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Transcutaneous Spinal Cord Stimulation for Voluntary Movement After Spinal Cord Injury: Current State of the Research.

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Introduction:

In the 1800s, the French neurologist Guillaume-Benjamin Duchenne published a treatise exploring the effects of electrical stimulation on paralysis.[1] In 1982, in uninjured participants, Marsden and colleagues[2] verified that electrical stimulation, delivered through the skin, was able to excite neural structures of the spinal cord. In 2007, Minassian et al[3] demonstrated that transcutaneous spinal cord stimulation (TSCS) of the posterior roots at the thoracolumbar region altered lower extremity reflexes. Given this finding, this same research group effectively used TSCS to reduce spasticity in persons with spinal cord injury (SCI).[4]

Early in the past decade, researchers used non-invasive spinal cord stimulation to activate spinal cord central pattern generators in uninjured participants.[5–7] Thus, TSCS showed potential to not only reduce spasticity, but possibly improve motor output in people with SCI. In a parallel scientific development, Harkema et al[8] published a case study in 2011 demonstrating that an individual with a motor complete SCI recovered voluntary movement below their lesion in the presence of spinal cord stimulation delivered through a surgically-implanted epidural stimulator.

Within the past ten years, research evaluating the impact of TSCS on voluntary motor control after SCI has rapidly expanded. The purpose of this narrative review is to summarize the current state of TSCS research as it applies to volitional control (motor output, bladder function) following SCI.

Objectives:

1. Describe the current state of the research in transcutaneous spinal cord stimulation for enabling voluntary movement and improving bladder function after SCI.
2. Describe the potential mechanisms underlying this innovation.
3. Compare and contrast this form of stimulation to spinal cord epidural stimulation.

Target Audience

The primary target audience for this Current State of the Research paper is physical therapists and other therapists working with individuals whom have sustained spinal cord injury.

Brief Summary: Collectively, TSCS studies have demonstrated improvements in voluntary function previously thought impossible in individuals diagnosed with severe SCIs, indicating that a shift in the management of these patients – from compensation to recovery-based interventions – may be warranted. Repetitive, task-specific training and/or pharmacologic management in combination with TSCS may re-engage diminished neural connections between the brain and spinal cord and meaningfully improve voluntary motor activation which may lead to improved function.

Objective 1: Describe the current state of the research in transcutaneous spinal cord stimulation for enabling voluntary movement and improving bladder function after SCI.

Lower extremity and trunk motor function

Led by Drs. Gerasimenko and Edgerton, TSCS-mediated restoration of voluntary lower extremity control over standing and stepping motions in people with motor-complete SCI has been demonstrated in multiple reports.[9–11] Participants regained voluntary step-like motions after a four-week period of step training (gravity-neutral position) coupled with TSCS, targeting the lumbo-sacral enlargement.[11] Additionally, the use of serotonin agonist treatment was found to enhance voluntary movement in all of these participants.[11] In another study of fifteen individuals with SCI ranging from American Spinal Injury Association Impairment Scale (AIS) A (motor complete) to C (motor incomplete), all participants regained the ability to stand upright with the use of their upper extremities for balance and minimal to no assistance when TSCS was applied.[10]

Stimulation can be applied at various levels of the spinal column to activate specific motor pools and interneurons. Electrode placement is dependent on the goal of the motor task. When TSCS is applied to vertebral levels T11-T12, a motor response in the lower extremities is evoked, which is an area known to be closely associated with spinal cord central pattern generators.[12] Stimulation at vertebral levels T10-T11 has been shown increase activation of the quadriceps, while stimulation at vertebral levels T12-L1 preferentially activates the hamstrings.[13]

TSCS has also been shown to improve trunk stability. Rath and colleagues[14] reported that TSCS applied to the thoracolumbar region in individuals diagnosed with SCI (AIS A to C) significantly improved trunk posture in sitting, stability in sitting, and ability to perform postural adjustments after perturbation.

Upper extremity motor function

In the upper extremity, a combination of TSCS and pharmacologic treatment was found to increase average grip strength over 300% in participants with tetraplegia.[15] Participants also made significant improvements in the Action Research Arm Test and in upper extremity motor scores.[15] Some carryover of these effects was demonstrated in voluntary upper extremity movement without application of the stimulation, indicating potential neuroplastic changes.[15]

A separate study demonstrated a similar carryover effect, reporting a 325% increase in grip strength with stimulation and a 225% increase in grip strength that persisted without stimulation.[16] Gains in upper extremity function from combined TSCS and physical therapy are shown to be maintained three months after treatment has been completed.[17] All studies that have demonstrated successful facilitation of upper extremity motor function applied stimulation to the C4-C7 segments of the spinal cord.[12]

Bladder function

Along with motor function, another top priority for individuals whom have sustained SCI is the recovery of bladder function.[18] Transcutaneous Electrical Spinal Stimulation for Lower Urinary Tract Functional Augmentation (TESSLA) has been shown to reactivate the spinal circuitry needed for lower urinary tract and urethral sphincter function in those with SCI by decreasing detrusor muscle overactivity, decreasing detrusor-sphincter dyssynergia, and increasing both bladder capacity and voiding.[19] Confirmed using an animal model, TSCS targets activation of spinal cord neural pathways controlling the detrusor muscle, pelvic floor muscles, and urethral and anal sphincter.[20] This recent research demonstrates potential for TSCS to help restore some lower urinary tract function which may result in reducing incontinence, kidney infection, and urinary tract infection for these individuals.

Objective 2: Describe the potential mechanisms underlying this innovation.

