Transcranial Magnetic Stimulation for Diagnosis of Residual Limb Neuromas

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ABSTRACT. Paysant J, André J-M, Martinet N, Beis J-M, Datié A-M, Henry S, Dap F. Transcranial magnetic stimulation for diagnosis of residual limb neuromas. Arch Phys Med Rehabil 2004;85:737-42.

Objective: To analyze the mechanism and examine the potential diagnostic contribution of transcranial magnetic stimulation (TMS) in diagnosing painful, clonic, and/or autonomic manifestations in amputees' residual limbs.

Design: Prospective study.

Setting: Regional rehabilitation institute at a medical school in France.

Participants: Thirty-four amputees (24 with myoclonus, stump pain, or trophic skin disorders; 10 controls with no stump symptoms).

Interventions: Not applicable.

Main Outcomes Measures: TMS performed before and after correcting prosthesis adaptation.

Results: TMS induced pain in 12 amputees, clonic manifestations in 4, and autonomic manifestations in 2. Twelve patients underwent magnetic resonance imaging that showed neuromas in all 12. After neuroma resection in 9 amputees, TMS no longer provoked abnormal manifestations. TMS did provoke abnormal manifestations after resection in 3 patients who had postoperative recurrent neuromas. The response to TMS was negative in subjects with a clinically silent neuroma (n=7). The response was also negative in all patients with other stump anomalies whose clinical manifestations fully regressed after conservative treatment. There was a highly significant correlation between the presence of a pathologic neuroma and TMS-induced abnormal manifestations ($P<.0001$).

Conclusions: TMS can provoke symptoms in patients who experience spontaneous or evoked symptoms related to a neuroma. Induced symptoms are proportional to spontaneous symptoms. Removing the neuroma can stop stump symptoms and reverse the TMS effect. The response to TMS was negative in the control subjects with clinically silent neuromas; conservative treatment was successful in these cases. TMS-induced abnormal manifestations underlying mechanisms are discussed (ephaptic transmission in neuromas).

Key Words: Amputation; Amputation stumps; Magnetic resonance imaging; Neuroma; Pain; Rehabilitation.

TRANSCRANIAL MAGNETIC STIMULATION (TMS) is a technique used to activate cortical motor areas and the corticospinal tract to generate motor-evoked potentials (MEPs) without causing a person discomfort.[1] TMS has been used very infrequently with amputees.[2,3]

We have observed that, in addition to the expected motor response to TMS, certain amputees present with other clinical manifestations such as pain, paresthesia, myoclonus, or vasomotor skin reactions. There have been rare reports of paresthesia, or an illusion of movement, in addition to the elicited motor response in normal or pathologic situations, a response attributed to extensive stimulation of the parietal cortex.[4,5] To our knowledge, however, no other team has reported pain elicited by TMS.[4,5] In amputees, elicitation of such symptoms in the stump suggests aberrant repair of sectioned nerves with crosstalk between motor nerve fibers and sensory and/or autonomic nerve fibers.

The purpose of this study was to analyze the effects of TMS in amputees with symptoms suggestive of a residual limb neuroma to determine the usefulness of TMS as a diagnostic tool.

A neuroma is a normal consequence of nerve repair after section.[6] All limb amputees have neuromas. In the first month after nerve section, they experience pain and paresthesia spontaneously or in response to minimal stimulation. Hormone factors and "artificial synapses" at the cut nerve ends have been hypothesized to be the cause.[6,7] These symptoms are usually transient and regress within a few weeks, spontaneously or with desensitization, and are followed by formation of a neuroma.

