Scrambler Therapy: Effective use of artificial neurons for the treatment of chronic neuropathic pain

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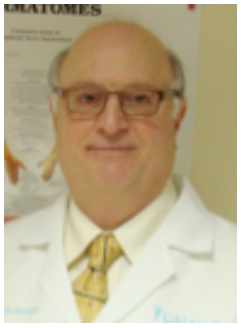

The experience of pain is a normal sensation existing as an expedient mechanism for preservation of life, reduction of injury and/or the initiation of healing. It is formally defined in many research studies as an unpleasant sensory and emotional experience associated with real or potential tissue damage (Merskey & Bogduk, 1994). When pain persists beyond the reasonable timeframe of healing (e.g., six months) and seems to have separated from its purpose of warning, it is labeled as chronic.

Chronic pain, for the most part, does not seem to have a specific purpose. While acute pain is usually time-limited, chronic pain can persist for decades. Chronic pain persists beyond a point when natural healing and in some cases surgical healing has resolved. Subjective components seem to increase in importance and the behaviors or responses of the individual appear disproportionate to underlying pathophysiology and often become the disorder itself.

Chronic pain disrupts every aspect of life and over time produces significant emotional and behavioral changes. People experiencing chronic pain seem to report the pain as treatment-resistant, thereby increasing exposure to more and more treatment approaches, including the use of opioids in combination with various cocktails of anticonvulsants, anti-inflammatories and antidepressants. As pain persists in the presence of varying and increasing interventions, the focus of treatment begins to move toward the psychological. Referrals are often made for "behavioral pain management," usually focused on improvement in coping as well as improvement of specific psychophysiological manifestations of the pain (e.g., muscle tension).

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Theories of pain control

The theoretical basis of most chronic pain treatment approaches is the *gate-control theory* (Melzak and Wall, 1966). The use of this theory has led to the development of treatments designed to suppress pain in the theoretical gating system in the dorsal horn of the spinal cord and brain and suppressing pain from an assumed sensory source in the periphery. Melzak (1999) has suggested the gate-control theory is more effective in understanding acute and sub-acute pain than chronic pain.

The *neuromatrix theory* proposes a sequentially established central source for pain that becomes independent of the initial sensory source (e.g., phantom limb pain). The neuromatrix theory suggests that key brain structures (anterior cingulate, insular, parietal lobes and perhaps other structures) are involved in the perpetuation of pain, and it is only when this pain matrix is interfered with and the brain returns to homeostasis that pain is reduced or eliminated. The neuromatrix theory has led to numerous investigations on the role of the brain in chronic pain.

Current methods of treatment for chronic pain, such as surgery, epidural steroid injections, medications, various forms of exercise, alternative treatment methodologies, and psychotherapy, are based on the gate-control model. Unfortunately, they have less than stellar levels of efficacy. Neuroscience advances have produced significant evidence, now widely accepted, that chronic pain is the result of a *central nervous system dysregulation,* with hyperexcitabilty and expansion of peripheral and central receptive fields and cerebral reorganization. These are often associated with *hyperalgesia* (Martelli et al., 2003).

> Neuroscience advances have produced significant evidence, now widely accepted, that chronic pain is the result of a central nervous system dysregulation.

Marineo et al. (2003) stated that, "the *pain system* … is characterized by a high level of information content which forms its essence." He states that specific neural receptors are biological elements capable of converting chemical, physical or mechanical events into specific pain information. Over time this biological system reestablishes homeostatic equilibrium. The purpose of the pain is achieved and the system returns to a "silent state" (Marineo et al., 2003).

This pain system is sometimes challenged, and the silent state is not achieved, resulting in chronic pain. This challenge is due to either the inability to

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remove the biological pathology or "intrinsic damage to the pain system itself (neuropathies) (Marineo et al. 2003)."

When this occurs, complex reactions set up a circular process that ultimately makes treatment approaches ineffective. Marineo postulated that it is reasonable to assume the lower levels of complexity in the pain system (e.g., chemical reactions regulating the coding of pain information and subsequent feedback) could be influenced by manipulating the "information" variable alone, but at higher levels of complexity. The chemical reactions are in essence a black box. Knowing the input and output of the black box does not require complete knowledge of its contents.

