PAIN MEDICINE CASE REPORTS

ISSN 2768-5152

Volume 7, Number 3, pp. 151-155

Scrambler Therapy for the Treatment of Pain and Sensory Symptoms in Corticobasal Syndrome: A Case Series

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Background: Corticobasal syndrome (CBS) is a rare atypical parkinsonian disorder. Pain occurs in one-third of patients; current pain treatment options are often inadequate. Scrambler therapy (ST) is a noninvasive cutaneous method of neuromodulation that has shown success in other refractory neuropathic pain syndromes.

Case Report: We treated 3 patients with CBS with one to 3 40-minute sessions of ST, capturing the terminal arborization of the peripheral nerves within the affected painful dermatomes. All patients reported rapid and complete relief of their pain, with one patient having 4 months of ongoing relief, along with complete resolution of alien limb phenomenon. Another patient experienced 11 months of relief, with resumption of pain relief with retreatment after symptoms gradually returned. None have experienced complications or adverse effects to date.

Conclusion: ST may represent a new noninvasive treatment for central pain associated with CBS. Further studies with longer follow-ups are warranted.

Key words: Scrambler therapy, atypical parkinsonism, corticobasal syndrome, chronic pain, central pain

BACKGROUND

Corticobasal syndrome (CBS) is a rare atypical parkinsonian disorder usually caused by a 4-repeat tauopathy (corticobasal degeneration or progressive supranuclear palsy). CBS symptom onset is usually in the seventh decade of life. It has an estimated prevalence of 5 to 7 per 100,000 individuals (1).

While the classic symptoms of CBS include asymmetric rigidity, dystonia, myoclonus, dyspraxia, bradykinesia, cortical sensory loss, and alien limb phenomenon, pain is a common presenting symptom, occurring in at least one-third of patients (2). The pain is often described as electric-like shocks radiating from the cervical spine to the arms in a "coat hanger" distribution, followed by intense muscle spasms. Pain also frequently accompanies dystonia and rigidity, severely impairing sleep and quality of life. Treatments for pain associated with CBS are often ineffective or associated with adverse effects (such as sedation). More treatment options are needed for this patient population (2).

Scrambler therapy (ST) is a novel form of cutaneous neuromodulation that targets the terminal arborization of nociceptive fibers in specific dermatomes and sends "nonpain" signals to replace nociceptive signals (3). ST

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Disclaimer: This work was supported by NCI grant P 30 006973; 1 R01 CA245054-01A1; 1 R01 CA177562-01A1; PCORI IHS 1609-36518; PCORI 2020C3-21247-el-Jawari (PI, MGH), Douglas Smith and Tom Smith, site co-PIs, Hopkins; The Harry J. Duffey Family Fund for Palliative Care; The Lerner Foundation, Washington DC (all TS); The Rosenbloom Foundation, Baltimore MD (LB). These funding sources had no involvement in the study design, data collection, analysis and interpretation of data, or writing of the report.
Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.
Patient consent for publication: Case reports of 3 or fewer people do not need Institutional Review Board approval at Johns Hopkins. All patients gave written permission for use of their stories and photographs.
Authors adhere to the CARE Guidelines for writing case reports and have provided the CARE Checklist to the journal editor.
Accepted: 2023-03-22, Published: 2023-05-31

is fundamentally different from transcutaneous electric neurostimulation (TENS). TENS devices are designed to stimulate afferent Aβ fibers, inhibiting nociception transmission as a secondary effect (4). In comparison, ST induces neuromodulation by transmitting low-frequency electrical signals to C-fibers using surface electrodes at each patient's specific pain areas. These signals are interpreted as both "nonpainful" and endogenous by the central nervous system (3).

ST has been used successfully to treat other types of refractory neuropathic pain such as chemotherapy-induced peripheral neuropathy-associated pain (5) and central pain associated with diseases such as Dejerine-Roussy syndrome (6), poststroke central pain (7), neuromyelitis optica (8), and transverse myelitis (8,9).

Here we describe 3 consecutive patients with CBS who were referred for ST for pain treatment. Each achieved dramatic and sustained relief after 3 or fewer 40-minute ST sessions. We used the Calmare™ MC5-A Scrambler Therapy device (Competitive Technologies, Inc.), which is US Food and Drug Administration 510(k)-cleared and European CE mark-certified for the noninvasive treatment of chronic neuropathic and oncologic pain. All patients gave written informed consent for use of their stories and photographs.

