

Access to de-identified participant data may be requested by contacting the first author. For the purpose of replicating procedures, the study protocol is published, and the statistical analysis is available through the King's College London institutional repository.

Results

A total of 10 participants were recruited and consented. One participant (child 2) withdrew before baseline assessment. For completeness and to reflect the a priori recruitment strategy, details of this participant are included in the results tables. Table 1 provides demographic and clinical characteristics of all 10 participants. There were no changes to medication or DBS measures for any participant for the duration of their involvement in the study. Standard occupational therapy and physiotherapy interventions were not interrupted during the study. Only 2 participants had an allocated occupational therapist who was providing advice and consultation or equipment. Physiotherapy was provided for 5 participants and focused on gross motor skills development in 4 participants and stretching in 1 participant. Details of the self-selected CO-OP goals are shown in table 2.

- (a) Visual analysis: Results are presented graphically in the following order: (1) trained goals: baseline, treatment, posttreatment (acquisition), and 3-month follow-up

(maintenance); and (2) untrained goals: baseline and transfer phases (posttreatment and 3-month follow-up). The figure provides illustrative PQRS-i scores for the first participant ($n = 1$). The graphs for the 8-replication cases are presented in figures e-2–e-9 (doi.org/10.5061/dryad.5r06h3c). The visual data provide evidence on means, levels, trends, variability, latency, and consistency across the different phases of the study for each participant and for each individual goal (each point representing a repetition). Also shown is the OLS regression line and 95% confidence range.

For ease of representation, table 2 contains a summary of statistical and clinical significance, with tables 3 and 4 showing more detailed individual statistical measures and results.

- (b) Quantitative analysis of performance change: Differences between means in baseline and postintervention using t test supported the visual inspections and indicated that the majority of participants achieved significant improvement on the trained goals at posttest (18/24) and follow-up (23/27) (tables 2 and 3) (one participant was lost to assessment at postintervention, hence only 24 goals were evaluated at posttest). Three participants improved on all 3 trained goals, 4 participants improved on 2 goals, and 1 participant improved on a single trained goal. At follow-up, 6 participants improved on all 3 trained goals, 2 improved on 2 goals, and 1 showed change only on a single trained goal. For the untrained goals, 3 children improved on at least one of the untrained goals (5/18).

Baseline trend data were found in 12 out of the 45 goals assessed and therefore the use of Tau-U correction for baseline trend was used. All participants achieved at least one goal with moderate or large effect size. A large effect (≥ 0.93) ("very

Table 1 Demographic and clinical characteristics (n = 10)

Child	Age	Sex	Diagnosis	Etiology	Phenotype	DBS duration	GMFCS	MACS
1	9 y 8 mo	Male	Primary unknown	Idiopathic (primary)	Dystonia	3 y	I	II
2 ^a	8 y 8 mo	Female	DYT-11	Inherited (primary-plus)	Dystonia and myoclonus	2 y	I	II
3	17 y 4 mo	Female	CP post meningitis	Acquired (secondary)	Dystonia	1 y 2 mo	I	II
4	17 y 6 mo	Male	HIE CP	Acquired (secondary)	Dystonia and choreoathetosis	1 y 5 mo	II	III
5	15 y 2 mo	Male	Ex prem CP	Acquired (secondary)	Dystonia and choreoathetosis	4 y	IV	IV
6	13 y 11 mo	Female	HIE CP	Acquired (secondary)	Dystonia and choreoathetosis	6 mo	II	II
7	18 y 11 mo	Female	BHC	Inherited (primary)	Dystonia and myoclonus	1 mo	I	II
8	13 y 10 mo	Female	Kernicterus CP	Acquired (secondary)	Dystonia	1 y 2 mo	II	IV
9	13 y 6 mo	Male	Primary unknown	Idiopathic (primary-plus)	Dystonia and tremor	7 mo	I	III
10	12 y 3 mo	Female	Primary unknown	Idiopathic (primary-plus)	Dystonia and myoclonus	4 y	III	II

Abbreviations: BHC = benign hereditary chorea; CP = cerebral palsy; DBS = deep brain stimulation; Ex Prem = extreme prematurity; GMFCS = Gross Motor Function Classification System; HIE = hypoxic-ischemic encephalopathy; MACS = Manual Ability Classification System.

^a Patient 2 withdrew for personal reasons after initial recruitment.

Table 2 Significant and nonsignificant outcomes (mean change, effect size): Clinical significance for each child for each trained and untrained goal

