The Case for CI Therapy

Dear Editor:

In a recent issue of this journal (vol. 40, issue No. 1, pp. vii–ix), Alexander Dromerick, MD, contributed an editorial on "Evidence-based rehabilitation: The case for and against constraint-induced movement therapy." We strongly endorse the first part of the editorial that speaks to the importance of basing clinical practice in neurorehabilitation on a solid foundation of experimental evidence.

In the second part of the editorial, Dr. Dromerick states that there is insufficient data to permit the conclusion that CI therapy is an effective therapy and that the data available are "unconvincing." We are puzzled by this opinion, since Dr. Dromerick is the medical director and main professional figure of a clinical CI therapy program at the Stroke Center of Barnes-Jewish Hospital, Washington University School of Medicine. As of the submission of this letter, the web site (www.neuro.wustl.edu/smart/citp.htm) representing Dr. Dromerick's program states, "In our research we have found that the group treated with CI therapy showed significantly improved hand function when compared to those treated with standard rehabilitation techniques." Moreover, prospective patients are informed that "our goal is to help you learn how to use your arm more during your everyday life."

We understand the enthusiasm for the results of CI therapy that must have underlain Dr. Dromerick's decision to open a clinic to provide this intervention. Six reasons might be mentioned:

1. Controlled experiments. In an initial study, the CI therapy group (n = 4) showed large improvements in real-world arm use and arm motor ability relative to a placebo control group (n = 5) [1]. These results were confirmed in a larger study with a fitness training control group (n = 20) who received the same amount of therapist attention and time in motor training as the CI therapy group (n = 21) [2]. Three months after the end of their placebo intervention, the fitness training control subjects were crossed over to CI therapy and displayed a similarly large motor improvement.
2. Replications. The results from this laboratory have been replicated with quantitatively similar results in studies from three other laboratories [3–5]. In one of the replications [3], the experimental intervention was compared to a no-treatment control period; no changes occurred over the control period.
3. Successful transfer to clinical settings. To date, approximately 150 research participants in our laboratory and over 120 patients in our clinic have received CI therapy for the upper limbs with substantial and clinically meaningful improvement recorded in more than 95% of cases [6]. Furthermore, we know of over 1,000 patients treated on a clinical basis with positive results in the United States, Germany, Sweden, Italy, United Kingdom, and elsewhere. Although control data are not available for these patients, the number of individuals having positive outcomes is not irrelevant and supports the successful transfer of CI therapy from laboratory to clinical settings.
4. Evidence of change against a stable baseline. Prior to our work, which began in 1987, the wisdom in neurorehabilitation, based on clinical experience and several published studies, was that patients reach a plateau in their motor recovery after approximately 1-year poststroke. Therefore, the motor ability of chronic stroke patients was considered unmodifiable. Given this view, the possibility is small that the positive experimental and clinical results just cited, which were all obtained with chronic stroke patients, were due to placebo or other nonspecific effects, to spontaneous recovery, or to differences in the distribution of subject variables between treatment and control groups.
5. Basis in animal research. The CI therapy intervention developed in this laboratory stems directly from basic research with monkeys done by Taub and coworkers [7,8]. This animal model provides rigorous evidence for the mechanisms thought to be responsible for the effects of CI

therapy and support for the results obtained with humans.

6. Physiological correlates of behavioral changes. Converging brain imaging and brain mapping evidence from seven studies from five laboratories indicate that CI therapy produces "massive" changes in brain organization and function that parallel the large increases in limb use that CI therapy patients exhibit from pre- to posttreatment [6]. While these brain reorganization phenomena do not themselves indicate that CI therapy is clinically efficacious, they, at a minimum, suggest that CI therapy is not producing its reported results because of placebo, nonspecific effects.

We disagree with the three reasons that Dr. Dromerick gives in the editorial for doubting the efficacy of CI therapy. He cites two studies that employ restraint along with an attenuated form of CI therapy, suggesting that the effects of CI therapy are smaller than indicated by publications from our group [9,10]. However, a study cannot claim to be a valid test of an intervention unless the treatment protocol is closely replicated. Both studies referenced by Dr. Dromerick have protocol differences that depart substantially from our laboratory's CI therapy. The studies differ in the intensity and amount of training provided, and van der Lee et al. changed the format (group versus one-on-one) in which therapy was administered [9], while Dromerick et al. reduced the duration of training [10]. Furthermore, Dromerick et al. not only provided an attenuated amount of CI therapy but also worked with patients with acute stroke (<7 to 14 days postevent) [10], while we have worked primarily with patients with chronic stroke (>1-year postevent). Because patients with acute stroke are generally more cognitively impaired, more easily fatigued, and less medically stable than patients with chronic stroke, comparing the results of rehabilitation in acute versus chronic patients is a case of comparing apples to oranges.