A practical analogy for ST

Marineo has offered a practical analogy to explain scrambler therapy to clarify this: the *traffic control model*.

Imagine an observer who is not familiar with traffic lights. He stands watching the flow of traffic through an intersection. Think of his position and this intersection as subsystem of the entire city's traffic control system. The entire city's complex traffic control system is made up of many of these subsystems.

Being able to correctly describe the whole traffic system depends on whether he can accurately understand its smaller parts. Our observer, in time, will probably learn to recognize and understand the way the colored lights regulate the flow of vehicles by color and timing: He has discovered the function of the traffic lights at one intersection, and now he can generalize that to the whole city's system.

Now, our observer understands that if he wants to arbitrarily change the city's traffic flow, all he has to do is to change the colors of the lights, perhaps by choosing his own sequence of colors instead of the programmed one.

If traffic lights suddenly stop working, traffic will probably go haywire. Since our observer has figured out how the traffic light system works, now he can imagine traffic going from an extremely disordered state (due to a breakdown in color code information) to a more orderly one, as soon as the information has been correctly re-established.

He can also imagine replacing the traffic lights with his own system, the characteristics of which are sufficiently compatible with the one it replaces. Although he might not know anything about the overall city traffic control system, he can make replacement system because he has learned its processing logic, which, in the final analysis, is what really regulates the traffic flow.

Once our observer has figured out the traffic rules, he doesn't need to know why lights stopped working

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properly to be able to restore them if they become disordered. All that is important to know is which electric cables are involved, the voltage of the lights themselves, and how to program the correct color sequences. Then he can develop his own control panel to replace a defective original, while respecting the original established rules. If he does this correctly, the drivers will not notice any difference, and traffic will resume normal flow.

Based on this simple example, Marineo infers:

- Increase in the disorder of traffic flow is strictly related to bad information, in this case, traffic light colors that drivers can't understand.
- Subsystems are part of a more complex system. This complexity itself amplifies and extends a disorder, even when it is initially small and localized, eventually increasing disorder throughout the city. A disorder caused by bad information grows and spreads, expanding with time and involving other systems (side streets) even if their local traffic lights function properly.
- The only way to avoid uncontrolled chaos caused by information errors is to correct them. This will work regardless of the method used to do it, although outcome will depend on the accuracy of the coding and its output.

Scrambler therapy is a way to deceive the brain into reading non-pain signals as real, thus blocking pain perception.

Scrambler Therapy

Scrambler therapy uses this principle. When long-lasting pain information loses its protective or informational value and becomes something else, a pathological event itself, greater disorder results. We see its serious consequences (chronic pain, neuralgia, causalgia) in people with indescribable suffering.

Having thus characterized the pain system in terms of its information content, both in the active phase and in the remission or quiescent phase, Marineo developed a way to create a synthetic antagonistic signal delivered through skin surface electrodes to deceive the nerve centers that decode information and recognize it as pain.

Marineo et al. (2003) applied his theory of pain modulation and elimination by using a device that uses a low amperage electrical stimulation applied to the healthy skin above and below the pain focus of an individual suffering from chronic pain. The electrical stimulation provides information to the CNS (using 16 different types of nerve action potentials, resembling endogenous ones, using

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agorithms to assemble them into sequences) through the dorsal horn and up to the brain via C-fibers.

In ST, bioelectrical non-pain information goes to the CNS, deceiving the brain into reading this non-pain information as real, as if it were generated by the body. When this occurs, there is an immediate reduction of the chronic pain, and in some cases it is eliminated. This is scrambler therapy.

Clinical researchers further postulate that due to repeated exposure to the non-pain code, changes in the brain (CNS plasticity) will result in a long-term relief of perceived pain, and the individual will continue to have this positive response for months or years following treatment.

Outcome studies in the literature

In one of the first published investigations of ST, Marineo (2003) reported on the treatment of 11 terminal cancer patients suffering from drug-resistant neuropathic pain. He applied ten treatment sessions of ST to these patients and reported that 81.8% of the patients were able to discontinue pain medications and 18.2% were able to reduce their dosage of pain medication.