Patient	Trained goals	t Test difference in means		Effect size (Tau-U)		CSC		Untrained goals	t Test difference in means		Effect size (Tau-U)		CSC	
		Pre-post	Pre, f-up	Pre-post	Pre, f-up	Pre-post	Pre, f-up		Pre-post	Pre, f-up	Pre-post	Pre, f-up	Pre-post	Pre, f-up
1	G1: Catching a tennis ball	✓	✓	✓	✓	✓	✓	G4: Bouncing a ball	✓	✓	✓	✓	✓	✓
	G2: Buttering and cutting toast	✓	✓	✓	✓	✓	✓	G5: Making a drink	✓	✓	✓	✓	✓	✓
	G3: Tying tie	✓	✓	✓	✓	✓	✓							
2	G1: Not set	NT	NT	NT	NT	NT	NT	G4: Not set	NT	NT	NT	NT	NT	NT
	G2: Not set	NT	NT	NT	NT	NT	NT	G5: Not set	NT	NT	NT	NT	NT	NT
	G3: Not set	NT	NT	NT	NT	NT	NT							
3	G1: Ponytail	✓	✓	✓	✓	✓	✓	G4: Cutting bagels in half	×	×	×	×	×	×
	G2: Shoelaces	✓	✓	✓	✓	✓	✓	G5: Peeling and cutting carrots	×	×	×	×	×	×
	G3: Painting nails on dystonic hand	×	×	×	×	×	×							
4	G1: Opening a pot of yogurt	×	×	✓	×	✓	✓	G4: Cutting with knife and fork	×	×	×	×	×	×
	G2: Carrying a bowl of cereal	✓	✓	✓	✓	✓	✓	G5: Making a drink	×	×	×	×	×	×
	G3: Handwriting	×	✓	×	✓	×	✓							
5	G1: Picking up remote control from floor	✓	✓	✓	✓	✓	✓	G4: Buttoning small buttons	×	×	×	×	×	×
	G2: Making a drink	×	×	×	×	×	×	G5: Putting on trousers	×	×	×	×	×	×
	G3: Doing a zipper	✓	×	✓	✓	✓	✓							
6	G1: Bicycle riding	✓	✓	✓	✓	✓	✓	G4: Using key to open door	×	×	×	×	×	×
	G2: Buttoning small buttons	✓	✓	✓	✓	✓	✓	G5: Painting nails	×	×	×	×	×	×
	G3: Eating ice cream	×	✓	×	×	✓	✓							
7	G1: Applying eyeliner	✓	✓	✓	✓	✓	✓	G4: Drinking	×	×	×	×	×	×

Continued

Table 2 Significant and nonsignificant outcomes (mean change, effect size): Clinical significance for each child for each trained and untrained goal (*continued*)

Patient	Trained goals	t Test difference in means		Effect size (Tau-U)		CSC		Untrained goals	t Test difference in means		Effect size (Tau-U)		CSC	
		Pre-post	Pre, f-up	Pre-post	Pre, f-up	Pre-post	Pre, f-up		Pre-post	Pre, f-up	Pre-post	Pre, f-up	Pre-post	Pre, f-up
8	G2: Turning bacon on the grill	✓	✓	×	×	✓	✓	G5: Doing pony tail	×	×	×	×	×	×
	G3: Carrying a hot drink and a plate	×	✓	×	✓	×	✓							
	G1: Brushing teeth	NT	✓	NT	✓	NT	✓	G4: Drinking	×	×	×	×	×	×
	G2: Making a chocolate spread sandwich	NT	✓	NT	✓	NT	✓	G5: Making a drink	×	×	×	×	×	×
9	G3: Putting a t-shirt on	NT	✓	NT	✓	NT	✓							
	G1: Cutting with knife and fork	✓	✓	✓	✓	✓	✓	G4: Drinking	✓	✓	✓	✓	✓	✓
	G2: Tying shoelaces	✓	✓	✓	✓	✓	✓	G5: Making a drink	✓	✓	✓	✓	✓	✓
	G3: Carrying a drink	✓	✓	✓	✓	✓	✓							
10	G1: Swimming	✓	✓	✓	✓	✓	✓	G4: Ponytail	✓	✓	✓	✓	✓	✓
	G2: Painting toenails	✓	✓	✓	✓	✓	✓	G5: Tying shoelaces	×	×	×	×	×	×
	G3: Cutting with knife and fork	✓	✓	✓	✓	✓	✓							

Abbreviations: CSC = clinically significant change; f-up = follow-up; G = goal; NT = not tested.

Figure Child 1: Results with ordinary least squares regression line superimposed

The figure indicates poor and relatively stable baseline performance for all 5 goals. During training of goals 1–3 (A–C), performance was highly variable, but showed overall improvement for goal 1 (A) and goal 3 (C), but less so for goal 2 (B). Posttreatment, all 3 goals showed improvement relative to baseline, although performance remained variable. Improvement tended to be maintained at follow-up. For the untrained goals, goals 4–5 (D, E), improvement was also observed at the end of the intervention and at follow-up indicating successful transfer of learned skill. The overall trend to improvement is further reflected by the slope of the regression line. B = baseline; F = follow-up; P = postintervention; PQRs = Performance Quality Rating Scale; tx = treatment.

effective intervention”) was obtained in 88% of participants postintervention and in 89% at follow-up in at least one goal. In total, the effect size was large for 62% of trained goals posttreatment and 55% at follow-up. For the remainder of trained goals (other than those showing large effect), moderate effects (0.66–0.92) (“effective intervention”) were obtained in 12% and 26% of trained goals at post and 3-month follow-up, respectively. Weak effects (≤ 0.65) were seen in 6 goals (25%) across 5 children at postintervention and 3 goals (11%) across 3 children at follow-up. Moderate negative effects (deterioration) were seen in 2 goals for 2 different children at follow-up. For untrained goals, large or moderate effect was seen in 5/16 (31%) goals posttreatment and 5/18 (28%) at follow-up. Table 4 summarizes results for effect size using nonoverlapping index, Tau-U.

- (c) Clinically significant change: All participants showed a positive change of at least 2 PQRs-i points (based on the difference between the phase means) on at least one goal, at end of treatment or at follow-up (tables 2 and 4).

Following intervention, 4 out of the 8 participants improved on 2 of their trained goals while the remainder improved on all trained goals. At follow-up, 7 out of the 9 participants improved for all trained goals (78%). For untrained goals, 3 children showed signs of transfer on at least one goal at post and 3-month follow-up.

