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Changes in diffusion tensor tractographic findings associated with constraint-induced movement therapy in young children with cerebral palsy

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HIGHLIGHTS

- We showed that constraint-induced movement therapy (CIMT) is an effective treatment in young children with unilateral cerebral palsy.
- CIMT might lead to a change in the corticospinal tract properties in young children with cerebral palsy.
- Young developing human brains might have the potential to change their neural properties in response to external stimulation such as CIMT.

ABSTRACT

Objective: The objective of the study was to determine whether constraint-induced movement therapy (CIMT) could lead to changes in diffusion tensor tractography (DTT) associated with clinical improvement in young children with unilateral cerebral palsy (CP).
Methods: A standardized pediatric CIMT protocol (4 weeks, 120 h of constraint) was used on 10 children with unilateral CP who were younger than 5 years. DTT was performed in five participants before and after the intervention. Clinical outcome was measured by using the Pediatric Motor Activity Log (PMAL), Quality of Upper Extremity Skills Test (QUEST), and self-care domain of the Pediatric Evaluation of Disability Inventory.
Results: In two patients, the affected corticospinal tract (CST) visible on pretreatment DTT became more prominent on posttreatment DTT. In one patient, the affected CST was not visible on pretreatment DTT, but was visible on posttreatment DTT. All the clinical outcomes significantly improved in the CIMT group compared with the control group. Changes in the PMAL how often scale (PMAL-HO) score significantly differed between the CIMT and control groups.
Conclusions: Changes in the properties of the affected CST on DTT were accompanied with improved arm function after CIMT in the children with CP.
Significance: CIMT might lead to CST reorganization in young children with CP.

1. Introduction

Constraint-induced movement therapy (CIMT) involves the application of constraint applied to the unimpaired upper limb coupled with intensive training of unimanual skills in the hemiplegic arm (Hoare et al., 2007). CIMT has been studied extensively and

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found to be effective in the treatment of adult hemiparetic stroke (Sirtori et al., 2009). Several randomized clinical trials performed on children with cerebral palsy (CP) also demonstrated immediate gain in the frequency of use and improved movement efficacy of the impaired upper limb (Deppe et al., 2013; Hoare et al., 2007; Rostami and Malamiri, 2012). The intervention duration has varied between studies, ranging from 60 to 120 h, delivered either intensively for up to 6 h per day for 10–21 days or following a schedule of 2–3 h per day over a 2-month period (Hoare et al., 2007).

Known mechanisms considered responsible for the increased use of the more affected extremity as a result of CIMT in children with CP include overcoming developmental disregard and inducing use-dependent cortical reorganization (Sutcliffe et al., 2009). Several case series have detected cortical changes after cerebral infarction in adult stroke patients, by using functional magnetic resonance imaging (fMRI) and transcranial magnetic stimulation (TMS) (Park et al., 2004; Sheng and Lin, 2009; Szaflarski et al., 2006). Sutcliffe et al. (2007, 2009) reported clinical improvement and a shift in the laterality index from the ipsilateral to contralateral hemisphere after modified CIMT(continuous casting and 1 h of occupational therapy for 3 weeks) in children with hemiplegic CP. Juenger et al. (2007) reported that a 12-day CIMT (wearing a glove and sling for 10 h and performing 2 h of occupational therapy) induced changes in cortical activation in 10 patients with congenital hemiparesis. The participants of the study by Juenger et al. were relatively older (age: range; 10–30 years; median, 14 years), and they all had cortical–subcortical infarction in the middle cerebral artery territory acquired during the late third trimester of pregnancy or perinatally.