Dr. Dromerick also argues that studies are necessary in which CI therapy is compared to other available motor treatments applied with the same intensity and duration. These types of data are only relevant, however, when the other available treatments have been shown to be efficacious; such is not the case in this situation [11]. Moreover, the intensity and duration of an intervention ought to be an integral part of its protocol; the appropriate comparison would be CI therapy to another treatment at each of their respective optimal doses rather than CI therapy to another treatment at the dose specified for the alternate treatment or vice versa.

Dr. Dromerick ends his editorial with the argument that data from multicenter trials are necessary to determine the effectiveness of CI therapy. While positive results from randomized, multisite clinical trials are strong evidence of efficacy, clearly, this evidence is not the only type that has standing for the resolution of doubt in this regard. This is especially the case when converging evidence of many different types exists, including placebo-controlled clinical studies, replications of quantitative results, and physiological data as just outlined—all of which support the conclusion that CI therapy is an efficacious therapy. Convergence of different types of evidence is a significant factor and, in our view, amply justifies Dr. Dromerick's decision to establish and direct a clinic whose primary purpose is to provide CI therapy. However, we find it difficult to understand the marked dissonance between his clinical activity and his negative opinions about CI therapy.

Sincerely yours,

Edward Taub, PhD
Director, CT Thearpy Research Group

Gitendra Uswatte, PhD
Associate Director, CT Therapy Research Group

University of Alabama at Birmingham and Birmingham Veterans Affairs Medical Center

Address all correspondence to Edward Taub, PhD; Department of Psychology, University of Alabama at Birmingham, 1530 3rd Avenue South, CH 415, Birmingham, AL 35294-1170.

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RESPONSE

I appreciate the close reading of my editorial and the extended response by Drs. Taub and Uswatte. We agree that constraint-induced-movement therapy (CIMT) has potential for the treatment of hemiparesis. We disagree on whether currently available evidence establishes CIMT as an effective treatment and on whether the data demonstrate a treatment effect specific to CIMT. Data that are persuasive in a primate study may not withstand the greater demands of evidence-based practice. Lines of convergence regarding a physiological process suggest, but do not demonstrate, an effective treatment protocol. Those who advocate for a treatment, particularly those who sponsor seminars to recruit patients paying out of pocket, must be prepared to submit to an objective and critical evaluation of that treatment.

A few points:

1. Readers can make their own judgments about the CIMT data. The 1999 publication is a review article of previously published data, with a small summary presentation of data that may be new. It seems to be a case series, but the methods and analysis are not presented in detail sufficient to evaluate. The 1993 study is a reasonable pilot of a potential clinical treatment, but hardly the type of data that establishes the effectiveness of CIMT. It lacks a prespecified primary end point. The "real-world" end point referred to is the unblinded Motor Activity Log, a subjective rating of arm use by a subject heavily invested in the treatment. The potential for biased scoring is obvious. The treatment group is small and highly selected; the generalizability of these results is unknown.
2. That the 1993 study has been replicated in other centers is good; however, these replications do not overcome the problems of the 1993 study. That 1,000 patients have been satisfactorily treated with CIMT is a cause for concern. Tens of thousands of patients were treated with estrogen supplementation, extracranial/intracranial bypass surgery for stroke prevention, and dozens of other ineffective or harmful treatments that were eventually rejected after well-done clinical trials. Not all patients emerged unscathed. CIMT seems safe, but how will we know until rigorous trials are performed?
3. The choice of the control treatment is key. The standard of care in chronic hemiparesis varies, but in sophisticated centers, it includes intermittent pulses of therapy services. Clinically documented improvements occur after such interventions. This routine treatment, delivered in similar amounts to controls, would address whether any treatment effect was specific to CIMT, or a less specific treatment effect that could be obtained with any motor intervention.
4. The motor representation data support the notion that CIMT has an effect on the motor system, an exciting prospect. However, these data do not demonstrate that CIMT is a superior treatment to

conventional ones already provided to patients.

5. One of the advantages of evidence-based analysis is that it imposes an intellectual discipline. I began the evidence-based evaluation that led to my editorial just over a year ago, and we have not treated a patient with CIMT outside of a research protocol since. Fewer than 10 patients have ever been treated at our center outside of a research protocol; all revenues went to those providing the treatment, and not to my salary or laboratory.

Dispassionate work to eliminate ineffective treatments and to refine effective ones will most effectively advance restorative care and help patients. I am excited by the prospects for CIMT, but I await a rigorous demonstration of its effectiveness.

Sincerely,

Alexander Dromerick, MD
Associate Professor of Neurology, Occupational Therapy, and Physical Therapy

Washington University, St. Louis, Missouri

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I currently receive salary and research support from the National Institutes of Health, the Washington University Physician Practice Plan, and the McDonnell Foundation. The National Institutes of Health, the McDonnell Foundation, and the American Heart Association have supported my CIMT work. Over the last three years, I have provided consulting services in stroke trial design and training to Eli Lilly, Ono Pharmaceuticals, and Bayer. I do not participate in speaker's bureaus or in industry-sponsored publications.