Videos 1–3 show a self-selected goal of attempted riding of a 2-wheeled bicycle for 10 meters on a straight line at baseline (video 1), postintervention (video 2), and at 3 months follow-up (video 3).

Discussion

Current practice and guidelines for rehabilitation interventions with children and young people with HMD are based on consensus opinion in the absence of robust trial evidence. This study explored the potential of CO-OP with childhood-onset HMD and provide preliminary evidence of its feasibility and potential efficacy in advance of further clinical trials.

Table 3 Results including statistical *t* test analysis and changes in slope

Patient (GT)	AC (S/NS)	Baseline, mean (SD)	Post Rx, mean (SD)	Post, CSC	Follow-up, mean (SD)	Follow-up, CSC	Trend	t Test pre-post		t Test pre follow-up		Slope β (p value)
								Mean shift (95% CI)	p Value	Mean shift (95% CI)	p Value	
Trained goals												
1 (1)	2.169 (NS)	1.83 (0.41)	7.67 (1.51)	Yes	8.17 (1.33)	Yes	↑	−5.83 (−7.40, −4.26)	<0.001	−6.33 (−7.73, −4.94)	<0.001	0.792 (<0.001)
1 (2)	3.166 (negative AC)	1.17 (0.41)	7.17 (2.32)	Yes	7.33 (2.50)	Yes	↑	−6.00 (−8.43, −3.57)	0.001	−6.17 (−8.79, −3.54)	0.002	0.801 (<0.001)
1 (3)	2.883 (negative AC)	2.00 (0.71)	7.34 (2.31)	Yes	6.67 (1.37)	Yes	↑	−5.33 (−10.69, 0.021)	0.050	−4.67 (−6.15, −3.18)	<0.001	0.452 (0.27)
3 (1)	2.168 (NS)	1.00 (0.0)	9.67 (0.52)	Yes	7.00 (2.00)	Yes	↑	−8.67 (−9.21, −8.12)	<0.001	−6.00 (−10.97, −1.03)	0.035	0.729 (<0.001)
3 (2)	Constant variable	3.17 (1.17)	9.50 (0.84)	Yes	7.75 (1.50)	Yes	↑	−6.33 (−7.66, −5.01)	<0.001	−4.58 (−6.82, −2.35)	0.003	0.699 (<0.001)
3 (3)	Constant variable	5.00 (2.10)	4.83 (1.33)	No	2.75 (0.50)	Worse	↓	0.167 (−2.15, 2.48)	0.873	2.25 (0.05, 4.45)	0.046	−0.429 (0.059)
4 (1)	2.968 (negative AC)	4.33 (3.27)	8.00 (3.16)	Yes	7.33 (3.78)	Yes	↑	−3.67 (−7.51, 0.18)	0.060	−3.00 (−7.55, 1.55)	0.172	0.389 (0.033)
4 (2)	1.802 (NS)	3.33 (2.16)	7.83 (1.72)	Yes	9.00 (1.55)	Yes	↑	−4.50 (−7.03, −1.97)	0.003	−5.67 (−8.12, −3.21)	0.001	0.702 (<0.001)
4 (3)	1.884 (NS)	2.67 (1.51)	4.43 (1.90)	No	5.33 (1.03)	Yes	↑	−1.76 (−3.84, 0.32)	0.090	−2.67 (−4.36, −0.98)	0.006	0.538 (0.005)
5 (1)	2.088 (NS)	1.20 (0.45)	10.00 (0.0)	Yes	10.00 (0.00)	Yes	↑	−8.80 (−9.36, −8.24)	<0.001	−8.80 (−9.36, −8.24)	<0.001	0.783 (<0.001)
5 (2)	3.070 (negative AC)	4.67 (2.58)	5.00 (1.00)	No	3.33 (1.15)	No	NC	−0.33 (−3.18, 2.52)	0.790	1.33 (−1.62, 4.28)	0.321	−0.161 (0.582)
5 (3)	2.695 (negative AC)	1.33 (0.82)	9.00 (1.00)	Yes	5.33 (4.04)	Yes	↑	−7.67 (−9.65, −5.68)	0.001	−4.00 (−13.77, 5.77)	0.227	0.493 (0.032)
6 (1)	1.749 (NS)	2.00 (0.00)	9.17 (0.41)	Yes	10.00 (0.00)	Yes	↑	−7.17 (−7.60, −6.74)	<0.001	−8.00 (N/A)	<0.001	0.933 (<0.001)
6 (2)	1.719 (NS)	2.17 (2.86)	9.67 (0.82)	Yes	10.00 (0.00)	Yes	↑	−7.50 (−10.49, −4.51)	0.001	−7.83 (−10.83, −4.83)	0.001	0.862 (<0.001)
6 (3)	2.914 (negative AC)	6.83 (1.60)	8.67 (1.63)	Yes	9.00 (1.55)	Yes	↑	−1.83 (−3.91, 0.25)	0.078	−2.17 (−4.19, −0.14)	0.039	0.434 (0.24)
7 (1)	2.120 (NS)	4.50 (1.25)	8.17 (1.60)	Yes	9.17 (0.75)	Yes	↑	−3.67 (−5.35, −1.99)	0.001	−4.67 (−5.53, −3.80)	<0.001	0.695 (<0.001)
7 (2)	2.146 (NS)	3.03 (1.87)	6.5 (0.55)	Yes	6.5 (0.55)	Yes	↑	−3.46 (−4.33, −2.60)	<0.001	−3.46 (−4.33, −2.60)	<0.001	0.569 (<0.001)
7 (3)	1.733 (NS)	7.62 (2.12)	8.17 (1.33)	No	10.00 (0)	Yes	↑	−0.54 (−2.05, 0.97)	0.450	−2.38 (−3.27, −1.48)	<0.001	0.403 (0.015)
8 (1)	Constant variable	2.50 (0.84)	NT	NT	6.75 (0.50)	Yes	↑	NT	NT	−4.25 (−5.23, −3.27)	<0.001	0.786 (<0.001)
8 (2)	Constant variable	3.17 (1.83)	NT	NT	7.20 (1.10)	Yes	↑	NT	NT	−4.03 (−6.08, −1.98)	0.002	0.713 (0.003)
8 (3)	3.166 (negative AC)	1.67 (1.63)	NT	NT	8.80 (0.45)	Yes	↑	NT	NT	−7.13 (−8.84, −5.42)	<0.001	0.872 (<0.001)
9 (1)	1.799 (NS)	1.83 (0.41)	4.83 (1.60)	Yes	7.00 (1.00)	Yes	↑	−3.00 (−4.68, −1.32)	0.005	−5.17 (−7.42, −2.91)	0.008	0.603 (0.004)