These results were encouraging. Another investigation was conducted and published in 2003 (Marineo, Spaziani, Sabato & Marotta, 2003) in which 33 patients suffering from drug-resistant chronic neuropathic pain were treated with 10 sessions of ST. The entire sample responded positively to the treatment with significant declines in VAS (Visual Analog Scale) scores. Seventy-two percent of the patients stopped taking pain medications. The remaining 28% significantly reduced their medications after ST.

Sabato, Marineo & Gatti (2005) treated 226 patients with various forms of neuropathic pain (e.g., sciatic and lumbar pain, post-herpetic pain, post-surgical nerve injury pain, pudendal neuropathy, brachial plexus neuropathy, and others). They applied only 5 ST treatments of 30 minutes and were able to demonstrate significant improvement with 80% of the sample reporting a better than 50% relief from pain, and only 9% with no positive response to the treatment.

More recently several studies have continued to demonstrate efficacy of ST. In a study of 40 cancer patients and 33 non-cancer pain patients VAS scores were compared at the initiation of treatment, after the 10-session treatment and again at 2 weeks following treatment (Ricci et al. 2011). In their sample the average VAS score was 6.2 just prior to treatment. After ten treatment sessions the average VAS was 1.6. Two weeks following treatment the average VAS score was 2.9.

Marineo et al. (2012) conducted a clinical trial with patient randomized to either guideline-based pharmacological treatment or ST. Patients were

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matched by type of pain (i.e. post-herpetic neuralgia, postsurgical neuropathic pain, and spinal canal stenosis). The VAS score was recorded prior to the initiation of the first treatment and after each of ten treatment sessions. The control group VAS was 8.1 and the ST group 8.0. At one month following the past ST treatment session the ST group VAS score was 0.7 while the control group was 5.8. At two and three months, the mean VAS scores in the control group were 5.7 and 5.9; the ST group scores were 1.4 and 2. These results clearly suggest that ST is far superior at relieving neuropathic pain than drug management.

The mechanism for this treatment effect may be raising the gate threshold for pain at the spinal cord, reducing wind-up (central sensitization of the spinal cord and brain that amplifies the abnormal feelings), reducing impulses from the damaged nerve, and reducing psychological maladaptation to pain (Jenson, 2010).

The most recent investigation (2012) has demonstrated similar levels of treatment efficacy in the treatment of post-herpetic pain with ST (Smith, Marineo, Coyne and Dodson 2012). Sparadeo, Kaufman & D'Amato (2012) recently published an outcome study comparing the impact of ST on three diagnostic groups (spine pain, complex regional pain syndrome, and complicated multi-site cases). They found that ST was equally effective for spine pain and CRPS, with six-month follow-up demonstrating improvement significant improvement lasting more than six months in more than 75% of these patients.

Implanted devices result in only a 50% reduction in pain and involve invasive procedures.

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Comparison to other methods No direct investigations comparing ST to implanted devices (i.e., intrathecal morphine pump and spinal cord stimulator) have been conducted to date. However, it is important to note that implanted devices result in only a 50% reduction in pain at best (Harke, Gretenkort, Ladleif et al., 2002; Kumar, Taylor, Jacques, et al. 2007; Smith, Staats, Pool et al., 2005) and involve invasive procedures with risk for infection and other surgical and technical problems. There is also a subset of patients that are successfully treated initially, only to request the implanted device be removed as the pain returns. It is quite clear that the use of ST before considering the use of an expensive surgically implanted device should be part of the protocol for these procedures.

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Pain rating measures used in this study

Brief Pain Inventory (BPI) *(Cleeland & Ryan, 1995) 7-item rating scale from 0 to 10 to rate the degree of negative pain effect, with 10 most severe. Variables: activity level, mood, ability to walk, ability to work or conduct household chores, interpersonal relations, sleep and life enjoyment Add*

Visual Analog Scale (VAS) *10-point scale to measure subjective level of pain. Numerous studies have demonstrated the validity and reliability. (Price, McGrath, Rafii & Buckingham, 1983)*

Recent Applied Data Analysis

Calmar Pain Relief is a free standing pain treatment center in Rhode Island exclusively dedicated to the treatment of chronic neuropathic pain. As part of ongoing evaluation of program efficacy, a data analysis was conducted in late 2013 on 46 consecutive admissions for the treatment of complex regional pain syndrome (CRPS) and 49 consecutive admissions for the treatment of single site spine-based pain.

