Calabrò RS, Naro A, Russo M, et al. Shaping neuroplasticity by using powered exoskeletons in patients with stroke: a randomized clinical trial. *J Neuroeng Rehabil*. 2018;15(1):35. Published 2018 Apr 25. doi:10.1186/s12984-018-0377-8

This study focuses on rehabilitation of patients with hemiparesis due to chronic stroke, acknowledging that many of these individuals struggle with functional mobility, and particularly gait, post-stroke.[1] These authors explain that asymmetry in these patients' gait mechanics results from a combination of dysfunctions including impaired balance, walking speed, and patterns of muscular activation. They then assert that despite being such a common impairment, overground gait training (OGT) does not consistently help these patients to recover a normalized gait pattern and typically only benefits those who are already ambulatory.[1] With this in mind, therapists are looking toward other options, particularly neurorobotic devices for robot-assisted gait training (RAGT). However, these researchers identify a key challenge of RAGT in its poor capacity for use in real-world settings. A newer solution to this problem has been the development of exoskeletons, robotic devices that can be worn during OGT, but there is little evidence thus far regarding the benefits of this technology for ambulation.[1]

With the argument that neurorobotics are especially beneficial when used with both high frequency and high intensity, they speculate that this could induce stronger and longer-lasting neuroplasticity during motor learning than previous interventions. These researchers cite one study suggesting that the Ekso™ in particular may improve ambulation in stroke patients.[1] In turn, they aim to 1) compare the efficacy of the Ekso™ against OGT, and 2) identify possible neurophysiological mechanisms for any improvements seen with Ekso™ use for patients with chronic stroke, with the argument that this could facilitate improved individualization of rehabilitation for this population: Because most spontaneous recovery of motor function will occur in the first 6-months post stroke, the focus on patients with chronic stroke significantly increases the likelihood that motor gains are a result of the rehabilitation interventions.[1] Given the large number of individuals who face dysfunctional gait and mobility post-stroke, this search for a more effective way to return patient independence is an important undertaking and worthwhile subject for research.

Patients were selected from the researchers' own neurorobotic rehabilitation unit, with 40 subjects eligible for participation. Subjects had to be at least 55 years old and 6 months or more post-supra-tentorial stroke, with limited muscle strength no greater than the ability to move against gravity, intact cognition, minimal lower extremity muscle tone, and requiring physical assistance to walk.[1] A randomized controlled trial design was used, and of the 40 participants, all received the allocated intervention and were analyzed, with none lost in follow-up. Patients were randomly assigned, and 20 subjects underwent Ekso™ gait training (EGT), while the other 20 underwent therapist-assisted OGT, and both groups attended 60-minute physical therapy sessions five times per week for eight weeks. Assessors were also blinded to group allocation, which reduced potential bias.[1] When using the Ekso™, patients are aided by motors at their hips and knees and spring-loading at the ankles. It facilitates walking by prompting steps in response to patient weight shifts, with or without the aid of assistive devices, a tether to the ceiling, or physical assistance; patients were progressed throughout the eight weeks. Subjects in the OGT group were able to use their chosen assistive devices but were required to maintain the same walking speed as those in the EGT group.[1] A sample of only 40 is certainly on the small side, and it raises questions for me regarding the transferability of the results to a wider and more diverse population, given the lack of demographic information listed beyond age and sex. However, these researchers assert that their statistical calculations indicate that 40 subjects is sufficient to achieve valid MCID data.[1]

Outcome measures taken pre- and post-intervention included the 10-Meter Walk Test, Rivermead Mobility Index (RMI), and the Timed Up and Go.[1] While I was initially unfamiliar with the RMI, after further investigation, these are all appropriate for use in chronic stroke. In addition to these physical tests, EMG data was gathered to assess participants' gait patterns, EEG data for frontoparietal connection, and Transcranial Magnetic Stimulation (TMS) to assess corticospinal excitability and sensorimotor integration, which allowed for quantification of potential mechanisms of plasticity.[1] With use of TMS, researchers administered pulses adjusted for each subject to both the involved and uninvolved legs to calculate modulations induced in corticospinal and sensorimotor magnitudes. With EEG, researchers identified instances in which gait training resulted in cortical activation in gray matter of the brain. In combination with structural equation modeling, this allowed for measurement of effective connectivity of these cortical activations and the ways in which brain areas influenced each other.[1] To analyze gait, researchers recorded EMG activity from major lower extremity muscles of the quadriceps, hamstrings, and calves. Key measures included cadence, duration of the gait cycle, stance/swing ratio, and an overall index of gait quality for both the involved and uninvolved sides.[1]