Continued

Table 3 Results including statistical *t* test analysis and changes in slope (*continued*)

Patient (GT)	AC (S/NS)	Baseline, mean (SD)	Post Rx, mean (SD)	Post, CSC	Follow-up, mean (SD)	Follow-up, CSC	Trend	t Test pre-post		t Test pre follow-up		Slope β (p value)
								Mean shift (95% CI)	p Value	Mean shift (95% CI)	p Value	
9 (2)	1.815 (NS)	2.00 (0.00)	9.50 (0.55)	Yes	10.00 (0)	Yes	↑	-7.50 (-8.07, -6.93)	<0.001	SD is 0		0.870 (<0.001)
9 (3)	2.488 (NS)	2.17 (0.41)	6.17 (2.40)	Yes	5.00 (0.00)	Yes	↑	-4.00 (-6.51, -1.49)	0.009	-2.83 (03.26, -2.40)	<0.001	0.608 (0.004)
10 (1)	3.001 (negative AC)	1.00 (0.00)	8.38 (1.06)	Yes	9.75 (0.50)	Yes	↑	-7.38 (-8.26, -6.49)	<0.001	-8.75 (-9.55, -7.95)	<0.001	0.869 (<0.001)
10 (2)	2.591 (negative AC)	1.50 (0.55)	5.20 (1.30)	Yes	4.67 (1.15)	Yes	↑	-3.70 (-5.29, -2.11)	0.002	-3.17 (-5.71, -0.63)	0.031	0.532 (0.019)
10 (3)	1.668 (NS)	5.17 (1.83)	9.83 (0.41)	Yes	9.00 (1.55)	Yes	↑	-4.67 (-6.59, -2.75)	0.001	-3.83 (-6.03, -1.64)	0.003	0.702 (<0.001)

Patient (GUT)	AC (S/NS)	Baseline, mean (SD)	Post Rx, mean (SD)	Post, 2p	Follow-up, mean (SD)	Follow-up, 2p	Trend	t Test pre-post		t test Pre-F-up		Slope β (p value)
								Mean shift (95% CI)	p Value	Mean shift (95% CI)	p Value	
Untrained goals												
1 (4)	2.638 (negative AC)	1.33 (0.52)	5.11 (2.85)	Yes	5.00 (3.61)	Yes	↑	-3.78 (-5.99, -1.57)	0.004	-3.67 (-12.50, 5.16)	0.219	0.580 (0.12)
1 (5)	1.668 (NS)	4.00 (0.00)	8.17 (2.14)	Yes	8.33 (1.37)	Yes	↑	-4.17 (-6.41, -1.92)	0.005	-4.33 (-5.77, -2.90)	0.001	0.775 (<0.001)
3 (4)	Constant variable (NS?)	7.67 (1.03)	7.67 (2.25)	No	7.33 (1.15)	No	NC	0.00 (-2.39, 2.39)	1.00 (0)	0.33333 (-1.93, 2.60)	0.696	-0.59 (0.833)
3 (5)	2.169 (NS)	6.50 (2.12)	7.40 (2.07)	No	8.00 (2.92)	No	NC	-0.90 (-9.14, 7.34)	0.664	-1.50 (-8.25, 5.25)	0.511	0.235 (0.461)
4 (4)	2.551 (negative AC)	6.00 (2.76)	6.83 (2.48)	No	7.50 (2.43)	No	NC	-0.83 (-4.21, 2.55)	0.594	-1.50 (-4.85, 1.85)	0.341	0.252 (0.313)
4 (5)	3.007 (negative AC)	7.33 (2.66)	8.67 (1.63)	No	7.50 (1.87)	No	NC	-1.33 (-4.25, 1.59)	0.325	-0.17 (-3.17, 2.84)	0.903	0.089 (0.726)
5 (4)	3.334 (negative AC)	1.13 (0.35)	1.00 (0.00)	No	1.00 (0.00)	No	NC	0.13 (-0.17, 0.42)	0.351	0.13 (-0.17, 0.42)	0.351	-0.211 (0.455)
5 (5)	2.012 (NS)	1.00 (0.00)	1.00 (0.00)	No	1.00 (0.00)	No	NC	NT	NT	NT	NT	Constant variable
6 (4)	2.169 (NS)	8.17 (2.14)	8.33 (3.14)	No	9.67 (0.82)	No	↑	-0.17 (-3.69, 3.35)	0.917	-1.50 (-3.75, 0.75)	0.156	0.255 (0.307)
6 (5)	3.043 (negative AC)	5.17 (2.99)	4.17 (2.32)	No	5.67 (1.03)	No	NC	1.00 (-2.47, 4.47)	0.533	-0.50 (-3.64, 2.64)	0.712	0.041 (0.871)
7 (4)	1.824 (NS)	6.29 (0.855)	6.5 (1.22)	No	7 (0)	No	NC	-0.21 (-1.50, 1.07)	0.701	-0.71 (-1.10, -0.33)	0.001	0.296 (0.095)
7 (5)	2.035 (NS)	7.48 (2.08)	8 (1.55)	No	8.17 (2.04)	No	NC	-0.52 (-2.18, 1.15)	0.500	-0.68 (-2.83, 1.47)	0.478	0.138 (0.376)
8 (4)	2.8280 (negative AC)	2.83 (2.23)	NT	NT	5.83 (3.37)	Yes	↑	NT	NT	-3.00 (-6.75, 0.75)	0.104	0.498 (0.099)
8 (5)	2.6380 (negative AC)	4.33 (2.25)	NT	NT	7.00 (2.10)	Yes	↑	NT	NT	-2.67 (-5.47, 0.13)	0.060	0.557 (0.060)