CASE SERIES PRESENTATION

Case One

This 70-year-old man presented to the movement disorders neurology clinic with more than 11 years of atypical parkinsonian symptoms, including visuospatial abnormalities (difficulty with reading and writing numbers and certain letters), an asymmetric postural/action tremor of the left arm, rigidity, dystonia, limb dyspraxia, cortical sensory loss, left-sided alien limb phenomenon, myoclonus, and gait difficulties due to intermittent right lower extremity pain. He met clinical diagnostic criteria for probable CBS (10).

Magnetic resonance imaging of the brain demonstrated asymmetric parietal lobe atrophy and lack of significant vascular ischemia. The patient lacked clinical findings to suggest progressive supranuclear palsy, multiple system atrophy, or Parkinson disease as more likely diagnoses. He described left-sided alien arm syndrome, paroxysmal left arm pain, bilateral upper extremity dystonia, and paroxysmal "coat-hanger" distribution pain that was worse on the left. He was unable to tolerate levetiracetam and had neither analgesic nor functional benefit with carbidopa/levodopa. He had an initial improvement of symptoms with oral morphine, but the analgesic efficacy decreased over time and he sought to avoid using opioids to minimize any potential risk of developing opioid use disorder.

Because there is some evidence that clonazepam and botulinum toxin injections may be beneficial for alien limb phenomena (11), he had tried them with modest pain relief over the previous 5 years, but with declining benefit over the past year. He began to require higher doses of botulinum toxin injections, which resulted in his left arm experiencing significant postinjection weakness. Mirror therapy attempted by occupational therapy yielded only transient relief for his alien limb phenomena and paroxysmal left upper extremity pain. He reported a 7/10 chronic baseline pain score.

The patient was treated with 3 total sessions of ST over 4 days. One set of electrodes was placed corresponding to his left upper extremity pain, which was approximately within the C6 dermatome (Fig. 1a); another 3 sets were positioned corresponding to his "coat-hanger" distribution pain, approximately along the C2 to T2 dermatomes bilaterally (Fig. 1b); and another set was placed corresponding to his low back and intermittent right leg and foot pain, which was approximately along the L5 dermatome (Fig. 1c).

After his first ST session, he slept through the night without pain or muscle spasms for the first time in more than 2 years. After completing 3 total ST sessions, he has remained pain-free for more than 4 months and ongoing, reporting a pain score of 0/10 (Fig. 2). His alien limb phenomenon has resolved and he reports a significant decrease in diffuse numbing sensations. He continues to receive botulinum toxin injections in the regions of his upper extremities where ST treatments had not been applied, but he reports that his botulinum toxin doses have been reduced by more than 60%.

Case 2

This 75-year-old woman presented to the movement disorders neurology clinic with more than 5 years of poor balance and mechanical falls, and at least 3 years of right-sided loss of upper and lower extremity motor coordination. She met the clinical diagnostic criteria for probable CBS.

She had notable motor symptom progression in the previous 3 months and lost most of her ability to move her right upper and lower extremities. She was becoming increasingly frustrated and despondent, expressing