Method

Sampling and Procedures

This investigation analyzed the pre- and post-treatment data of 95 individuals entering a ST program for the treatment of chronic neuropathic pain. The patients were divided into two diagnostic groups: those with complex regional pain syndrome (CRPS) and those with chronic spine-based pain. Each patient was asked to rate their pain using the Visual Analog Scale (VAS) before initiation of ST. Each patient was also asked to rate the impact pain was having on their life using the Brief Pain Inventory (BPI, a 10-point rating scale in which a higher score represents greater pain impact). Each patient was asked to report the number of hours of pain relief between ST applications.

All patients were weaned from opioids and anticonvulsant medications being used for pain reduction. The data were composed of pretreatment pain levels using the 10-point VAS and BPI. Each treatment session included a VAS measure before ST was applied and following the ST. At 6 to 12-month post treatment patients were telephoned and VAS pain levels were requested along with the administration of the BPI.

Data Analysis

Means and standard deviations of pretreatment VAS and BPI measures were calculated and plotted graphically representing pre- and post-treatment states. Paired comparisons using T-tests were conducted comparing pretreatment VAS mean levels to post-treatment levels as well as pretreatment BPI results to post-treatment results (means). A simple

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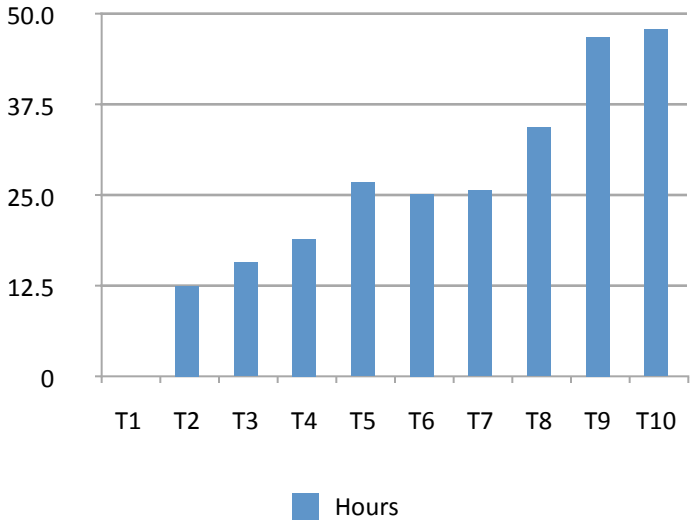
analysis of the number of hours of pain relief between treatment sessions was also computed and graphed.

Results

In the first analysis the subjects were asked to keep track of the number of hours of pain relief between sessions. This data was plotted on a graph across 10 ST Sessions (graph 1).

Graph 1. Mean number of hours of pain relief reported by patients in ST between sessions.



Analysis of variance (ANOVA) was conducted in which VAS means were compared between subjects with CRPS and those with spine pain. No differences were found between these diagnostic groups before treatment or at follow-up. There were statistically significant differences within subjects comparing VAS levels before treatment and at follow-up using paired comparisons (t-tests).

Table 1. Means and Standard deviations by diagnosis for Pre and post treatment VAS.

	CRPS (N=46)		Spine Pain (N=49)	
	Mean	SD	Mean	SD
Pre Treat VAS	7.9	1.9	7.4	1.6
Post Treat VAS	3.4	3.4	2.8	2.5

ANOVA was conducted on the total score means pre and post-treatment for both diagnostic groups. No statistical differences were present prior to the initiation of ST and likewise at follow-up. Within subjects differences were significant. The following table includes means and standard deviations for both diagnostic groups prior to ST and at follow-up.

Table 2. Means and Standard Deviations for Pre and Post ST BPI total scores

	CRPS (N=46)		Spine Pain (N=49)	
	Mean	SD	Mean	SD
Pre Treat BPI	46	14	52	11
Post Treat BPI	20	18	14	20

An analysis of success versus failure was conducted using a cutoff of 30% relief. Specifically, those patients reporting less than 30% relief at follow-up were considered failures and those reporting 30% or greater were considered successes. Table 3 summarizes the results of this analysis.

