Constraint-Induced Movement Therapy in Parkinson's Disease

Constraint-induced movement therapy (CIMT), or forced limb use, is a rehabilitation technique that restricts movement of an unaffected upper extremity to force use of a paretic limb. CIMT has been shown to induce cortical reorganization and functional improvement in patients with stroke,[1] as well as those with focal hand dystonia.[2–4]

Parkinson's disease (PD) is managed with pharmacotherapy and adjunctive physical therapy. Initial work with 6-hydroxydopamine-lesioned rats hinted that CIMT may be beneficial in PD, and suggested that function may be improved via sparing of striatal dopamine, its metabolites, and the expression of the monoamine transporter.[5,6] To date, no systematic clinical trials have investigated the effects of CIMT in PD patients.

We now report the results of an open-label nonrandomized treatment trial of CIMT in mild-to-moderate PD. The effects of CIMT were assessed with the Unified Parkinson's Disease Rating Scale (UPDRS), patient and evaluator clinical global impression (CGI) of disease severity, and a motor function assessment (MFA) test of upper limb function. The MFA test was based on previous work[7,8] and examined the kinematics of discrete and rhythmical flexion/extension movements of the elbow and wrist. We hypothesized that CIMT of the less-affected arm in PD would improve function of the more severely affected unrestrained arm. The study was approved by the Institutional Review Board of Fairview-University Medical Center, Minneapolis, Minnesota.

Six PD patients, Hoehn and Yahr stage II to III, all right-handed with right-sided symptom onset, were enrolled. Patients were excluded if they had atypical parkinsonism, dementia, clinically significant depression or other psychiatric diagnoses, significant medical illness that might interfere with study participation, or an inability to adhere to the study protocol.

The study followed a nonrandomized, repeated-measures, clinical open-label pilot study design with multiple baseline measurements. Subjects came in for the first baseline assessments within 10 days before the start of the CIMT sessions (for a standard history and neurological examination, Mini-Mental status examination, UPDRS, CGI, and kinematic MFA of the upper extremities). MFAs were conducted with a custom-made manipulandum that allows flexion and extension of the wrist (see Fig. 1). Each arm was tested in an aiming task (35 flexion or extension) and a task of synchronizing wrist movement to a distinct tone at two frequencies (2.5 and 4 Hz). Reaction time, movement time, peak velocity, and frequency error (mean difference between produced and required frequency in the synchronization task) were calculated based on the recorded time-position data. Patients refrained from taking antiparkinsonian medications for 12 hours before this assessment (i.e., *off* assessment). The second visit (baseline 2) included UPDRS, CGI, and MFA measurements in the *off* state, and occurred within 2 days before initiating CIMT.

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Therapy sessions ran for 3 hours, 5 days a week, for 2 consecutive weeks. During the intervening weekend, patients were asked to wear their restraint mitten but did not attend therapy sessions. Once therapy commenced and until post-therapy assessments, subjects were asked to wear their mitten for a total of 10 hours per day or for 90% of their waking hours. CIMT was conducted based on shaping therapy, as has been used in previous studies.[1,9] *Off* follow-up assessments were carried out within 2 days after the completion of the 2 weeks of CIMT therapy.

Within subjects, pre- to post-CIMT comparisons of mean values (over trials) were computed. To detect changes between baseline and posttest performance, difference scores were computed and entered into univariate analysis of variance. Correlation analyses were also conducted to determine the strength of the association between baseline motor function and behavioral improvements after CIMT.

There were no significant effects of CIMT on UPDRS or CGI scores. We found small but nonsignificant changes in physician and subject ratings. There was no apparent relationship between changes in UPDRS or CGI scores and any demographic variable, although it is noteworthy that both subjects who had changes of at least 2 points on the UPDRS had been diagnosed with PD $\leq$5 years before testing.

In regards to the aiming task, the mean group peak velocity for the left wrist (i.e., the less-affected side) was expectedly faster than the right (right, 249.5 degrees/sec; left, 219.1 degrees/sec). Mean reaction times were longer for the right than for the left arm (right, 240.4 msec; left, 220.4 msec). Conversely, movement times on average were quicker for the right than for the left arm (right, 724.6 msec; left, 682.9 msec). For the group, CIMT did not systematically improve motor performance of the affected upper limb on any kinematic measure relative to baseline (mean improvements: 2.3% for reaction time; 9.1% for movement time; 6% for peak velocity). Individual patients revealed changes in their kinematics, but these changes were not consistent enough to state that a subgroup of patients might have benefited significantly from CIMT (see Fig. 1B). Finally, we found no consistent effects of the CIMT on the unaffected limb.

To our knowledge, this open-label pilot study is the first to explore the effects of CIMT in PD. Overall, we found no substantial or consistent kinematic improvements in the affected limb. The lack of effect was not the result of learning, but could have been related to the study parameters, the patient characteristics, or small sample size.

The main result of this study is that CIMT does not seem to benefit those with PD. Given the limited scope of the study, however, we cannot exclude that CIMT may show benefits if conducted over a longer period. In addition, possible benefits might have been masked by our small sample that did not account for individual differences (e.g., gender, age, medication history, and disease severity). In practice, CIMT can be employed relatively easily as it is noninvasive and can be carried out at the patient's home.

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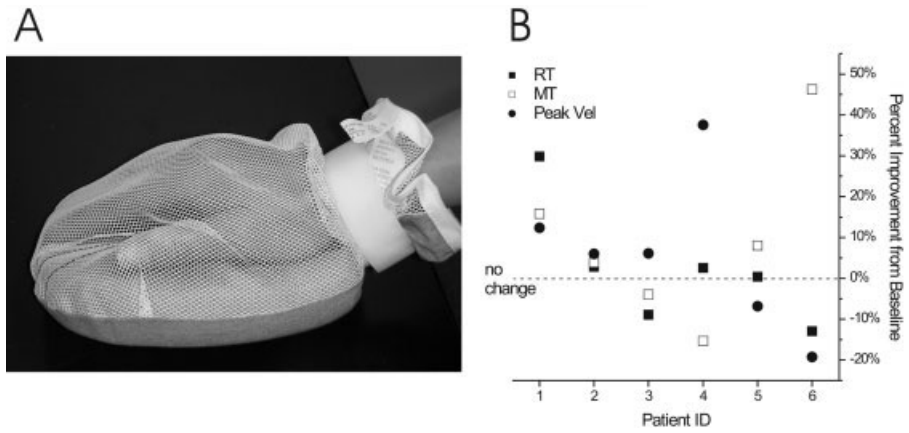

FIG. 1. A: Device to restrict use of the less-affected hand. The palmar surface of the glove consisted of a 2.5-cm-thick foam pad. **B:** Individual change in kinematic performance for all 6 patients in the aiming task. Data points represent the average improvement at the posttest with respect to a patient's baseline performance for the affected arm. RT, reaction time; MT, movement time; Peak Vel, Peak angular velocity. Some patients improved performance; however, only Patient 1 showed a consistent improvement in all kinematic variables.

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