As compared against healthy controls, both the OGT and the EGT group initially demonstrated slower gait speeds and worse scores on the TUG and the RMI. At baseline, they also demonstrated qualitatively poor gait consisting of long cycles, asymmetric stance/swing ratios, and abnormal activations of lower extremity musculature that resulted in decreased hip, knee, and ankle flexion during swing phase, and reduced hip extension in stance.[1] Baseline for the neurophysiologic measures included low corticospinal excitability in the affected hemispheres of the brain, as well as reduced effective connectivity between prefrontal, supplementary motor, and centroparietal areas of the brain. At the same time, stronger motor evoked potentials (MEP) and hyperconnectivity were noted in the other areas as conditioned responses. Importantly, these researchers found that the differences between patients at baseline were not statistically significant.[1]

Following intervention, all EGT participants met the MCID for all physical outcome measures, while OGT participants did not, and in some cases, did not even achieve the MDC.[1] Furthermore, researchers were able to associate these improvements in the EGT group with changes seen in neurophysiologic measures: After gait training, muscle activation amplitudes were higher, effective connectivity had normalized, and MEP amplitudes in the involved hemispheres had increased - this was true in both groups, but to a greater extent in EGT subjects, who experienced rebalanced sensorimotor integration between their brain hemispheres.[1] While it is always important for results to meet levels of clinical significance, it improves my confidence in the results that this data also demonstrated statistical significance with low *p* values and moderate to large effect sizes.[1]

These results demonstrate that patients who received gait training with the Ekso™ experienced greater and clinically significant improvements in their overall quality and mechanics of gait, balance, and functional mobility than those in the OGT group. Patients in the EGT group who had initially presented with gait asymmetries and compensatory alterations in muscle activation on both sides also saw greater pattern normalization than OGT subjects.[1] This exemplifies the potential of Ekso™ to produce greater recovery of gait in patients with chronic stroke than more conventional forms of gait training typically used in inpatient rehabilitation or outpatient neuro settings. While not new, it further supports previous Ekso™ data that evaluated other functional outcome measures. It is important to note that other studies that also used exoskeletons in patients with chronic stroke found no difference between EGT and OGT groups.[1] However, these studies only made stationary use of the device, which requires less patient engagement and participation that may be less likely to induce plasticity. It is also important to recognize that the neurophysiological data implies that Ekso™ use did induce neuroplasticity by rebalancing corticospinal excitability and sensorimotor integration between the hemispheres - and EGT subjects saw corticospinal changes in both hemispheres (i.e. it also affected the pieces that were compensating), while OGT participants only experienced changes in the affected side.[1]

With these conclusions, I do find this data exciting and potentially applicable to future clinical practice, but there are a number of limitations worth noting. The study itself identifies an important limitation in that they did not perform any long-term follow up with these patients - but they do believe that the neurophysiologic changes that occurred will be retained. They also acknowledge that the differing data presented from other studies presents a call for larger, multi-center trials.[1] However, I am left with a number of other questions. Based on the frequency and intensity required, I would anticipate that use of an Ekso™ would be more feasibly performed in an inpatient rehabilitation setting. However, the patients in this study are at least 6 months post-injury and fall within the category of chronic stroke, which does not tend to be the patient population available in inpatient rehab. If this technology were to be used in an outpatient neuro setting, it would be worth future study to determine if a lower frequency of use remains effective and produces clinically significant results. Otherwise, I anticipate that the session duration and frequency of 5 times per week for 60 minutes at a time[1] would not be feasible for most outpatient candidates to consistently attend, due to employment, financial, or insurance challenges. Another concern is the very high price of the device and the cost of training therapists in its use. Will this be covered by the clinic? And will this sort of therapy intervention be acceptable to and reimbursable by major insurances? If not, this presents another significant barrier. If these questions are satisfactorily answered, then I do think that EGT would be worthwhile in rehabilitation for stroke patients who match the population characteristics of those in the study, given that higher performance in gait improves mobility in a way that is key to maximizing quality of life.

Additional Reading:

I was not familiar with the Rivermead Mobility Index, so I searched for the measure itself and data supporting its use. See references 2, 3, and 4, which helped confirm for me its validity and retest reliability for use in patients with chronic stroke. This helped me to decide whether this was an appropriate outcome measure, given that it is not one that has been emphasized in school or in the clinic. I also wanted a more in-depth review of how TMS worked, and reference 5 turned out to be a nice overview necessary to my understanding of the methods this study used for measuring neurophysiologic responses.

References

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