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Table 3. Success v. failure and % of pain decrease at follow-up

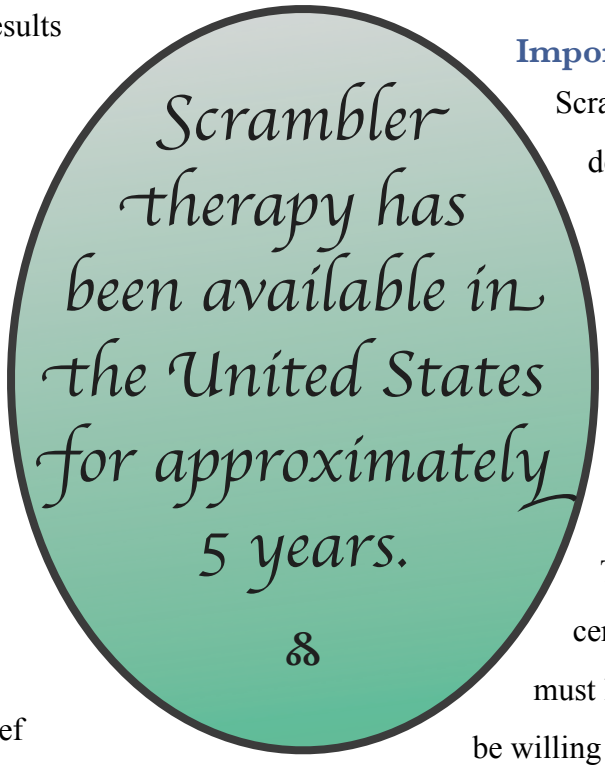
	N	Percent	% pain decrease
Success	67	70	76
Failure	28	30	13

Discussion

The data analysis is consistent with previous program evaluation data analyses (Sparadeo et al., 2012) indicating that ST is highly effective for chronic neuropathic pain. The results indicate that six to 12 months following treatment, 70% of patients had an average improvement of 76% in their pain levels. Even those patients considered failing treatment reported an average level of improvement of 13%. The analysis indicated that during the treatment process the vast majority of patients experienced significant pain relief between sessions in an ascending pattern to 48 hours of relief by the final (10th) treatment session. There does not appear to be any other treatment for chronic pain with the same levels of positive impact.

Implications

Scrambler therapy has been available in the United States for approximately 5 years. At the Calmar Pain Relief Center in Rhode Island over 700 patients have been treated with success rates over 70%, depending on the diagnosis and complexity of the case. Scrambler therapy is a non-invasive direct treatment of the chronic pain with no known side effects. The use of ST in chronic pain is cost-effective and more effective than any other form of direct treatment for chronic pain. This treatment will likely be used in more cases, especially as more reports appear in sientific literature.



Important factors to consider

Scrambler therapy is very operator-dependent. While the MC-5A ST device manual describes electrode placement sites derived from knowledge of dermatomes, standardized placement does not seem to result in the best outcomes. The physician, nurse, or certified technician applying ST must listen to the every patient and be willing to move the electrodes if the results are not satisfactory.

Electrode placement is at the pain margins above and below the pain location. These margins can change from session to session and therefore successful electrode placements one day may not be the same the next day. Patients using anticonvulsant medications or patients on high doses of opiate

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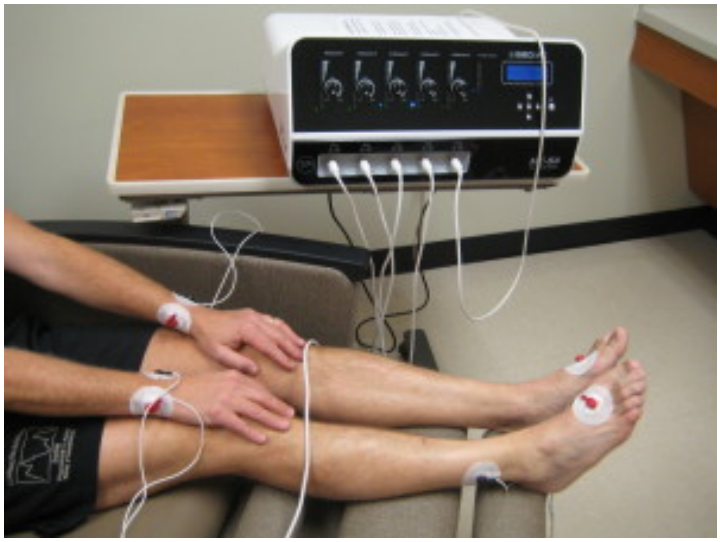
analgesics seem to have delayed responses to the ST, and therefore it is necessary to reduce or eliminate these medications before initiating ST. Patients with surgical hardware still in place may experience significant improvement, if not optimal results. Implanted electrical devices, such as spinal cord stimulator or medication pump, are contraindications for ST. Patients who have such devices removed will experience the same results as the general population. Patients with significant psychiatric illness are less likely to have good results with ST; this includes patients with active major depressive disorder, psychotic disorder, and somatoform disorder.