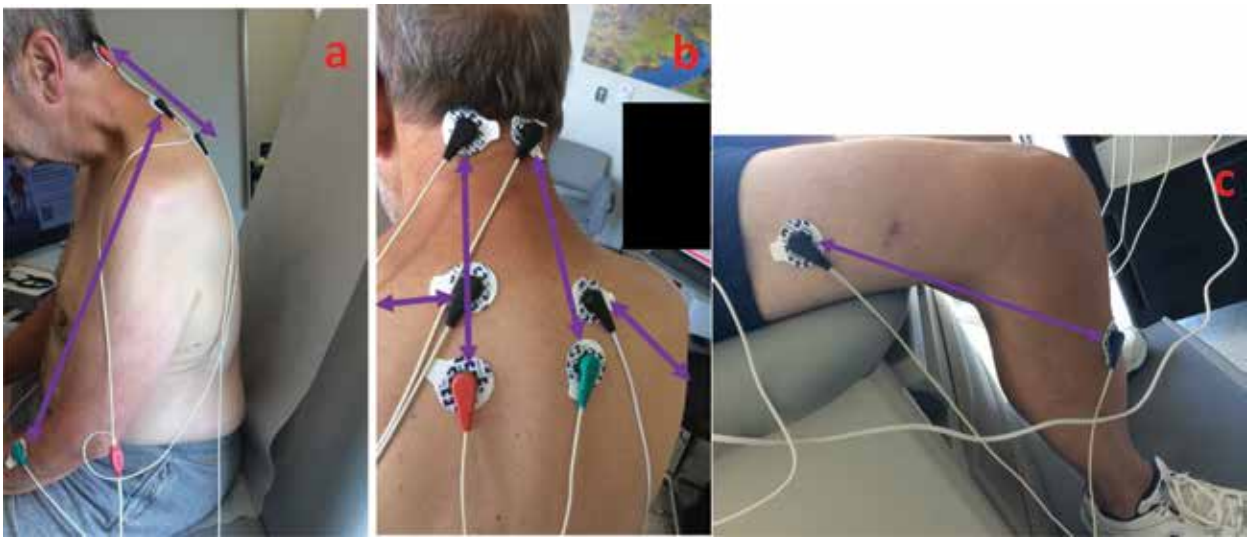

Fig. 1. Placement of scrambler therapy electrodes along the dermatomes approximating the patient's areas of pain. 1a): Left C6 dermatome; 1b): Bilateral C2 to T2 dermatomes; 1c): Right L5 dermatome, above the patient's reported region of numbness.

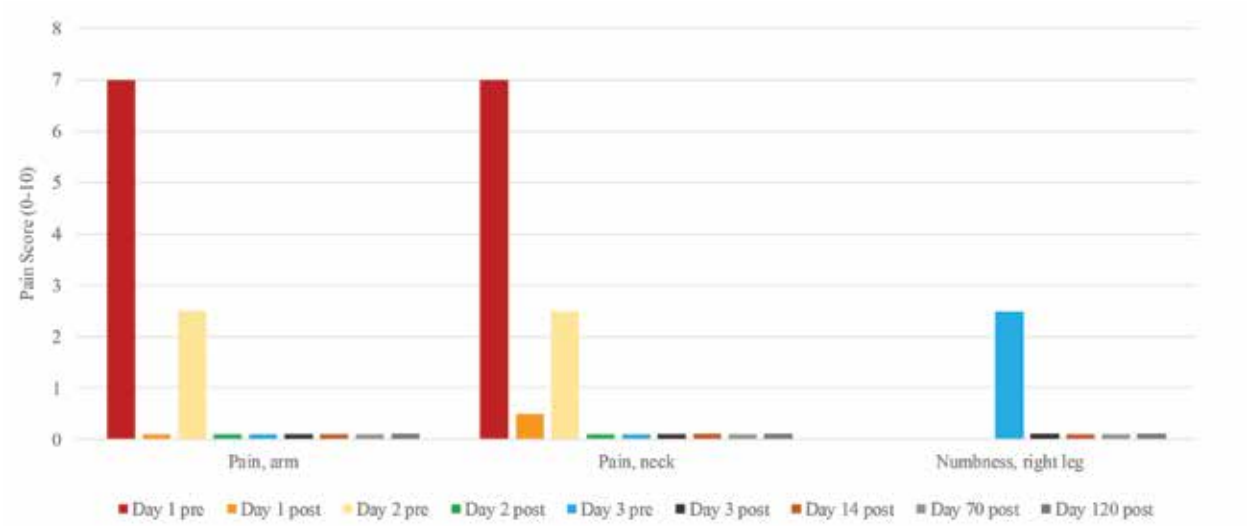

Fig. 2. Pretreatment and posttreatment pain scores for Patient One via the 0-10 Numer Rating Scale (NRS-11). Numbness was only assessed beginning treatment day 3.

passive suicidal ideation the day before her first ST session. Her pain level at minimum was 5/10, but worsened as the day progressed and peaked in the early evenings. Botulinum toxin injections temporarily relieved her pain for only a few days each time.

The patient was treated with 3 total sessions of ST over 3 consecutive days. We placed electrodes within the dermatomal distributions that most approximated her areas of pain. At her first treatment session, we placed electrodes along her C6 dermatome bilaterally, between her C3 to T8 dermatomes bilaterally along her neck and upper back, and along her right L5 dermatome to her right foot. After 40 minutes, the patient reported that her pain had decreased to 0/10 and that her baseline right upper extremity hyperalgesia had resolved. At her second treatment session, ST electrodes were placed at identical locations, and her symptoms of numbness in her right upper and right lower extremities completely resolved. At her third treatment session, we adjusted the ST electrodes to also cover the C8 dermatome in

her right upper extremity. After this third session, she reported that her right foot was no longer abnormally inverting, and as a result she experienced marked improvement in her ability to walk. At a 2-week follow-up evaluation, she reported a greatly improved mood and ongoing 0/10 pain. Her pain relief lasted 11 months before her symptoms gradually returned over a duration of 2 weeks. After she was treated with 3 additional ST sessions, she again reported complete pain relief.