Continued

Table 3 Results including statistical *t* test analysis and changes in slope (continued)

Patient (GUT)	AC (S/NS)	Baseline, mean (SD)	Post Rx, mean (SD)	Post, 2p	Follow-up, mean (SD)	Follow-up, 2p	t Test pre-post		t test Pre-F-up	
							Trend	Mean shift (95% CI)	p Value	Slope β (p value)
9 (4)	2.5510 (negative AC)	1.83 (1.33)	7.33 (2.34)	Yes	7.33 (2.31)	Yes	↑	-5.50 (-8.04, -2.96)	0.001	-5.5 (-10.40, -0.60) 0.038
9 (5)	3.0070 (negative AC)	2.67 (1.86)	5.50 (1.64)	Yes	6.00 (1.00)	Yes	↑	-2.83 (-5.10, -0.57)	0.019	-3.33 (-5.61, -0.55) 0.011
10 (4)	2.1690 (NS)	1.83 (0.41)	5.33 (1.86)	Yes	3.67 (0.58)	No	↑	-3.50 (-5.45, -1.55)	0.005	-1.83 (-3.01, -0.66) 0.015
10 (5)	3.0430 (negative AC)	2.50 (2.26)	2.00 (0.63)	No	2.00 (0.00)	No	↓	0.50 (-1.86, 2.86)	0.621	0.50 (-1.87, 2.87) 0.611

Abbreviations: ↑ = ascendant; ↓ = descendant; AC = autocorrelation; CI = confidence interval; CSC = clinically significance change; GT = goal trained; GUT = goal untrained; N/A = not applicable; NC = no change; NS = not significant; NT = not tested; S = significant; 2p = 2 point change. Participant number is shown with goal number in parentheses.

Three major findings should be highlighted. First, CO-OP was acceptable and feasible to implement with a range of children and young people with HMD and their families. Young people were willing to participate, with all 10 participants approached agreeing to take part. All participants completing treatment were followed up and there were no further dropouts once the assessment and intervention had started.

Second, skill improvement following CO-OP was seen in all children and young people who participated in the study, independent of their baseline characteristics and with a broad range of goals. The majority (18/24; 75%) of goals addressed in therapy improved by the end of the CO-OP intervention; at 3-month follow-up, gains were found not only to have been maintained but also continued to improve in some cases (22/27; 81%). This was achieved with a relatively low dose of therapy intervention (less than 10 hours). While all children achieved at least one goal, some goals were not achieved, potentially linked to the varying difficulty of the self-selected goals. It is important to note that a considerable number of goals related to feeding, which are goals accessible on a daily basis. It will be important in future work to explore the relationship between child or goal characteristics and goal achievement. This suggests that outcome may relate more to the chosen goal itself and baseline score. Goal improvement was maintained for all participants at the 3-month follow-up, except for one goal for one participant that did not achieve clinical significance. Improvement for one participant did not achieve significance at the postintervention review but the goal had improved at the 3-month follow-up.

The third major finding is that skill transfer was noted, albeit only in 22% of untrained goals at follow-up. Such transfer is one of the main objectives of all rehabilitation approaches and is explicit in CO-OP, which focuses on generalizable strategies while supporting specific skill acquisition. That some transfer was observed provides valuable proof of concept of the approach in children and young people with HMD following DBS. However, the low rate of transfer found here, relative to studies of CO-OP in other populations, needs further investigation. A number of potential explanations can be explored. In some instances, the untrained goals tended to have higher baseline scores (i.e., were performed better) and therefore reduced room for improvement. This might suggest that participants choose those goals that were more pressing for them. The relationship between the trained and untrained goal needs to be considered; for example, in some instances trained goals were more similar to each other, perhaps offering less of an opportunity to model a more difficult transfer. In a similar vein, in some instances the trained goals were more similar to the untrained goals, requiring a less difficult transfer. This exploration of the relationship between goals from a transfer perspective will be important in future work. For example, participant 9 chose a trained goal of carrying a drink and had 2 untrained goals for therapy that also included handling liquids. Therefore, the transfer might be expected to

