Motor Cortex Stimulation

Number: 0755

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.

Aetna considers motor cortex stimulation experimental and investigational for the treatment of the following indications (not an all-inclusive list) because its effectiveness has not been established:

- Amyotrophic lateral sclerosis
- Chronic refractory pain (e.g., central pain syndromes, complex regional pain syndrome, peripheral neuropathic pain, phantom limb pain, and trigeminal neuropathic pain)
- Dysphagia
- Dystonia secondary to a focal basal ganglia lesion
- Movement disorders
- Obsessive compulsive disorder
- Parkinson's disease
- Post-stroke hemiparesis
- Traumatic brain injury

Background

Motor cortex stimulation (MCS) has been used to treat various chronic refractory pain conditions such as trigeminal neuralgia, post-stroke pain (PSP), and other nerve/brain injury pain.

Policy History

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Review History

Definitions

Additional Information

Clinical Policy Bulletin Notes
syndromes. It entails implantation of electrodes over the primary motor cortex. One or more electrodes are placed extra-durally over the motor cortex via a burr hole or a small craniotomy, and these electrodes are then connected to an implantable, battery-powered, neurostimulator. This procedure is usually performed in two separate operations: (i) computer-aided neuro-navigation techniques and magnetic resonance imaging (MRI) images are used to guide implantation of electrode(s); and (ii) a second operation is performed for implantation of a neurostimulator if stimulation of the motor cortex is successful in alleviating the patient’s pain. The neurostimulator placed subcutaneously near the clavicle, and is connected to the electrode(s). An external radio transmitter is used to adjust the electrical impulses depending on the level of pain. Maarrawi et al (2007) noted that MCS is associated with focal cerebral blood flow changes involving regions with high density of opioid receptors. These researchers suggested that MCS-related pain relief is probably due to MCS-induced release of endogenous opioids in brain structures involved in the processing of pain.

While MCS has been employed in the treatment of a variety of chronic refractory pain conditions, there is only limited evidence regarding its effectiveness. Available evidence is largely derived from small, uncontrolled, case studies.

Ebel et al (1996) reported the results of MCS in treating severe trigeminal neuropathic pain (TNP) (n = 7). In all but one case the impulse-generator was implanted after a successful period of test stimulation. "Successful" means a pain reduction of more than 50 % as assessed with a visual analog scale (VAS). Excluding one case, in which a prolonged focal seizure resulting in a post-ictal speech arrest occurred during test stimulation, there have been no operative complications and the post-operative course was uneventful. In all the other patients the pain inhibition appeared below the threshold for producing motor effects. Initially these patients reported a good-to-excellent pain relief. In 3 of 6 patients a good-to-excellent pain control was maintained for a follow-up period of 5 months to 2
In the remaining 3 patients the positive effect decreased over several months.

Nguyen et al (2000) studied the use of MCS in the treatment of central pain (n = 32). The mean follow-up was 27.3 months. Ten of the 13 patients (77 %) with central pain and 10 of the 12 patients (83.3 %) with neuropathic facial pain experienced substantial pain relief. One of the 3 patients with post-paraplegia pain was clearly improved. A satisfactory result was obtained in 1 patient with pain related to plexus avulsion and in 1 patient with pain related to intercostal herpes zoster. None of the patients developed epileptic seizures. The authors concluded that chronic MCS is an effective method in treating certain forms of refractory pain.

Mogilner and Rezai (2001) noted that chronic epidural MCS has been shown to have promise in the treatment of patients with refractory deafferentation pain. A total of 5 patients underwent MCS in which functional imaging guidance was used. Prior to surgery, patients underwent MRI with skin fiducial markers placed on standard anatomical reference prints, followed by magneto-encephalography mapping of the sensory and motor cortices. In 2 patients, functional MRI was also performed using a motor task paradigm. The functional imaging data were integrated into a frameless stereotactic database by using a 3-dimensional co-registration algorithm. Subsequently, a frameless stereotactic craniotomy was performed using the integrated anatomical and functional imaging data for surgical planning. Intra-operative somato-sensory evoked potentials (SSEPs) and direct stimulation were used to confirm the target and final placement of the electrode. Direct stimulation and SSEPs performed intra-operatively confirmed the accuracy of the functional imaging data. Trial periods of stimulation successfully reduced pain in 3 of the 5 patients who then underwent permanent internal placement of the system. At a mean 6-month follow-up, these patients reported an average reduction in pain of 55 % on a VAS.

Devulder and colleagues (2002) noted that amitriptyline and
sodium channel blockers are the drugs of first-choice for the treatment of central pain. If oral or transdermal drug delivery is not indicated or ineffective, the intra-thecal administration route can be attempted with baclofen, clonidine, opioids and midazolam. Invasive electro-stimulation is the last treatment option. Thalamic stimulation can be tried in spinal cord injuries, and MCS is sometimes the last resort. Rainov and Heidecke (2003) reported long-term follow-up of 2 patients with unilateral facial neuropathic pain due to idiopathic trigeminal neuropathy and surgical trauma to the glosso-pharyngeal nerve, respectively. These patients failed other modalities for pain relief. Electrical stimulation of the motor cortex with a quadripolar electrode contralateral to the painful area of the face was tried and resulted in immediate analgesia with more than 50% pain reduction. During a follow-up period of 72 months, a sufficient (greater than 50%) and stable analgesic effect of MCS was observed.