Residual limb neuromas, which develop during the normal healing process of the injured nerve after amputation, are generally silent. Occasionally, neuromas may be a source of persistent residual limb symptoms. This pathologic situation is believed to result from structural anomalies, called ephapses, that occur within the neuromas.[8,9] Ephapses consist of anastomoses or contacts between nerve fibers that may be of the same or different types.[10,11] This leads to persistent short circuits or ephaptic crosstalk between neighboring sensory (eg, somatognosis, nociception, proprioception) nerve fibers, autonomic nerve fibers, or motor nerve fibers, or any combination thereof. Anomalous nerve response or shunted nerve impulses[8] are also observed in other neurologic diseases, including facial hemispasm, the most common and widely studied condition[10,12]; peripheral neuropathies with chronic denervation[13]; or after nerve injury.[14] Activation of autonomic nerve fibers via ephapses[15] or with TMS[16] has been proposed as an explanation of complex regional pain syndrome. The clinical symptoms depend both on the efferent nerve fibers involved and on the antidromic nature of the excitation of certain nerve fibers in the neuroma's environment.[17] Crosstalk can result from (1) the indirect effect of afferent fibers (which may or may not be recurrent) and (2) ephaptic afferents (generally motor afferents). This leads to a situation where, for example, a motor impulse destined to stimulate muscle contraction in the residual

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limb could induce pain, paresthesia, or vasomotor skin reactions in the stump.

In clinical practice, it is difficult to recognize the pathologic nature of a neuroma. Magnetic resonance imaging (MRI) provides a good diagnostic clue by showing the presence of the neuroma and subcutaneous anomalies of the residual limb,[18,19] but it cannot show the cause-and-effect relationship between the neuroma and the clinical manifestations. Silent neuromas have the same MRI aspect as pathologic neuromas. Several electrophysiologic tests have been proposed to make a distinction, but TMS does not appear to have been studied.

In this study, we hypothesized that (1) TMS will cause symptoms in amputees who experience spontaneous or evoked stump symptoms when these residual limb symptoms are caused by a neuroma; and (2) TMS will have no effect when residual limb symptoms are not the result of ephaptic transmission in neuromas and will respond to conservative treatment.

METHODS

Participants

This prospective study was conducted with consecutive amputees who attended a specialized outpatient clinic between January 1, 2001, and January 1, 2002. Patients were divided into 2 groups. Group 1 included 24 patients over the age of 18 years who had had a prosthesis for at least 6 months and who had complained of pain, abnormal movements, and/or vasomotor disorders of the stump for at least 2 months, regardless of the level of or the reason for the amputation. Patients with epilepsy, a contraindication for TMS (1 amputee who underwent neuroma resection during the study period), or a stump wound were excluded. Group 2 was considered the control population and included 10 amputees over the age of 18 with a prosthesis for at least 6 months who had been chosen randomly from among patients without abnormal clinical manifestation of the residual limb. Complaints concerning phantom limbs were not considered. All patients were given both written and oral information describing the protocol and their participation was voluntary.

Study Protocol

The protocol included (1) a physical examination with a precise description of pain, (2) an MRI study of the residual limb to detect neuromas (detection limit, $<$10mm)[18] and signs of mechanical stress (bursitis, adventitious bursa, localized soft-tissue inflammation, bone marrow edema),[19] and (3) TMS. Subjects' prostheses were refit after they completed the study protocol. A second evaluation (physical examination, TMS) was performed 4 weeks later. Surgical resection was proposed if a neuroma was identified by MRI and the response to TMS was positive. A follow-up TMS was performed 6 weeks after surgical resection.

Transcranial Magnetic Stimulation

TMS was performed with a Mag-Lit machine.[a] This stimulator has a high-power generator (400–3000V), operating at 4000 to 20,000A and connected to a 5-cm stimulation coil (MC 125). The coil was placed on the patient's scalp, over the rolandic region, which was exposed to a magnetic field of 1 to 10T. Motor potentials were recorded with 2 surface electrodes placed on the stump. A salvo of ten 200-ms supramaximal stimulations was delivered. The operator was blinded to the history of the patients and was not informed of their complaints or of the clinical observations made before, during, or after the stimulation.

