

GUEST EDITORIAL

Evidence-based rehabilitation: The case for and against constraint-induced movement therapy

Along with much of psychiatry and complementary therapies, the field of rehabilitation lacks the solid foundation of empirically derived data demonstrating the efficacy of key interventions. Rehabilitation research lags behind drug development, in which at least one multicenter trial with adequate statistical power is required before regulatory approval is granted. Rehabilitation even lags behind many surgical fields, where many expensive or commonly performed procedures are eventually put to the test of a randomized controlled trial. Many widely performed procedures, hailed by their advocates as so obviously effective that randomized controlled trials were not needed or were even unethical, litter the medical literature. Once performed by the thousand, procedures such as extracranial-intracranial bypass for stroke prevention and irrigation of knees for degenerative joint disease are now abandoned because objective clinical trials showed no benefit to the participants.

Rehabilitation has several features that make it peculiarly susceptible to the acceptance of treatments with little or no direct evidence of efficacy. First is the lack of obvious and catastrophic clinical failure to force rehabilitationists to test and refine ideas and treatments. While rehabilitation probably does reduce long-term morbidity and mortality, patients do not obviously and immediately die from bad rehabilitation, as they might from poor surgical techniques or ineffective drugs. Thus, rehabilitationists do not face the same discipline of clinical failure that many other clinicians face. Second, treatment often has no hard end points, such as survival time in oncology trials or the counting of seizure events in epilepsy trials. Since rehabilitationists strive to promote independence, quality of life, and other difficult-to-measure goals, development of clinical trials has been hampered by difficulties in methodology—how do we measure what we claim to be improving? A third problem is that the nature of most rehabilitation interventions makes standardizing the treatment intervention difficult; a behavioral treatment such as a motor therapy or a memory-retraining strategy is much more operator-dependent than simply giving the patient a drug or device. Finally, rehabilitation



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lacks the type of industry interest that drives the development of new drugs and devices. Though there is no shortage of for-profit rehabilitation enterprises, they spend minuscule bits of their revenue on research and development. This is a striking contrast to the pharmaceutical and medical-device companies that view new treatments as their lifeblood and spend accordingly.

Constraint-induced movement therapy (CIMT) is a rehabilitation treatment with some promise and is

accompanied by extravagant fanfare. CIMT has a significant basic science rationale. The idea is an old one, dating back at least to the early 20th century, when Ogden and Franz attempted constraint on primates with pyramidal tract lesions [1]. The work was expanded upon by Knapp, Taub, and others beginning mid-century [2,3]. These workers showed that lesioned primates had latent motor abilities and that certain kinds of motor learning paradigms could access these abilities. Other investigators showed that primate motor cortex had significant plasticity that could be altered by training or by lesioning [4]. These animal findings are tempered by the observation that early constraint of the unaffected forelimb in rodents increased infarct size and was associated with worsening of function [5].

The first report of CIMT for hemiparesis in humans was by Ostendorf and Wolf in 1981 [6]. A large number of case reports and case series followed. All of these reports were positive, reporting improvements in people with stroke, brain trauma, and cerebral palsy. A report that CIMT might alter cortical motor representation in humans with chronic hemiparesis generated an outpouring of press attention [7]. Treatment programs have sprung up all around the world, implying or explicitly stating that CIMT is an effective treatment for restoring motor function. Most recently, studies comparing various modifications of CIMT are being published, again lending the impression that the basic data demonstrating the effectiveness of any CIMT protocol actually exist.

What data are available? A search of the literature on CIMT reveals dozens of publications, but none are multicenter trials. Only a few randomize subjects, and fewer use a separate control group of patients instead of using subjects as their own controls. If we screen the literature for trials that are published in peer-reviewed journals that use a randomized design with a separate control group and that involve at least 20 subjects, only two studies are left. The first is by van der Lee and colleagues [8], which involved 66 subjects with chronic hemiparesis who were randomized to CIMT or a neuro-developmental treatment control. A small improvement in motor impairment was found, but was judged to be of potential clinical significance only in the subjects with sensory loss or neglect. The second study, by Dromerick, Edwards, and Hahn, occurred during inpatient

stroke rehabilitation, with treatment beginning within 14 days of stroke onset [9]. Twenty subjects were randomized to CIMT or a "traditional" treatment control, and the CIMT group did demonstrate a robust improvement in motor impairment. However, the end point was measured only at the end of the 14-day treatment, and the differences in motor impairment did not clearly translate into improvements in activities of daily living function. In short, the randomized controlled trials demonstrating the effectiveness of CIMT are unconvincing. Both studies were positive, but only in a qualified way. Moreover, both are too small to rule out the possibility of falsely positive results [10].

The path to proving or disproving the effectiveness of CIMT is clear. Multicenter trials that randomize subjects to either CIMT or another active motor treatment are needed to determine the effectiveness of CIMT; these studies must be directed both at chronic and at acute hemiparesis. Multicenter trials are necessary because the intervention depends on the interaction between the therapist and participant. If CIMT can be executed only in a few tightly controlled programs, then the widespread application in many other centers may not actually improve patient treatment in the clinic. An active motor treatment is needed as a control because of the implication that CIMT is superior to other available motor treatments. Unless CIMT is compared with other motor treatments in similar doses (treatment time and intensity), the superiority of CIMT over other motor therapies cannot be demonstrated. Finally, while the treatment is being tested in subjects with chronic hemiparesis, it is most likely to be applied during inpatient rehabilitation because of the availability of both the patient and the necessary funding. If so, trials of CIMT during inpatient rehabilitation phase are essential, because the brain is undergoing rapid changes early after injury, and the treatment response may differ from the chronic phase.

The performance of well-done multicenter randomized controlled trials will allow us to unambiguously abandon unsuccessful treatments and to refine and improve successful ones, just as in other clinical fields. The potential of CIMT is exciting, but the widespread routine use of it cannot be supported in the absence of well-done multicenter randomized controlled trial. The EXCITE trial (www.excite.wustl.edu),

a small multicenter trial of CIMT applied a few months after stroke, is an important step toward determining the effectiveness of treatment. Similarly, the VECTORS study (www.strokecenter.org/vectors) will allow the development of a badly needed trial of CIMT during acute rehabilitation. Studies at other centers are also underway. With the completion of these studies, clinicians will be able to examine the data and make their own judgments, rather than be forced to simply accept a glowing case report or a press release. CIMT may be among the first rehabilitation treatments to undergo rigorous testing, but let us hope that it is not the last.

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