Henderson et al (2004) stated that MCS may serve as an adjunct in managing neuropathic pain after other conservative and interventional methods have failed. However, the magnitude and duration of the benefit are highly variable, with a significant percentage of patients losing pain relief over time. These researchers examined if intensive re-programming could re-capture the beneficial effects of MCS (n = 6). Patients' average age was 50 years (range of 26 to 71). The diagnoses were TNP (n = 2), complex regional pain syndrome (CRPS) I (n = 2), phantom limb pain (n = 1) and PSP (n = 1). The mean duration of pain was 6 years. The MCS benefit had initially lasted for a mean of 7.16 months (range of 2 to 18 months). After re-programming, 5 of 6 patients experienced improvement in pain. Average VAS scores decreased from 7.44 to 2.28 (p < 0.001) in those patients who responded to re-programming. Three patients experienced seizures during re-programming. No patient experienced seizures at their therapeutic settings. Pain control was maintained after discharge. These researchers found that intensive re-programming can re-capture the benefit of MCS in patients who have lost pain control.
Tirakotai et al (2004) noted that MCS is an alternative treatment for central pain syndromes. A total of 5 patients suffering from central pain underwent MCS with the guidance of a frameless stereotactic system. The neuro-navigation was used for identification of the pre-central gyrus and accurate planning of the single burr hole. The exact location was re-confirmed by an intra-operative stimulation test. Post-operative clinical and neuro-radiological evaluations were performed in each patient. The navigation system worked properly in all 5 cases. Determination of the placement of stimulating electrode was possible in every case. All patients obtained post-operative pain relief. No surgical complication occurred, and the post-operative course was uneventful in all patients.

In a prospective study (n = 10), Brown and Pilitsis (2005) used the McGill Pain Questionnaire, VAS, and an inventory of drug consumption to review the results of treating patients with TNP by means of MCS. Implantation of electrodes was performed via intra-operative neuro-navigation and cortical mapping for stimulation site targeting. Nine patients had TNP from post-herpetic neuralgia, surgical injury, or unknown cause, and 1 patient had pain of central origin. Patients were evaluated with multi-modality scales before, immediately after, and at designated intervals after surgery. Eight patients underwent permanent implantation after a trial evaluation. In 2 patients, the stimulating electrodes were removed after an unsuccessful trial: 1 had a lateral medullary infarct leading to central pain, and in the other patient, there was no explanation for the pain. The average duration of pain before surgery was 6 years. Post-operatively, there was an 88 % rate of immediate pain relief (greater than 50 % on VAS score) and a 75 % rate of pain relief at mean follow-up of 10 months (range of 3 to 24 months). Mean pre-operative McGill Pain Questionnaire total pain rating index was 57 (higher than that observed in causalgia) for patients who did not undergo implantation and 53 for those who underwent implantation. Mean McGill Pain Questionnaire pain rating index at mean follow-up of 10 months was 24 (55 % decrease). Mean VAS score
pre-operatively was 9 in patients with stimulator implants and 8 in those whose stimulator was removed after the trial. Immediate post-operative mean VAS score was 1. This score stabilized 3 months after surgery. Patients with implanted stimulators reduced their pain medication dose by a mean of more than 50%. Three patients with facial weakness and sensory loss regained both strength and discriminative sensation during stimulation. In another patient, dysarthria improved. In a review of the literature, 29 (76%) of 38 patients with neuropathic facial pain treated with MCS achieved greater than 50% pain relief. The authors concluded that these results provided support for the use of MCS in facial neuropathic pain and document pain improvement as measured by multi-dimensional scales.

In a prospective study, Nuti et al (2005) evaluated the effects of MCS in the treatment of refractory neuropathic pain (n = 31). The long-term outcome was evaluated using 5 variables: (i) rate (%) of pain relief, (ii) pain scores as assessed on VAS, (iii) post-operative decrease in VAS scores, (iv) reduction in analgesic drugs intake, and (v) a dichotomic (yes/no) response to the question whether the patient would accept, under similar circumstances, to be operated on again. Pain relief was rated as excellent (greater than 70% pain relief) in 10% of cases, good (40 to 69%) in 42%, poor (10 to 39%) in 35% and negligible (0 to 9%) in 13%. Intake of analgesic drugs was decreased in 52% of patients and unchanged in 45% (unavailable data in 3%), with complete withdrawal of analgesic drugs in 36% of patients. Twenty-one patients (70%) declared themselves favorable to re-intervention if the same beneficial outcome could be guaranteed. Neither pre-operative motor status, pain characteristics, type or localization of lesions, quantitative sensory testing, SSEPs, nor the interval between pain and surgery were found to predict the effectiveness of MCS. The level of pain relief, as evaluated in the first month following implantation was a strong predictor of long-term relief (regression analysis, $r = 0.744; p < 0.0001$). These results indicated that MCS can be a satisfactory and durable alternative to medical treatments in patients with
refractory pain, and suggested that the effectiveness of MCS may be predicted in the first month of therapy.

Rasche et al (2006) analyzed retrospectively 17 patients with chronic neuropathic pain who were treated with contralateral epidural stimulation electrodes; TNP was diagnosed in 10 cases and PSP in 7 cases. The placement of the electrodes was performed in local anesthesia using neuro-navigation and intra-operative neuro-monitoring. A test trial of minimum 1 week including double-blind testing was conducted and pain intensity was measured using a VAS. Correct placement of the electrode was achieved in all patients using intra-operative neurophysiological monitoring. Double-blind testing was able to identify 6 (35 %) non-responders. In 5 of 10 (50 %) with TNP and 3 of 7 (43 %) with PSP, a positive effect with pain reduction greater than or equal to 50 % was observed. The mean follow-up period was 3.6 years (range of 1 to 10 years) and included 1 patient with 10 years of positive stimulation effect. The authors concluded that MCS is a treatment option for patients with chronic neuropathic pain localized in the face or upper extremity.