Table 4 Effect size calculation for trained and untrained goals

Participant (GT)	Baseline to post			Baseline to follow-up		
	Tau-U value	p Value (90% CI)	Effect size	Tau-U value	p Value (90% CI)	Effect size
Trained goals						
1 (1)	1.00	0.004 (0.43, 1)	Strong	1.00	0.004 (0.43, 1)	Strong
1 (2)	1.00	0.004 (0.43, 1)	Strong	1.00	0.004 (0.43, 1)	Strong
1 (3)	1.00	0.03 (0.264, 1)	Strong	1.00	0.006 (0.4, 1)	Strong
3 (1)	1.00	0.004 (0.43, 1)	Strong	1.00	0.02 (0.29, 1)	Strong
3 (2)	1.00	0.004 (0.43, 1)	Strong	1.00	0.01 (0.36, 1)	Moderate
3 (3)	0.08	0.81 (−0.49, 0.65)	Weak	−0.88	0.03 (−1, −0.23)	Moderate (worse)
4 (1) ^a	0.65	0.045 (0.12, 1)	Moderate	0.64	0.07 (0.07, 1)	Weak
4 (2)	0.89	0.01 (0.32, 1)	Moderate	0.94	0.01 (0.37, 1)	Strong
4 (3)	0.60	0.07 (0.047, 1)	Weak	0.92	0.01 (0.346, 1)	Strong
5 (1)	1.00	0.03 (0.26, 1)	Strong	1.00	0.03 (0.26, 1)	Strong
5 (2) ^a	−0.5	0.25 (−1, 0.21)	Weak worse	−0.72	0.09 (−1, −0.01)	Moderate worse
5 (3)	1.00	0.02 (0.29, 1)	Strong	0.89	0.04 (0.18, 1)	Moderate
6 (1)	1.00	0.004 (0.43, 1)	Strong	1.00	0.004 (0.43, 1)	Strong
6 (2)	0.97	0.005 (0.40, 1)	Strong	1.00	0.004 (0.43, 1)	Strong
6 (3)	0.58	0.09 (0.01, 1)	Weak	0.61	0.08 (0.04, 1)	Weak
7 (1)	0.95	0.0004 (0.51, 1)	Strong	1.00	0.0002 (0.56, 1)	Strong
7 (2) ^a	0.40	0.13 (−0.03, 0.83)	Weak	0.40	0.13 (−0.03, 0.83)	Weak
7 (3)	0.09	0.74 (−0.35, 0.53)	Weak	0.75	0.005 (0.31, 1)	Moderate
8 (1) ^a	NT	NT	NT	0.71	0.07 (0.07, 1)	Moderate
8 (2) ^a	NT	NT	NT	0.73	0.0446 (0.13, 1)	Moderate
8 (3)	NT	NT	NT	1.00	0.0062 (0.40, 1)	Strong
9 (1) ^a	0.86	0.01 (0.29, 1)	Moderate	0.72	0.09 (0.01, 1)	Moderate
9 (2)	1.00	0.0039 (0.43, 1)	Strong	1.00	0.02 (0.29, 1)	Strong
9 (3)	1.00	0.0039 (0.43, 1)	Strong	1.00	0.02 (0.30, 1)	Strong
10 (1)	1.00	0.0019 (0.47, 1)	Strong	1.00	0.01 (0.36, 1)	Strong
10 (2)	1.00	0.006 (0.40, 1)	Strong	1.00	0.02 (0.29, 1)	Strong
10 (3)	1.00	0.0039 (0.43, 1)	Strong	0.89	0.01 (0.32, 1)	Moderate
Untrained goals						
Participant (GUT)	Tau-U baseline to post			Tau-U baseline to f-up		
	Tau-U value	p Value (90% CI)	Effect size	Tau-U value	p Value (90% CI)	Effect size
1 (4)	1.00	0.004 (0.43, 1)	Strong	1.00	0.004 (0.43, 1)	Strong
1 (5)	1.00	0.004 (0.43, 1)	Strong	1.00	0.004 (0.43, 1)	Strong
3 (4) ^a	−0.19	0.58 (−0.77, 0.38)	Weak	−0.61	0.16 (−1, 0.10)	Weak
3 (5)	0.3	0.56 (−0.55, 1)	Weak	0.5	0.33 (−0.35, 1)	Weak
4 (4) ^a	0.14	0.69 (−0.432, 0.710)	Weak	−0.19	0.58 (−0.77, 0.38)	Weak
4 (5)	0.22	0.52 (−0.35, 0.79)	Weak	0.36	0.30 (−0.21, 0.93)	Weak

Continued

Table 4 Effect size calculation for trained and untrained goals (*continued*)