Clinical use

The application of ST begins at intake. The patient's past medical record is read, records are reviewed by the physician, and the patient is interviewed and examined. The patient is then educated about ST. This visit can take two hours. During this visit the patient is allowed to see the ST device and to feel the electronic signal. If the patient is cleared to begin treatment, ten sessions will be planned.

On the first session the physician and nurse apply the treatment by placing electrodes on non-involved areas but along dermatomes as close to the dermatome(s) at the epicenter of the pain (but not on the pain), usually 1 or 2 dermatomes above and



below it. This guarantees that the ST electronic code will travel along healthy fibers. The device is turned on and the patient gives the clinician feedback regarding what he/she feels. If the placements are in the correct position, the patient will report a precipitous drop in pain to zero, usually within two minutes. Once this occurs the patient will be treated for an additional 45-60 minutes. This process will be repeated for 9 more visits applied on consecutive days, usually with a two-day hiatus after the first five treatments.

After the series is complete, the patient is offered an opportunity to return for booster sessions should they experience an increase in their pain level. Most patients returning for booster sessions do so at approximately 6 months following the treatment. Booster sessions seem to re-stimulate the non-pain memory that was created in the initial treatment process, and therefore the number of booster sessions is minimal.

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Differentiating ST from TENS

- Standard transcutaneous electrical nerve stimulation (TENS) transmits an electronic signal through the skin to the spinal cord. Scrambler therapy is a neuromodulation procedure using electricity on the surface of the skin to transmit a coded signal to the spinal cord and ultimately to the brain through C-fibers.
- Scrambler therapy voltage is significantly lower than TENS and ST cannot burn the skin.
- ST is placed above and below the pain and never on the pain, whereas TENS is placed on the pain.
- ST sends information to the cord and brain (coded action potentials indistinguishable from real human action potentials). TENS transmits individual wave forms (which are not codes).
- TENS is an attempt to "close the gates" and reduce the pain experience, based on gate control theory. ST serves as a source of information that transmits this information ultimately to the brain where it is decoded as non-pain.
- ST is assumed engineered to capture A-delta and C-fibers only. TENS is designed to stimulate beta fibers and therefore the brain will accommodate to these electronic signals rendering the treatment ineffective over time.

Indications for ST

- Neuropathic pain
  - Spine-based pain (radicular pain, stenosis, sciatica, cervicalgia)

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Nursing Diagnoses to Consider *NANDA-I Nursing Diagnosis, 2012-2014*

- ***Readiness For Enhanced Sleep:*** *A pattern of natural, periodic suspension of consciousness that provides adequate rest, sustains the desired lifestyle, and can be strengthened (Domain 4, Activity/Rest; Class 1, Sleep/Rest)*
- ***Activity Intolerance:*** *Insufficient physiological or psychological energy to endure complete required or desired daily activities (Domain 4 Activity/Rest, Class 4: Cardiovascular/Pulmonary Responses)*
- ***Readiness for Enhanced Self-Care:*** *A pattern or performing activities for oneself that helps to meet health-related goals and can be strengthened (Domain 4, Activity/Rest; Class 5, Self-Care)*
- ***Risk for Powerlessness****: At risk for perceived lack of control over a situation and/or one's ability to significantly affect an outcome (Domain 9: Coping/Stress Tolerance; Class 2: Coping Responses)*
- ***Impaired Comfort****: Perceived lack of ease, relief, and transcendence in physical psychospiritual, environmental, and social dimensions (Domain 12: Comfort, Class 1: Physical comfort*
- ***Chronic Pain:*** *Unpleasant sensory or emotional experience arising from actual or potential tissue damage or described in terms of such damage (International Association for the Study of Pain); sudden or slow onset of any intensity from mild to severe without anticipated or predictable end and a duration of greater than 6 months (Domain 12: Comfort, Class 1: Physical comfort)*