In a review on neuro-stimulation for chronic non-cancer pain, Coffey and Lozano (2006) noted that neurostimulation to treat chronic pain includes approved and investigational therapies directed at the spinal cord, thalamus, peri-aqueductal or peri-ventricular gray matter, motor cortex, as well as peripheral nerves. Persistent pain following surgery and work-related or neural injuries are common indications for such treatments. In light of the risks, efforts, costs, and expectations associated with neuro-stimulating therapies, a careful re-examination of the methods used to gather evidence for this treatment’s long-term effectiveness is in order. The authors concluded that future analyses of emerging neuro-stimulating modalities for pain should require unambiguous diagnoses as an entry criterion and should involve the use of randomization, parallel control groups that receive sham stimulation, as well as blinding of patients, investigators, and device programmers. Given the chronicity of patient symptoms and stimulation
therapies, effectiveness should be studied for 1 year or longer following implantation of the device. Meticulous methods are especially important to evaluate new therapies such as MCS. Henderson and Lad (2006) noted that MCS is a relatively new technique that has shown some promise in the treatment of TNP. This technique has the potential to revolutionize the treatment of chronic pain. The authors stated that it is important to evaluate MCS critically in a prospective, controlled fashion.

Cheshire (2007) noted that MCS, although having shown initial promise for TNP, seemed to be ineffective for classical TN. Lazorthes et al (2007) reported that the results of MCS on phantom limb pain are promising; and the conclusions of ongoing multi-center randomized clinical trials (RCTs) will be very useful and are likely to promote further research and clinical applications in this field. Cioni and Meglio (2007) stated that the indications for MCS included TNP and other types of central/peripheral deafferentation pain. The results reported in the literature were quite good; the mean long-term success rate was 80 % in facial pain and 53 % in non-facial pain. However, results from these researchers were less impressive; 4 of 14 (28 %) patients with chronic non-malignant pain experienced a greater than 40 % pain relief, but in 2 of them the effect faded with time. These investigators stated that it is time for a large, multi-center, prospective, randomized, double-blind study evaluating not only the effect of MCS on pain, but also the optimal electrode placement and stimulation parameters.

Available guidelines indicate that RCTs are needed to ascertain the effectiveness of MCS in the treatment of chronic pain. The Reflex Sympathetic Dystrophy Syndrome Association's treatment guidelines on CRPS (2006) listed MCS as an experimental procedure in the treatment algorithm of this condition. Furthermore, the guideline on assessment and management of chronic pain by the Institute for Clinical Systems Improvement (2007) stated that neurosurgical techniques for chronic pain resistant to an adequate
A conservative approach holds promise, but has limited scientific evidence. These invasive approaches include ablative techniques such as cingulotomy and mesencephalotomy, as well as stimulation techniques such as deep brain stimulation and MCS. In addition, the European Federation of Neurological Societies' guidelines on neurostimulation therapy for neuropathic pain (Cruccu et al., 2007) stated that there is level C evidence (possibly effective, ineffective, or harmful) that MCS is useful in 50 to 60% of patients with central PSP as well as central or peripheral facial neuropathic pain, with small risk of medical complications. The evidence about any other condition remains insufficient. The authors stated that further controlled trials are needed for spinal cord stimulation in conditions other than failed back surgery syndrome and CRPS; and for MCS and deep brain stimulation in general. An assessment by the Institute for Clinical Effectiveness and Health Policy (Pichon-Riviere et al., 2007) concluded that MCS for central and neuropathic pain is an investigational technique.

More recently, MCS is also being studied for the treatment of other diseases. Several studies have specifically examined the use of MCS in treating Parkinson's disease (Cioni et al., 2007). Arle and Shils (2008) performed a literature search between 1991 and 2007 and found 512 cases using MCS. Although most of these addressed the treatment of pain (n = 422), 84 of them involved movement disorders. Moreover, Priori and Lefaucheur (2007) noted that the therapeutic effects of MCS in the treatment of movement disorders still need to be assessed in controlled studies. Arle and colleagues (2008) stated that although there have been some positive findings using MCS for Parkinson's disease, a larger study may be needed to better determine if it should be pursued as an alternative surgical treatment to deep brain stimulation.

Lima and Fregni (2008) conduct a systematic review and meta-analysis to quantify the efficacy of invasive and non-invasive MCS for the treatment of chronic pain. Medline and other databases were searched as data sources. Reference lists and conference abstracts were examined for further
relevant articles. A total of 11 studies using non-invasive brain stimulation and 22 studies using invasive brain stimulation met the inclusion criteria. The results showed that weighted responder rate was 72.6 % (95 % confidence interval [CI]: 67.7 to 77.4) for the invasive stimulation studies and 45.3 % (95 % CI: 39.2 to 51.4) for the non-invasive stimulation studies. This difference was significant. For the non-invasive stimulation studies, the random effects model revealed that the number of responders in the active group was significantly higher as compared with sham stimulation group (risk ratio of 2.64) (95 % CI: 1.63 to 4.30). The authors concluded that this meta-analysis shows that two different techniques of brain stimulation of motor cortex -- invasive and non-invasive -- can exert a significant effect on pain in patients with chronic pain. They discussed potential reasons that invasive brain stimulation showed a larger effect in this meta-analysis; these findings encourage continuation of research in this area and highlight the need for well-designed clinical trials to define the role of brain stimulation in pain management. These investigators stated that future studies should address several questions (e.g., the duration of the effects, parameters of stimulation, and the use of medications). More importantly, sham-controlled trials on invasive brain stimulation for pain treatment should be carried out. This is in agreement with the observations of Fontaine et al (2009) who stated that studies with a better design are mandatory to confirm the effectiveness of MCS for the treatment of chronic neuropathic pain.