Participant (GUT)	Tau-U baseline to post			Tau-U baseline to f-up		
	Tau-U value	p Value (90% CI)	Effect size	Tau-U value	p Value (90% CI)	Effect size
5 (4)	0	1 (−0.78, 0.78)	No change	0	1 (−0.78, 0.78)	No change
5 (5)	0	1 (−0.78, 0.78)	No change	0	1 (−0.78, 0.78)	No change
6 (4)	0.08	0.81 (−0.49, 0.65)	Weak	0.42	0.23 (−0.15, 0.99)	Weak
6 (5) ^a	−0.39	0.26 (−0.96, 0.18)	Weak-worse	−0.14	0.69 (−0.71, 0.43)	Weak negative
7 (4)	0.23	0.3977 (−0.22, 0.68)	Weak	0.48	0.08 (0.03, 0.92)	Weak
7 (5) ^a	−0.54	0.04 (−0.97, −0.11)	Weak worse	−0.46	0.08 (−0.89, −0.03)	Weak
8 (4)	NT	NT	NT	0.56	0.11 (−0.015, 1)	Weak
8 (5) ^a	NT	NT	NT	0.47	0.17 (−0.099, 1)	Weak
9 (4)	1.00	0.004 (0.43, 1)	Strong	1.00	0.02 (0.29, 1)	Strong
9 (5) ^a	0.56	0.11 (−0.015, 1)	Moderate	0.67	0.12 (−0.04, 1)	Moderate
10 (4)	1.00	0.0039 (0.43, 1)	Strong	1.00	0.02 (0.29, 1)	Strong
10 (5)	0.11	0.75 (−0.46, 0.68)	Weak	0.17	0.74 (−0.66, 0.99)	Weak

Abbreviations: CI = confidence interval; GT = goal trained; GUT = goal untrained; NT = not tested.

^a Baseline trend data considered for Tau-U analysis.

be high, as was observed. In contrast, participant 6 chose bike riding as one of the worked goals in therapy, and painting her fingernails and opening the door with a key as untrained goals. In this instance, little transfer was observed. Further analysis of transfer across a wider number of participants would be beneficial as well as finding a way to more accurately assess specific rather than general skill transfer.

This study used a single case experimental design rather than more traditional group comparison methodology. SCED offers a number of strengths applied to the rehabilitation arena in populations such as childhood HMD. With the heterogeneity that characterizes this group of children and young people (figures e-2–e-9; doi.org/10.5061/dryad.5r06h3c), the multiple baseline n-of-1 methodology allows a systematic way of testing the effect of interventions such as CO-OP on a within-subject basis. It enables researchers to economically but robustly trial new interventions where there is no current evidence (proof-of-concept) and provides a better understanding of the nature, size, and generalizability (within that person) of any effects of the intervention.

As with any study, there are limitations that warrant mentioning. Only one occupational therapist implemented the CO-OP and there is a risk of therapist effect that needs to be considered independent of the intervention itself. However, to improve generalizability of the findings, the research design included up to 3–5 replications for each different variable to further understand the efficacy of the intervention with each separate variable. Finally, the number of treatment sessions was based on the standard format for CO-OP based on other

clinical conditions. Although seemingly sufficient for learning and retention of the trained goals in HMD, transfer in this group may require a longer intervention period. Despite the above limitations, the presented results are promising as CO-OP and indeed cognition provide us with an evidence-based successful management approach for children and young people with HMD.

Replication across CO-OP trained therapists using the same methodology is warranted, as is investigation of the potential of CO-OP for children who have not had or who are not suitable for DBS or other medical interventions. Further exploration of baseline characteristics would help us with patient selection and would allow refinement of the intervention. Finally, in addition to testing efficacy, further research is needed to understand the most important “active ingredients” of the intervention that enable acquisition and transfer of skills in this population.

Current rehabilitation in childhood-onset dystonia, including dyskinetic CP, are based on outcomes from studies with other populations such as spastic CP¹ and typically motor-based interventions with children with unilateral involvement. Interventions for children and young people with bilateral involvement, and particularly dyskinetic CP, still have to be developed. This trial is the first attempt to systematically measure a rehabilitation intervention for children and young people with HMD including dystonia. This study shows that CO-OP is a feasible and acceptable approach to rehabilitation following DBS for children and young people with HMD and can achieve meaningful improvements for personalized goals.

In this trial, a cognitive approach, CO-OP, when added to deep brain stimulation, improved self-selected functional goals in a heterogeneous group of participants with childhood-onset hyperkinetic movement disorders. This is the only rehabilitation trial available to date and shows proof-of-concept and preliminary efficacy. The methodology used allows the systematic evaluation of rehabilitation interventions for populations with high heterogeneity and variability in performance.

DBS is an effective but invasive and expensive procedure for the management of childhood-onset hyperkinetic movement disorders. The use of CO-OP as an adjunct rehabilitation intervention might be a useful approach to augment the benefits of DBS more specifically in children and young people who have never previously been able to perform certain desirable functions, but confirmation and extension to other health care settings to deliver this rehabilitation intervention are needed.

Author contributions

Ms. Gimeno: research study conception, organization, and execution; writing of the first draft. Dr. Brown: research study conception; manuscript preparation, review, and critique. Dr. Lin: research study conception; manuscript preparation, review, and critique. Dr. Cornelius: research study conception; manuscript preparation, review, and critique. Dr. Polatajko: research study conception; manuscript preparation, review, and critique.

Acknowledgment

The authors thank the children, young people, and their families who participated in the study; and the blind raters, occupational therapists, Laura Ainaga, and Emily Fleischfresser.

Study funding

Hortensia Gimeno is funded by a National Institute for Health Research (NIHR/HEE) Clinical Doctoral Research Fellowship (CDRF-2013-04-039). This article represents independent research funded in part by the NIHR (H.G.) and the NIHR Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London (R.G.B.). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, or the Department of Health and Social Care.

Disclosure

The authors report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

Publication history

Received by *Neurology* December 10, 2017. Accepted in final form November 6, 2018.