- Complex Regional Pain Syndrome
- Pudendal pain
- Post-herpetic neuralgia
- Peripheral neuropathy
- Trigeminal neuralgia
- Chemotherapy induced peripheral neuropathy
- Post-surgical nerve pain
- Complex pain presentations with a neuropathic component
- Phantom limb pain

Contraindications for ST

- Scrambler therapy should not be used in patients who have an implanted electronic device (spinal cord stimulator or medication pump).
- Scrambler therapy is most effective in patients who are not using anticonvulsant medications for pain.
- Scrambler therapy does not work as well in patients on high doses of opiates. Once the medication is reduced or eliminated, a good response to the treatment is expected.
- Patients with a significant psychiatric history, especially those with a history of somatoform disorder, are not good candidates for ST. Patients who are actively psychotic or suffering from severe major depressive disorder are not good candidates
- Patients experiencing dementia are not good candidates.
- Patients with a history of traumatic brain injury may experience less than an optimal response to ST.
- Patients with non-neuropathic pain (arthritis, vascular pain, bone pain) do not respond as well to ST.

Cost

While there is a Category III CPT code for ST (0278T), there is no consistent universal reimbursement coverage. Severl workers compensation carriers and third-party administrators now cover ST. While some private insurance companies have been willing to cover the treatment, others have not, and those patients presently have to pay out of pocket. The cost per session varies depending on the provider but in general the costs-per-session is approximately $500.00. Patients who do well in the first few sessions usually will need only 7 treatment sessions (based upon data analysis at Calmar Pain Relief, 2011) and more complicated patients may require as many as 15 sessions.

Future

It is expected that research will continue to be conducted on ST. Currently, trials are being conducted at a number of institutions of higher learning including a sham study being designed at the University of Wisconsin. There is no doubt that more research is needed and it is likely that various modifications in treatment approaches will be developed. Currently, there are no studies on the use of ST with children, although the Calmar Pain relief Center has extensive experience using ST to treat children from age 8-18.

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There are no studies on ST comparing treatment responses of the elderly versus younger patients. A barrier to some of the research may be the subjective aspects of the treatment. As mentioned above, standardized electrode treatments often weaken the treatment response. This can be a barrier to double blind research designs.

The number of ST devices being used across the U.S. is increasing and such prestigious institutions as Mayo Clinic, Johns Hopkins University Medical School, the Massey Cancer Institute and the U.S. military are using the device. (For a list of civilian and military centers using Calmare ST throughout the US, see http://www.calmarett.com/locations.html) Physicians at other major institutions such as the Cleveland Clinic have been referring patients for ST regularly. It is anticipated that as the excellent treatment results continue the use of ST across the U.S. will continue to grow.

Late-breaking news: Federal judge opines "Medicare should cover ST"

February 7, 2014 Anson, P. *A federal judge has ruled that a novel medical device called the Calmare Scrambler is effective at relieving pain and should be covered under Medicare. The decision could lead to Calmare's non-invasive therapy becoming more affordable and more widely available to thousands of chronic pain patients.*

The ruling involved a 69-year-old breast cancer patient who suffered from chronic neurogenic pain after undergoing mastectomy and chemotherapy. She was treated with the Scrambler and 2011 at a pain clinic in Staten Island, New York, but her Medicare claim was initially denied because Calmare therapy wasn't included in the treatment code used when the claim was filed.

The pain clinic appealed the decision and Administrative Law Judge LeAnn R. Canter allowed the appeal, which permits the clinic to receive reimbursements for Calmare treatments on behalf of the woman.

http://americannewsreport.com/nationalpainreport/calmare-therapy-gets-favorable-medicare-ruling-8822947.html

Retrieved February 21, 2014

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