Plow and colleagues (2009) noted that residual motor deficits frequently linger after stroke. Search for newer effective strategies to promote functional recovery is ongoing. Brain stimulation, as a means of directing adaptive plasticity, is appealing. Animal studies and phase I and II trials in humans have indicated safety, feasibility, and efficacy of combining rehabilitation and concurrent invasive cortical stimulation. However, a recent phase III trial showed no advantage of the combination. These researchers critically reviewed results of various trials and discussed the factors that contributed to the distinctive result. Regarding cortical stimulation, it is important
to determine (i) the location of peri-infarct representations by integrating multiple neuro-anatomical and physiological techniques; (ii) the role of other mechanisms of stroke recovery; (iii) the viability of peri-infarct tissue and descending pathways; (iv) the lesion geometry to ensure no alteration/displacement of current density; and (v) the applicability of lessons generated from non-invasive brain stimulation studies in humans. In terms of combining stimulation with rehabilitation, the following points should be understood (i) the principle of homeostatic plasticity; (ii) the effect of ongoing cortical activity and phases of learning; and (iii) that subject-specific intervention may be necessary. The authors concluded that future cortical stimulation trials should consider the factors that may have contributed to the peculiar results of the phase III trial and address those in future study designs.

Lefaucheur et al (2009) presented the results of the first RCT using chronic MCS for the treatment of refractory peripheral neuropathic pain. A total of 16 patients were included with pain origin as follows: trigeminal neuralgia (n = 4), brachial plexus lesion (n = 4), neurofibromatosis type-1 (n = 3), upper limb amputation (n = 2), herpes zoster ophthalmicus (n = 1), atypical orofacial pain secondary to dental extraction (n = 1) and traumatic nerve trunk transection in a lower limb (n = 1). A quadripolar lead was implanted, under radiological and electrophysiological guidance, for epidural cortical stimulation. A randomized cross-over trial was performed between 1 and 3 months post-operative, during which the stimulator was alternatively switched "on" and "off" for 1 month, followed by an open phase during which the stimulator was switched "on" in all patients. Clinical assessment was performed up to 1 year after implantation and was based on the following evaluations: VAS, brief pain inventory, McGill Pain questionnaire, sickness impact profile and medication quantification scale. The cross-over trial included 13 patients and showed a reduction of the McGill Pain questionnaire-pain rating index (p = 0.0166, Wilcoxon test) and McGill Pain questionnaire sensory subscore (p = 0.01) when the stimulator was switched "on" compared to
the "off-stimulation" condition. However, these differences did not persist after adjustment for multiple comparisons. In the 12 patients who completed the open study, the VAS and sickness impact profile scores varied significantly in the follow-up and were reduced at 9 to 12 months post-operative, compared to the pre-operative baseline. At final examination, the mean rate of pain relief on VAS scores was 48% (individual results ranging from 0% to 95%) and MCS efficacy was considered as good or satisfactory in 60% of the patients. Pain relief after 1 year tended to correlate with pain scores at 1 month post-operative, but not with age, pain duration or location, pre-operative pain scores or sensory-motor status. Although the results of the cross-over trial were slightly negative, which may have been due to carry-over effects from the operative and immediate post-operative phases, observations made during the open trial were in favor of a real efficacy of MCS in peripheral neuropathic pain. Analgesic effects were obtained on the sensory-discriminative rather than on the affective aspect of pain. The authors concluded that these findings suggested that the indication of MCS might be extended to various types of refractory, chronic peripheral pain beyond TNP. The results of this small study needs to be validated by well-designed studies.

Anderson et al (2009) reported on a patient with a neuropathic facial pain syndrome, including elements of trigeminal neuralgia, glossopharyngeal neuralgia, and dysphagia. After failing medical and surgical decompressive treatments, the patient underwent implantation of a MCS system. The patient was a 54-year old woman who had a 14-year history of left sided facial pain, throat pain, and associated nausea and vomiting. She failed several open surgical and percutaneous procedures for her facial pain syndrome. Additionally, several medication trial attempts were unsuccessful. Imaging studies were normal. The patient underwent placement of a right-sided MCS system for treatment of her neuropathic facial pain syndrome. The procedure was well-tolerated, and the trial stimulator provided promising results. The permanent MCS generator needed to be re-programmed at the time of the
5-week follow-up visit to optimize symptom relief. The patient demonstrated dramatic improvements in her neuropathic facial and oral pain, including improvements in swallowing toleration, after the 5-week follow-up examination with sub-threshold MCS. A decline in treatment efficacy also occurred 2 years after implantation due to generator depletion. Symptom improvement returned with stimulation after the generator was replaced. The authors concluded that a novel implantable MCS system was used to treat this patient's neuropathic facial pain. Durable improvements were noted not only in her facial pain, but also in swallowing toleration. The ultimate role of MCS in the treatment of pain conditions is still not well-defined but might play a part in refractory cases and, as in this case, might improve other functional issues, including dysphagia.