References

- Gimeno H, Lin JP. The International Classification of Functioning (ICF) to evaluate deep brain stimulation neuromodulation in childhood dystonia-hyperkinesia informs: future clinical & research priorities in a multidisciplinary model of care. *Eur J Paediatr Neurol* 2017;21:147–167.
- Koy A, Lin JP, Sanger TD, Marks WA, Mink JW, Timmermann L. Advances in management of movement disorders in children. *Lancet Neurol* 2016;15:719–735.
- Burke RE, Fahn S, Marsden CD, Bressman SB, Moskowitz C, Friedman J. Validity and reliability of a rating scale for the primary torsion dystonias. *Neurology* 1985;35:73–77.
- Lumsden DE, Gimeno H, Tustin K, Kaminska M, Lin JP. Interventional studies in childhood dystonia do not address the concerns of children and their carers. *Eur J Paediatr Neurol* 2015;19:327–336.
- AACPDM. Dystonia Care Pathways. 2016. Available at: <https://www.aacpdm.org/publications/care-pathways/dystonia>. Accessed August 17, 2017.
- Polatajko H, Mandich A. Enabling Occupation in Children: The Cognitive Orientation to Daily Occupational Performance (CO-OP) Approach. Ottawa: CAOT Publications; 2004.
- McEwen SE, Donald M, Dawson D, et al. A multi-faceted knowledge translation approach to support persons with stroke and cognitive impairment: evaluation protocol. *Implement Sci* 2015;10:157.
- McEwen S, Polatajko H, Baum C, et al. Combined cognitive-strategy and task-specific training improve transfer to untrained activities in subacute stroke: an exploratory randomized controlled trial. *Neurorehabil Neural Repair* 2015;29:526–536.
- Polatajko HJ, McEwen SE, Ryan JD, Baum CM. Pilot randomized controlled trial investigating cognitive strategy use to improve goal performance after stroke. *Am J Occup Ther* 2011;66:104–109.
- McEwen SE, Polatajko HJ, Huijbregts MP, Ryan JD. Inter-task transfer of meaningful, functional skills following a cognitive-based treatment: results of three multiple baseline design experiments in adults with chronic stroke. *Neuropsychol Rehabil* 2010;20:541–561.
- McEwen SE, Polatajko HJ, Davis JA, Huijbregts M, Ryan JD. “There’s a real plan here, and I am responsible for that plan”: participant experiences with a novel cognitive-based treatment approach for adults living with chronic stroke. *Disabil Rehabil* 2010;32:540–550.
- McEwen SE, Polatajko HJ, Huijbregts MP, Ryan JD. Exploring a cognitive-based treatment approach to improve motor-based skill performance in chronic stroke: Results of three single case experiments. *Brain Inj* 2009;23:1041–1053.
- Cameron D, Craig T, Edwards B, Missiuna C, Schweltnus H, Polatajko HJ. Cognitive Orientation to daily Occupational Performance (CO-OP): a new approach for children with cerebral palsy. *Phys Occup Ther Pediatr* 2017;37:183–198.
- Jackman M, Novak I, Lannin N, Froude E. Parents’ experience of undertaking an intensive Cognitive Orientation to daily Occupational Performance (CO-OP) group for children with cerebral palsy. *Disabil Rehabil* 2017;39:1018–1024.
- Tate RL, Perdices M, Rosenkoetter U, et al. The Single-case Reporting Guideline in Behavioural Interventions (SCRIBE) 2016: explanation and elaboration. *Arch Sci Psychol* 2016;4:10–31.
- Gimeno H, Polatajko HJ, Cornelius V, Lin JP, Brown G. Protocol for N-of-1 trials proof of concept for rehabilitation of childhood-onset dystonia: study 1: protocole des essais de validation à effetif unique pour la réadaptation de la dystonie débutant dans l'enfance: étude 1. *Can J Occup Ther* 2018;85:242–254.
- Law M, Baptiste S, McColl MA, Opzoozer A, Polatajko H, Pollock N. The Canadian Occupational Performance Measure: an outcome measure for occupational therapy. *Can J Occup Ther* 1990;57:82–87.
- Thornton J, Farber J, Gimeno H, Polatajko H. Does it Measure up: Examining the Performance Quality Rating Scale. Nepean, Canada: Canadian Association of Occupational Therapists; 2016.
- Kratochwill TR, Levin JR. Enhancing the scientific credibility of single-case intervention research: randomization to the rescue. *Psychol Methods* 2010;15:124–144.
- Nourbakhsh R, Ottenbacher KJ. The statistical analysis of single-subject data: a comparative examination. *Phys Ther* 1994;74:768–776.
- Kazdin AE. Single-case Research Designs: Methods for Clinical and Applied Settings, 2nd ed. New York: Oxford University Press; 2011.
- Swaminathan H, Rogers HJ, Horner RH, Sugai G, Smolkowski K. Regression models and effect size measures for single case designs. *Neuropsychol Rehabil* 2014;24:554–571.
- Maggin DM, Swaminathan H, Rogers HJ, O’Keeffe BV, Sugai G, Horner RH. A generalized least squares regression approach for computing effect sizes in single-case research: application examples. *J Sch Psychol* 2011;49:301–321.
- Parker RI, Vannest KJ, Davis JL, Sauber SB. Combining nonoverlap and trend for single-case research: Tau-U. *Behav Ther* 2011;42:284–299.
- Law M, Baptiste S, McColl MA, Opzoozer A, Polatajko H, Pollock N. Canadian Occupational Performance Measure, 5th ed. Ottawa: CAOT Publications ACE; 2014.