In cases of SCI that are deemed clinically complete (AIS A), individuals present with no voluntary motor or sensory function below the level of injury.[21] In the majority of cases, remaining intact axons spanning the level of the lesion still exist,[22,23] but cannot send a strong enough signal to recruit lower motoneurons distal to the injury.[24] (see Figure 1) Spinal cord stimulation electrically excites primary afferent fibers of the posterior roots of the spinal cord,[25] which – at progressive stimulation intensities – increases the excitability of interneurons and motoneurons at the level of the stimulation.[11] The theory is that this increased excitability enables remaining intact descending axons to once again carry out voluntary motor commands.[9,24] (See Figure 2) The propriospinal system is known to be an important relay system between the brain and spinal cord as well as between spinal cord segments while also having direct involvement in locomotion.[26] It is also hypothesized to play a critical role in upregulating spinal cord activity specifically associated with standing and stepping when augmented with TSCS.[24] Following multiple sessions of TSCS and task-specific training, neuroplastic changes may occur that allow functional gains to persist even when the TSCS is turned off.[16,17] Further exploration of where and how these neuroplastic changes occur is warranted.

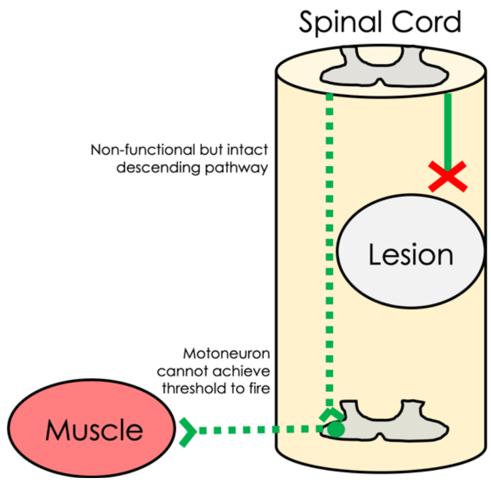

Figure 1: Following motor-complete spinal cord injury, some descending axons are still intact but non-functional. Lower motoneurons (below the level of injury) cannot become sufficiently excited to thresholds for firing action potentials.

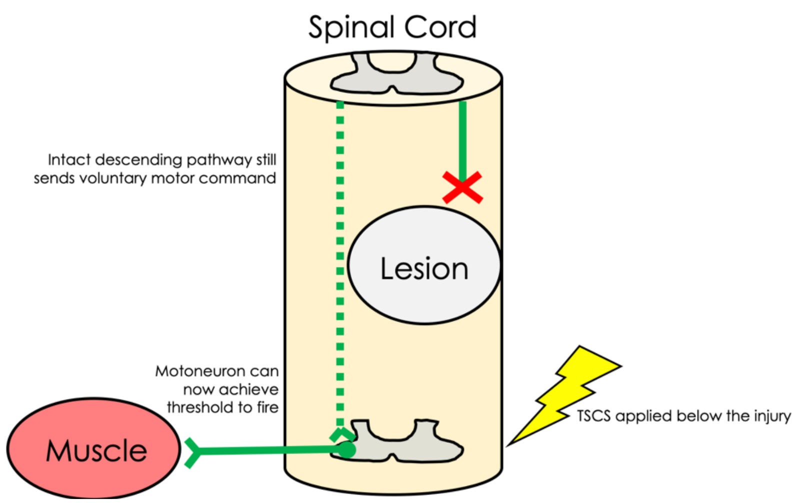

Figure 2: Transcutaneous spinal cord stimulation (TSCS) applied below the lesion is able to bring lower motoneurons to an increased state of baseline excitability. Now, intact descending voluntary motor commands may be able to sufficiently excite these motoneurons for voluntary movement.

Objective 3: Compare and contrast this form of stimulation to spinal cord epidural stimulation.

There has been considerable scientific and consumer interest in both TSCS and epidural spinal cord stimulation in recent years. Both technological advancements have demonstrated promise in restoring voluntary connections below the spinal cord lesion even in individuals diagnosed with the most severe SCIs.[24]

Epidural spinal cord stimulation involves a surgical procedure where the stimulating electrode array is implanted over the lumbo-sacral cord segments.[27] Three separate research groups demonstrated that epidural stimulation paired with task specific physical training was able to restore voluntary over-ground walking after SCI,[28–30] with two of these cases being motor-complete injuries.[29,30] To date, no TSCS studies have shown as much functional improvement as was found in these studies using epidural spinal cord stimulation. Further, the epidural stimulation electrode array may offer a higher degree of fine-tuning to activate specific motor pools, compared to surface electrodes.[27]

TSCS is non-invasive, which may be a considerable benefit to those with SCI, and may ultimately be more widely accessible due to its non-invasive nature. Epidural stimulation requires an invasive surgery that carries a financial burden as well as increased risk for surgical complications and post-surgical infection.[31] Even though both interventions have shown potential for improving spinal cord function, at this moment neither has received FDA approval for clinical use and continued research efforts must focus on safety, clinical feasibility and efficacy before they can be widely adopted.

Conclusion

Transcutaneous spinal cord stimulation is a promising non-invasive tool to augment voluntary movement below the level of injury, even in cases of severe SCI. Currently, a number of clinical trials are active to explore safety, efficacy, and mechanisms underlying TSCS in persons with SCI, both in the United States and internationally. According to the clinical trial identifier NCT04043715, one trial out of University of Washington will directly compare epidural stimulation versus TSCS in individuals with motor incomplete SCI. Innovations like TSCS show potential to fundamentally alter our profession's clinical management of patients with SCI.

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