In a double-blind, placebo-controlled trial, Di Lazzaro and colleagues (2009) tested the hypothesis that repetitive transcranial magnetic stimulation given as continuous theta burst stimulation (cTBS), repeated monthly for 1 year, would affect amyotrophic lateral sclerosis (ALS) progression. A total of 20 patients with ALS were randomly allocated to blinded real or placebo stimulation. Continuous theta burst stimulation of the motor cortex was performed for 5 consecutive days every month for 1 year. Primary outcome was the rate of decline as evaluated with the revised ALS functional rating scale (ALSFRS-R). Treatment was well-tolerated. There was no significant difference in the ALSFRS-R score deterioration between patients treated with real or placebo stimulation. ALSFRS-R mean scores declined from 32.0 (SD 7.1) at study entry to 23.1 (SD 6.3) at 12 months in patients receiving real cTBS and from 31.3 (SD 6.9) to 21.2 (SD 6.0) in those receiving placebo stimulation. Although cTBS proved a safe procedure, on the basis of the present findings a larger randomized confirmatory trial seems unjustified in ALS patients, at least in advanced stage of the disease.

Central pain syndrome is a neurological condition caused by damage to or dysfunction of the central nervous system (CNS), which includes the brain, brainstem, and spinal cord. This
syndrome can be caused by stroke, multiple sclerosis, tumors, epilepsy, brain or spinal cord trauma, or Parkinson's disease.  

Moreno-Duarte et al (2014) reviewed initial efficacy, safety and potential predictors of response by assessing the effects of neural stimulation techniques to treat spinal cord injury (SCI) pain. A literature search was performed using the PubMed database including studies using the following targeted stimulation strategies: transcranial direct current stimulation (tDCS), high-definition tDCS (HD-tDCS), repetitive transcranial magnetic stimulation (rTMS), cranial electrotherapy stimulation (CES), transcutaneous electrical nerve stimulation (TENS), spinal cord stimulation (SCS) and MCS, published prior to June of 2012. These researchers included studies from 1998 to 2012. A total of 8 clinical trials and 1 naturalistic observational study (9 studies in total) met the inclusion criteria. Among the clinical trials, 3 studies assessed the effects of tDCS, 2 of CES, 2 of rTMS and 1 of TENS. The naturalistic study investigated the analgesic effects of SCS. No clinical trials for epidural MCS or HD-tDCS were found. Parameters of stimulation and also clinical characteristics varied significantly across studies. Three out of 8 studies showed larger effects sizes (0.73, 0.88 and 1.86, respectively) for pain reduction. Classical neuropathic pain symptoms such as dysesthesia (defined as an unpleasant burning sensation in response to touch), allodynia (pain due to a non-painful stimulus), pain in paroxysms, location of SCI in thoracic and lumbar segments and pain in the lower limbs seem to be associated with a positive response to neural stimulation. No significant adverse effects were reported in these studies. The authors concluded that chronic pain in SCI is disabling and resistant to common pharmacologic approaches. Electrical and magnetic neural stimulation techniques have been developed to offer a potential tool in the management of these patients. Although some of these techniques are associated with large standardized mean differences to reduce pain, these researchers found an important variability in these results.
across studies. The authors concluded that there is a clear
need for the development of methods to decrease treatment
variability and increase response to neural stimulation for pain
treatment.

Bolognini et al (2013) stated that limb amputation may lead to
chronic painful sensations referred to the absent limb, i.e.,
phantom limb pain (PLP), which is likely subtended by
maladaptive plasticity. These researchers examined if tDCS, a
non-invasive technique of brain stimulation that can modulate
neuroplasticity, can reduce PLP. In 2 double-blind, sham-
controlled experiments in subjects with unilateral lower or
upper limb amputation, they measured the effects of a single
session of tDCS (2 mA, 15 mins) of the primary motor cortex
(M1) and of the posterior parietal cortex (PPC) on PLP, stump
pain, non-painful phantom limb sensations and telescoping.
Anodal tDCS of M1 induced a selective short-lasting decrease of
PLP, whereas cathodal tDCS of PPC induced a selective short-
lasting decrease of non-painful phantom sensations; stump pain
and telescoping were not affected by parietal or by motor
tDCS. These findings demonstrated that painful and non-
painful phantom limb sensations are dissociable phenomena.
Phantom limb pain is associated primarily with cortical
excitability shifts in the sensorimotor network; increasing
excitability in this system by anodal tDCS has an antalgic effect
on PLP. Conversely, non-painful phantom sensations are
associated to a hyper-excitation of PPC that can be normalized
by cathodal tDCS. The authors concluded that this evidence
highlighted the relationship between the level of excitability of
different cortical areas, which underpins maladaptive plasticity
following limb amputation and the phenomenology of
phantom limb, and it opens up new opportunities for the use of
tDCS in the treatment of PLP. Well-designed studies are needed
to ascertain the effectiveness of MCS in the treatment of PLP.

Moore et al (2014) noted that chronic neuropathic pain affects
8.2 % of adults, extrapolated to roughly 18 million people every
year in the United States. Patients who have pain that cannot
be controlled with pharmacologic management or less invasive techniques can be considered for deep brain stimulation or MCS. These techniques are not currently approved by the Food and Drug Administration for chronic pain and are, thus, considered off-label use of medical devices for this patient population. The authors stated that conclusive effectiveness studies are still needed to demonstrate the best targets as well as the reliability of the results with these approaches.