Case 3

This 74-year-old woman presented to the movement disorders neurology clinic. Approximately 3 years ago, she noticed that her handwriting had changed, and her right arm motor function gradually declined thereafter. She became unable to button her shirt, comb her hair, or hold objects with her right hand, and elbow extension and finger extension also became difficult. She met probable CBS diagnostic criteria.

As her dystonia and rigidity worsened, she began to have increasingly frequent episodes of paroxysmal severe pain in her right arm. She was taking tramadol 50 mg tablets twice a day and using several types of splints for her right hand. She had difficulty sleeping overnight due to severe pain and urinary urgency, both likely symptoms of her CBS. Her chronic baseline pain score was at least 3-4/10.

She was treated with one session of ST, with electrodes placed along her right upper extremity, approximating the C6-C8 dermatomal distributions. She was not having a paroxysmal episode of pain at the time of the treatment so it was not possible to assess the immediate effect of ST. However, she slept through the night that evening for the first time in several months, and she reported complete resolution of her paroxysmal right arm pain. She continued to report a pain score of 0/10 for approximately 8 weeks. Her pain has since gradually returned, but she plans to return for additional ST treatments because of the significant analgesic and functional benefit she experienced.

DISCUSSION

We present a series of 3 consecutive patients with probable CBS according to clinically established criteria who have thus far experienced immediate and sustained relief of their chronic pain and sensory impairment complaints using 3 or fewer sessions of ST. All patients had experienced inadequate pain relief or adverse effects from previous trials of medications or injections, and 2 patients had pain that was refractory to opioids.

These patients' pain and sensory symptoms are most likely centrally mediated given the prominent neurodegeneration of the sensorimotor cortex implicated in CBS. We propose that ST may modulate these central sensory pathways to ameliorate symptoms. Our promising findings with ST in CBS thus far address a crucial unmet need in this patient population and are similar to the results described in patients experiencing centrally mediated pain from other etiologies (6-9). Importantly, these results may also be applicable to patients with Parkinson disease, of whom 85% report pain with unsatisfactory pain relief (12).

The generalizability of our report is limited by the small sample size; we cannot rule out a contribution from the placebo effect. The proper administration of ST requires the operator to titrate the device settings to the maximum magnitude the patient can tolerate. As a result, a truly "sham" ST session is not possible, precluding blinding (3). However, each of our patients experienced significant and immediate analgesia with ST, with ongoing relief. It would be surprising if this pain relief were due to the placebo effect alone, as our patients had all been suffering from debilitating and refractory pain for several years in the context of a neurodegenerative disorder.

The ideal pain treatment modality would provide significant analgesia, have an immediate onset and prolonged duration of effect, and produce minimal adverse effects. ST achieves all of these goals. ST can yield pain relief within a single treatment session, provide analgesia for months, has no physiologic mechanism for inducing tolerance, and only uses cutaneous adhesive electrodes rather than needles or injections (3).

CONCLUSION

ST has a highly favorable risk-benefit profile and has great potential to improve pain and quality of life in patients with CBS, and possibly in other atypical parkinsonism syndromes and Parkinson disease. Our results warrant further investigation through controlled studies of ST in CBS, with larger sample sizes and longer follow-up.

Acknowledgments

We thank the patients and their family members in this case series for agreeing to provide us with relevant information.

Author Contributions

Eric J. Wang: This author helped with the analysis and interpretation of data, drafting, and revising the article for important intellectual content, and approving the final version to be submitted.

Lauren E. Berninger: This author helped with the analysis and interpretation of data, drafting, and revising the article for important intellectual content, and approving the final version to be submitted.

Thomas J. Smith: This author helped with the conception and design of the study, the analysis and interpretation of data, drafting, and revising the article for important intellectual content, and approving the final version to be submitted.

Alexander Y. Pantelyat: This author helped with the conception and design of the study, the analysis and interpretation of data, drafting, and revising the article for important intellectual content, and approving the final version to be submitted.

All authors approved the final submitted version of this manuscript.

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