Transtibial Amputation Management

Dear Editor:

We very much enjoyed reading the journal's review by Dr. DG Smith et al., "Postoperative dressing and management strategies for transtibial amputations: A critical review," in the 2003 May/June issue, on postoperative dressings for transtibial amputees, an area of medicine that continues to lack definitive evidence for any specific management strategy [1]. Two randomized trials were not included in the review, which may contribute to the small amount of evidence leaning toward a rigid or semirigid dressing in the postoperative period.

Wong and Edelstein compared Unna paste semirigid dressings to elastic (soft) bandages and found that the Unna dressing group had faster wound healing, earlier fitting with prostheses, and better ambulatory outcomes [2]. The study involved a majority of transtibial amputations (unfortunately not analyzed based on level of amputation because of small sample size). Dressings were applied only upon arrival to the inpatient rehabilitation unit, extending the apparent window of benefit of Unna dressings from the immediate postoperative period demonstrated in a nonrandomized study by MacLean and Fick [3]. While difficult to categorize, the notion of a semirigid dressing should be considered an option for postoperative management.

In addition, Vigier et al. compared plaster casting to soft dressings in patients with a recent open transtibial amputation and found that plaster cast dressings resulted in quicker healing times and decreased lengths of stay [4]. Although the application of this rigid dressing was delayed by an average of greater than 20 days and involved open stump wounds, this study contributes further evidence in favor of a rigid dressing.

We agree with the authors that the issue of postoperative amputation wound care requires further research if clinicians are to provide optimal care for this patient population. We also felt that Lynne McFarland's abstract painting included with the on-line paper was the perfect summary for such a confusing but crucial component of the rehabilitation process. It is unfortunate the painting is lost in the hard copy of this excellent review.

Sincerely,

Michael W.C. Payne
BscEng, MSc, MD

Meridith B. Marks
MD, MEd, FRCPC

Division of Physical Medicine and Rehabilitation, University of Ottawa

Address all correspondence to Dr. Michael W.C. Payne, The Rehabilitation Centre, 505 Smyth Rd, K1H 8M2, Ottawa, Ontario, Canada; 613-737-7350, ext. 5595; email: mipayne@ottawahospital.on.ca.

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RESPONSE

Drs. Payne and Marks identified three papers that also contribute to the body of literature on postoperative dressings and transtibial amputation management strategies and could be included in a comprehensive review on this topic. The first paper by Wong and Edelstein randomized 21 transtibial and transfemoral amputees to either Unna wrap, (Dome Paste®), a semirigid dressing or elastic bandages [1]. In this study, transtibial and transfemoral amputees were both enrolled following their rehabilitation hospital admission (within 30 days of amputation). Using data from the time interval where the investigators were able to observe study subjects, they reported 20.8 days until readiness to limb fitting in the Unna wrap group compared to 28.7 days in the elastic bandage group. The limitations in this study are the absence of observation in the immediate postoperative interval and the inclusion of 23% of patients with transfemoral amputations, which could bias results given differing management strategies by amputation level.

The second paper by MacLean and Fick describes 40 transtibial amputees who were alternatively assigned to either the Unna wrap or a soft dressing [2]. The authors report 40% of the study population were unable to complete the study. In an analysis on the remaining 60% of subjects, the authors conclude from Kaplan Meier survival curves that the time to readiness for prosthetic fitting is less than half in the Unna group compared to the soft dressing group. A primary outcome in both of these two papers investigating semirigid dressings was the determination by two trained therapists that the limb was ready for prosthetic fitting. Even with highly trained personnel, this outcome variable is very difficult to accurately quantify.

In the final paper by Vigier and colleagues [3], 56 patients were randomized to a plaster cast or elastic compression. The authors limited the study to a specific subgroup of transtibial amputees who underwent a surgical procedure that intentionally left open wounds from 8 to 24 cm^2 in size. The rigid dressings were worn only for periods ranging from 30 minutes to 5 hours a day in the intervention group; thus this protocol allowed the rigid dressing group to be a mixed exposure of rigid and soft dressings. These findings support a technique to improve healing of open amputation wounds. This however would not translate readily to other transtibial amputees where the incisions are surgically closed.

We thank Drs. Payne and Marks for their attention to detail in identifying these papers and for their kind words. They reconfirm our conclusion that arriving at the evidence-based treatments from the current literature on postoperative dressing and management strategies for transtibial amputation is difficult and more study is definitely needed.

Sincerely,

Douglas G. Smith, MD
Lynne V. McFarland, PhD, MS
Gayle E. Reiber, MPH, PhD
Bruce J. Sangeorzan, MD
Joseph M. Czerniecki, MD

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