In a double-blind, cross-over, multi-center, pilot study, Rieu et al (2014) evaluated the effectiveness of epidural MCS on dystonia, spasticity, pain, and quality of life in patients with dystonia secondary to a focal basal ganglia (BG) lesion. A total of 5 patients with dystonia secondary to a focal BG lesion were included in this study. Two quadri-polar leads were implanted epidurally over the M1 and the premotor cortex, contralateral to the most dystonic side. The leads were placed parallel to the central sulcus. Only the posterior lead over M1 was activated in this study. The most lateral or medial contact of the lead (depending on whether the dystonia predominated in the upper or lower limb) was selected as the anode, and the other 3 as cathodes. One month post-operatively, patients were randomly assigned to on- or off-stimulation for 3 months each, with a 1-month washout between the 2 conditions. Voltage, frequency, and pulse width were fixed at 3.8 V, 40 Hz, and 60 μs, respectively. Evaluations of dystonia (Burke-Fahn-Marsden Scale), spasticity (Ashworth score), pain intensity (VAS), and quality of life (36-Item Short Form Health Survey) were performed before surgery and after each period of stimulation. Burke-Fahn-Marsden Scale, Ashworth score, pain intensity, and quality of life were not statistically significantly modified by MCS. The authors concluded that bipolar epidural MCS failed to improve any clinical feature in dystonia secondary to a focal BG lesion.

Slotty et al (2015) reported a retrospective long-term analysis of patients neuropathic pain treated with MCS over a median follow-up of 39.1 months. A total of 23 closely followed patients treated with MCS were retrospectively analyzed. Reduction in
pain measured on a VAS was defined as the primary outcome parameter; VAS pain level and adverse events were documented at the 1-, 3-, 6-, 12-, 18- and 24-month follow-ups. The mean VAS under best medical treatment was 7.8 (SD 1.2, range of 5 to 9) with escalation to 9.3 (SD 0.9, range of 6 to 10) when the patients' medications were missed or delayed. About 50% of the patients experienced a satisfactory (greater than 50%) reduction in pain during the first month of treatment. The best treatment results were seen at the 3-month follow-up (mean VAS of 4.8, SD 1.9, -37.2% compared to baseline). A decline in the treatment effect was generally observed at the subsequent follow-up assessments; 6 patients had their devices explanted during the follow-up period due to loss of treatment effect. The authors concluded that MCS failed to provide long-term pain control for neuropathic pain. They noted that many aspects of MCS still remain unclear; and means must be developed to overcome the problems in this promising technique.

In a cross-over, double-blind, sham-controlled study, Bolognini et al (2015) examined the analgesic effects of tDCS over the motor cortex on post-amputation PLP. A total of 8 subjects with unilateral lower or upper limb amputation and chronic PLP were included in this study. For 5 consecutive days, anodal (active or sham) tDCS was applied over the motor cortex for 15 minutes at an intensity of 1.5 mA. The 5-day treatment with active, but not sham, tDCS induced a sustained decrease in background PLP and in the frequency of PLP paroxysms, which lasted for 1 week after the end of treatment. Moreover, on each day of active tDCS, patients reported an immediate PLP relief, along with an increased ability to move their phantom limb. Patients' immediate responses to sham tDCS, on the contrary, were variable, marked by an increase or decrease of PLP levels from baseline. The authors concluded that these results showed that a 5-day treatment of MCS with tDCS can induce stable relief from PLP in amputees. They stated that neuromodulation targeting the motor cortex appears to be a promising option for the management of this debilitating neuropathic pain condition, which is often refractory to classic
pharmacologic and surgical treatments.

Ngernyam et al (2015) examined the effects of tDCS in patients with neuropathic pain from SCI. This study tested the hypothesis that pain reduction with tDCS is associated with an increase in the peak frequency spectrum density in the theta-alpha range. A total of 20 patients with SCI and bilateral neuropathic pain received single sessions of both sham and anodal tDCS (2 mA) over the left primary motor area (M1) for 20 minutes. Treatment order was randomly assigned. Pre- to post-procedure changes in pain intensity and peak frequency of electroencephalogram (EEG) spectral analysis were compared between treatment conditions. The active treatment condition (anodal tDCS over M1) but not sham treatment resulted in significant decreases in pain intensity. In addition, consistent with the study hypothesis, peak theta-alpha frequency (PTAF) assessed from an electrode placed over the site of stimulation increased more from pre- to post-session among participants in the active tDCS condition, relative to those in the sham tDCS condition. Moreover, these researchers found a significant association between a decrease in pain intensity and an increase in PTAF at the stimulation site. The authors concluded that these findings were consistent with the possibility that anodal tDCS over the left M1 may be effective, at least in part, because it results in an increase in M1 cortical excitability, perhaps due to a pain inhibitory effect of MCS that may influence the descending pain modulation system. They stated that future research is needed to determine if there is a causal association between increased left anterior activity and pain reduction.