The diffusion tensor imaging (DTI) technique has allowed the evaluation of microstructural conditions of white matter tracts by virtue of its ability to visualize water diffusion characteristics (Basser et al., 1994). Meanwhile, diffusion tensor tractography (DTT), derived from DTI, can provide three-dimensional (3D) visualization of neural tracts, which is not possible in conventional MRI (Melhem et al., 2002). Recent advancements in DTI technology have facilitated the detailed assessment of the corticospinal tract (CST) status, and several previous studies have shown that DTT is useful for evaluating CST and somatosensory tract (SST) lesions in patients with CP (Chang et al., 2012; Cho et al., 2013; Hoon et al., 2002; Rha et al., 2012; Son et al., 2007; Trivedi et al., 2010; Yoshida et al., 2010). Furthermore, several reports showed significant increments of fractional anisotropy (FA) value in the CST and SST after long-term physiotherapy with medical intervention (Chaturvedi et al., 2013; Min et al., 2013). However, to the best of our knowledge, changes in DTT after short-term rehabilitative intervention such as CIMT in children with CP have not been reported in the medical literature.

We hypothesized that purposeful and intensive therapeutic exercise such as CIMT could induce use-dependent reorganization of the injured developing brain and result in changes in CST properties on DTT in children with CP. The purpose of this study was to determine whether 4 weeks of CIMT (6 h of constraint and 2 h of occupational therapy for a total of 120 h) could lead to CST reorganization associated with clinical improvement in young children with unilateral CP.

2. Methods

2.1. Patients

This study was approved by the institutional review board of the Samsung Medical Center. Informed consent was provided by parents or guardians before enrollment.

A total of 19 children younger than 5 years (age: mean, 36.9 ± 12.4 months; range, 18–60 months) with unilateral CP and gross motor function classification system level I or II were included in this study (Table 1). The exclusion criteria were as follows: (1) severe intellectual disability preventing participation in therapy, (2) botulinum toxin injection in the upper extremity during the past 6 months, (3) previous orthopedic surgery on the affected upper extremity, (4) epilepsy, (5) long-term use of medication, and (6) contraindication to MRI (for children who were undergoing MRI only). Unlike the study by Juenger et al. (2007), we did not exclude patients with brain malformations or periventricular leukomalacia. This study was a nonrandomized controlled trial. The children were allocated to either of the two treatment arms, namely the CIMT (10 children) and control groups (nine children) in an alternative way. DTI and conventional MRI were obtained from the five children in the CIMT group before and after the intervention, whose parents agreed on MRI studies.

2.2. Constraint-induced movement therapy

An occupational therapist applied a standardized pediatric CIMT protocol on 10 children in the CIMT group. The participants wore individually tailored plastic long-arm bivalved casts on the nonparetic arm for 6 h per day, 5 days per week for 4 consecutive weeks (total, 120 h), which limit all movements of the elbow, hand, and fingers. Occupational and physical therapists provided 2 h of therapy per day for 4 weeks. During the immobilization, concentrated, repetitive training of the affected upper arm was performed by using a technique to shape motor behavior following Taub's protocol (Morris et al., 2006). Nine children in the control group received 2 h of conventional occupational therapy per week for 4 weeks.

2.3. Clinical outcome measure

Evaluators were blinded to the treatment administered to the patients, and the patients' parents completed the Pediatric Motor Activity Log (PMAL), the Quality of Upper Extremity Skills Test (QUEST), and self-care domain of the Pediatric Evaluation of Disability Inventory pretreatment and posttreatment.

Table 1
Patients' demographic data.

	No.	Age (months)	Sex	GA (weeks)	Birth weight (g)	Affected arm
CIMT group	Case 1*	46	M	24	694	L
	Case 2*	34	M	39	3400	R
	Case 3*	35	M	40	3510	R
	Case 4*	36	M	36	2910	R
	Case 5*	33	F	29	1290	R
	Case 6	47	F	39	3080	R
	Case 7	34	M	38	3380	R
	Case 8	49	M	26	985	R
	Case 9	20	M	40	3100	R
	Case 10	39	F	40	3170	R
Control group	Case 1	19	M	40	3120	R
	Case 2	60	M	37	3060	R
	Case 3	25	M	30	1090	R
	Case 4	37	M	26	942	L
	Case 5	53	M	39	3890	R
	Case 6	56	F	29	1090	R
	Case 7	34	M	39	3150	L
	Case 8	26	M	30	1960	L
	Case 9	18	M	39	2300	L

GA, Gestational age; CIMT, constraint-induced movement therapy.
* Patients who participated in the imaging study.