Zanjani et al (2015) examined the effects of rTMS targeting the primary motor cortex (M1) in the treatment of motor signs in PD. Studies meeting inclusion criteria were analyzed using meta-analytic techniques and the Unified Parkinson's Disease Rating Scale (UPDRS) sections II and III were used as outcome measures. In order to determine the treatment effects of rTMS, the UPDRS II and III scores obtained at baseline, same day, to 1 day post-rTMS treatment (short-term follow-up) and 1-month
post-stimulation (long-term follow-up) were compared between the active and sham rTMS groups. Additionally, the placebo effect was evaluated as the changes in UPDRS III scores in the sham rTMS groups. A placebo effect was not demonstrated, because sham rTMS did not improve motor signs as measured by UPDRS III. Compared with sham rTMS, active rTMS targeting the M1 significantly improved UPDRS III scores at the short-term follow-up (Cohen's d of 0.27, UPDRS III score improvement of 3.8 points). When the long-term follow-up UPDRS III scores were compared with baseline scores, the standardized effect size between active and sham rTMS did not reach significance. However, this translated into a significant non-standardized 6.3-point improvement on the UPDRS III. No significant improvement in the UPDRS II was found. The authors concluded that rTMS over the M1 may improve motor signs; and further studies are needed to provide a definite conclusion.

**Obsessive-Compulsive Disorder:**

Saba and colleagues (2015) stated that rTMS and tDCS are non-invasive brain stimulation methods that became widely used as therapeutic tools during the past 20 years especially in cases of depression and schizophrenia. Low frequency rTMS and cathodal effect of tDCS inhibits cortical functioning while high frequency and anodal effect of tDCS have the opposite effect. Prolonged and repetitive application of either methods leads to changes in excitability of the human cortex that outlast the period of stimulation. Both rTMS and tDCS induce functional changes in the brain-modulating neural activity at cortical level. These investigators reviewed rTMS and tDCS effects in clinical trials for obsessive-compulsive disorder (OCD). Low frequency rTMS, particularly targeting the supplementary motor area and the orbital frontal cortex, seems to be the most promising in terms of therapeutic efficacy while older studies targeting the prefrontal dorsal cortex were not as successful. The authors concluded that tDCS clearly needs to be investigated in large scale and sufficiently powered RCTs. They stated that from a general point of view, these non-invasive
techniques hold promise as novel therapeutic tools for OCD patients.

Complex Regional Pain Syndrome:

Lopez and colleagues (2016) described a case of a 30-year old woman who suffered a traumatic injury of the right brachial plexus, developing severe complex regional pain syndrome type II (CRPS-II). After clinical treatment failure, SCS was indicated with initial positive pain control. However, after 2 years her pain progressively returned to almost baseline intensity before SCS. Additional motor cortex electrode implant was then proposed as a rescue therapy and connected to the same pulse generator. This method allowed simultaneous MCS and SCS in cycling mode with independent stimulation parameters in each site. At 2 years follow-up, the patient reported sustained improvement in pain with dual stimulation, reduction of painful crises, and improvement in quality of life. The authors concluded that the encouraging results in this case suggested that this can be an option as add-on therapy over SCS as a possible rescue therapy in the management of CRPS-II. However, they stated that comparative studies must be performed in order to determine the effectiveness of this therapy.

Traumatic Brain Injury:

Clayton and associates (2016) noted that there is growing evidence that electrical and magnetic brain stimulation can improve motor function and motor learning following brain damage. Rodent and primate studies have strongly demonstrated that combining cortical stimulation (CS) with skilled motor rehabilitative training enhances functional motor recovery following stroke. Brain stimulation following traumatic brain injury (TBI) is less well studied, but early pre-clinical and human pilot studies suggested that it is a promising treatment for TBI-induced motor impairments as well. These researchers discussed the evidence supporting brain stimulation efficacy derived from the stroke research field as proof of principle and
then reviewed the few studies exploring neuromodulation in experimental TBI studies.

**CPT Codes / HCPCS Codes / ICD-10 Codes**

*Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":*

**CPT codes not covered for indications listed in the CPB:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>61850</td>
<td>Twist drill or burr hole(s) for implantation of neurostimulator electrodes, cortical</td>
</tr>
<tr>
<td>61860</td>
<td>Craniectomy or craniotomy for implantation of neurostimulator electrodes, cerebral, cortical</td>
</tr>
<tr>
<td>61885</td>
<td>Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to a single electrode array</td>
</tr>
<tr>
<td>61886</td>
<td>with connection to two or more electrode arrays</td>
</tr>
<tr>
<td>64573</td>
<td>Incision for implantation of neurostimulator electrodes; cranial nerve</td>
</tr>
<tr>
<td>95961</td>
<td>Functional cortical and subcortical mapping by stimulation and/or recording of electrodes on brain surface, or of depth electrodes, to provoke seizures or identify vital brain structures; initial hour of physician attendance</td>
</tr>
<tr>
<td>+ 95962</td>
<td>each additional hour of physician attendance (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>95970</td>
<td>Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude and duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); simple or complex brain, spinal cord, or peripheral (i.e., cranial nerve, peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, without reprogramming</td>
</tr>
</tbody>
</table>

**Other CPT codes related to the CPB:**
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>+61781</td>
<td>Stereotactic computer-assisted (navigational) procedure; cranial, intradural (list separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>+61782</td>
<td>Cranial, extradural (list separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>61880</td>
<td>Revision or removal of intracranial neurostimulator electrodes</td>
</tr>
<tr>
<td>61888</td>
<td>Revision or removal of cranial neurostimulator pulse generator or receiver</td>
</tr>
<tr>
<td>70551-70553</td>
<td>Magnetic resonance (e.g., proton) imaging, brain (including brain stem)</td>
</tr>
<tr>
<td>70554-70555</td>
<td>Magnetic resonance imaging, brain, functional MRI</td>
</tr>
<tr>
<td>95927</td>
<td>Short-latency somatosensory evoked potential study, stimulation of any/all peripheral nerves or skin sites, recording from the central nervous system; in the trunk or head</td>
</tr>
<tr>
<td>95965-95967</td>
<td>Magnetoencephalography (MEG), recording and analysis</td>
</tr>
<tr>
<td>96020</td>
<td>Neurofunctional testing selection and administration during noninvasive imaging functional brain mapping, with test administered entirely by a physician or psychologist, with review of test results and report</td>
</tr>
</tbody>
</table>

**HCPCS codes not covered for indications listed in the CPB:**
- C1767  Generator, neurostimulator (implantable), nonrechargeable
- C1770  Imaging coil, magnetic resonance (insertable)
- C1778  Lead, neurostimulator (implantable)
- C1787  Patient programmer, neurostimulator
- C1816  Receiver and/or transmitter, neurostimulator (implantable)
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1820</td>
<td>Generator, neurostimulator (implantable), non high-frequency with rechargeable battery and charging system</td>
</tr>
<tr>
<td>C1883</td>
<td>Adaptor/extension, pacing lead or neurostimulator lead (implantable)</td>
</tr>
<tr>
<td>C1897</td>
<td>Lead, neurostimulator test kit (implantable)</td>
</tr>
<tr>
<td>E0745</td>
<td>Neuromuscular stimulator, electronic shock unit</td>
</tr>
<tr>
<td>L8680</td>
<td>Implantable neurostimulator electrode, each</td>
</tr>
<tr>
<td>L8681</td>
<td>Patient programmer (external) for use with implantable programmable neurostimulator pulse generator</td>
</tr>
<tr>
<td>L8682</td>
<td>Implantable neurostimulator radiofrequency receiver</td>
</tr>
<tr>
<td>L8683</td>
<td>Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver</td>
</tr>
<tr>
<td>L8685</td>
<td>Implantable neurostimulator pulse generator, single array, rechargeable, includes extension</td>
</tr>
<tr>
<td>L8686</td>
<td>Implantable neurostimulator pulse generator, single array, non-rechargeable, includes extension</td>
</tr>
<tr>
<td>L8687</td>
<td>Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension</td>
</tr>
<tr>
<td>L8688</td>
<td>Implantable neurostimulator pulse generator, dual array, non-rechargeable, includes extension</td>
</tr>
<tr>
<td>L8689</td>
<td>External recharging system for battery (internal) for use with implantable neurostimulator</td>
</tr>
<tr>
<td>L8695</td>
<td>External recharging system for battery (external) for use with implantable neurostimulator</td>
</tr>
</tbody>
</table>

**ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>F42</td>
<td>Obsessive-compulsive disorder</td>
</tr>
<tr>
<td>F51.8</td>
<td>Other sleep disorders not due to a substance or known physiological condition</td>
</tr>
<tr>
<td>F98.4</td>
<td>Stereotyped movement disorders</td>
</tr>
<tr>
<td>G10</td>
<td>Huntington's disease</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>------------</td>
<td>----------------------------------------------------------</td>
</tr>
<tr>
<td>G12.21</td>
<td>Amyotrophic lateral sclerosis</td>
</tr>
<tr>
<td>G20, G21.0 - G21.9</td>
<td>Parkinson's disease and secondary parkinsonism</td>
</tr>
<tr>
<td>G23.0 - G23.9</td>
<td>Other degenerative diseases of basal ganglia</td>
</tr>
<tr>
<td>G24.01 - G24.9</td>
<td>Dystonia</td>
</tr>
<tr>
<td>G25.0 - G26</td>
<td>Extrapyramidal and movement disorders</td>
</tr>
<tr>
<td>G47.61</td>
<td>Periodic limb movement disorder</td>
</tr>
<tr>
<td>G47.69</td>
<td>Other sleep related movement disorders</td>
</tr>
<tr>
<td>G50.0</td>
<td>Trigeminal neuralgia</td>
</tr>
<tr>
<td>G54.6 - G54.7</td>
<td>Phantom limb syndrome</td>
</tr>
<tr>
<td>G60.0 - G60.9</td>
<td>Hereditary and idiopathic neuropathy</td>
</tr>
<tr>
<td>G80.3</td>
<td>Athetoid cerebral palsy</td>
</tr>
<tr>
<td>G89.0</td>
<td>Central pain syndrome</td>
</tr>
<tr>
<td>G89.21 - G89.29</td>
<td>Chronic pain, not elsewhere classified</td>
</tr>
<tr>
<td>G89.3</td>
<td>Neoplasm related pain (acute) (chronic)</td>
</tr>
<tr>
<td>G89.4</td>
<td>Chronic pain syndrome</td>
</tr>
<tr>
<td>G90.3</td>
<td>Multi-system degeneration of the autonomic nervous system</td>
</tr>
<tr>
<td>I69.051 - I69.059, I69.151 - I69.159, I69.251 - I69.259, I69.351 - I69.359, I69.851 - I69.859, I69.951 - I69.959</td>
<td>Hemiplegia and hemiparesis, sequelae of cerebrovascular disease</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>R13.0, R13.10</td>
<td>Aphagia and unspecified dysphagia</td>
</tr>
<tr>
<td>R25.0 - R25.9</td>
<td>Abnormal involuntary movements</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:

7. Tirakotai W, Riegel T, Sure U. Image-guided motor cortex
Bloomington, MN: Institute for Clinical Systems Improvement (ICSI); March 2007.


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Amendment to
Aetna Clinical Policy Bulletin Number: 0755
Motor Cortex Stimulation

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania
Revised 04/2017