Pain, abnormal movements, and autonomic manifestations were recorded, as was total conduction time. The MEPs recorded in group 1 were compared with MEPs recorded in group 2, which were considered normal.

Assessment

Patients gave their subjective assessment of the clinical manifestations. Spontaneous paroxysmal residual limb pain was scored 0 (absent or tolerable pain, not requiring treatment) or 1 (intolerable pain, requiring treatment). Residual limb pain provoked by percussion was scored 0 (absent), L (local), or I (irradiation to the amputated limb segment). The patients' perceptions, as well as observations made during the physical examination or during stimulation, were used to assess other manifestations. Motor disorders were scored 0 (absent) or M (myoclonus), and autonomic disorders (sweating, skin reddening) were scored 0 (absent) or 1 (present). Paresthesia and illusions of movement were not considered, because it is known that such manifestations can be related to heightened sensitivity of the perceptual system to the motor cortical response to TMS.[4,5]

For each manifestation, it was noted whether the symptoms elicited by TMS were the same as the patient's usual complaints (spontaneous or evoked symptoms).

The total conduction time of the MEPs was the interval between stimulation of the motor cortex and the peripheral muscle response in an area recognized clinically near the stump. Response to TMS was considered positive (TMS+) when pain, abnormal movement, and/or skin reactions were generated and negative (TMS–) when no effect was observed.

Data Analysis

The statistical analysis was performed with GraphPad InStat[b] using the Fisher exact test (2-sided *P* value). Sensitivity and specificity were computed. A *P* value less than .05 was considered significant.

RESULTS

The characteristics of the study population are presented in table 1. Mean age of the 34 amputees (25 men, 9 women) was 50.7 years (range, 19–80y; median, 52y). The study protocol was performed a mean of 8 years after amputation (range, 1–53y; median, 4y). Amputation levels were leg (n=16), thigh (n=15), or forearm (n=3); 1 patient had bilateral lower-limb amputations. The condition leading to amputation was vascular disease in 13, trauma in 18, and tumor in 3.

Sixty-one sessions of TMS were performed with the 34 subjects. The morphology of the evoked potentials and the total conduction time were within the normal range in all patients in both groups.

Amputees Without Abnormal Stump Symptoms

MRI was normal in all 10 controls (group 2). TMS did not elicit pain, skin reaction, or clonic or abnormal movement of the residual limb in any of the controls (10 TMS–; 0 TMS+)

Amputees With Abnormal Stump Symptoms

The clinical data are presented in table 2. MRI showed 17 neuromas, 6 cases of bursitis or soft tissue inflammation, and 2 bone anomalies (group 1). MRI study results were normal in 3 patients and could not be interpreted in 2 because of artifacts.

Group 1 subjects with positive TMS responses. Magnetic stimulation elicited abnormal manifestations in 12 patients (TMS+). These manifestations were pain (n=10), myoclonus (n=8), and vasomotor skin reaction (n=3) and reproduced the

Table 1: Patients Characteristics

Group	No.	Age (y)	Gender	Etiology	Level/Side	Years After Amputation
1	10	53	M	Vasc	Femoral R	5
	13	36	F	Trauma	Tibial R/L	2
	15	33	M	Tumor	Femoral L	17
	12	52	F	Trauma	Tibial L	7
	2	50	M	Trauma	Forearm R	5
	29	56	F	Trauma	Femoral R	7
	23	34	M	Trauma	Finger R	3
	3	77	M	Trauma	Femoral L	53
	9	32	M	Tumor	Tibial L	12
	5	36	M	Trauma	Tibial L	20
	19	70	F	Vasc	Femoral R	1
	4	44	M	Trauma	Femoral R	12
	8	73	M	Vasc	Femoral L	7
	7	63	M	Vasc	Femoral L	5
	11	65	M	Vasc	Tibial R	4
	25	59	M	Vasc	Femoral R	4
	1	49	M	Trauma	Forearm L	8
	21	19	M	Trauma	Femoral L	1
	26	52	F	Vasc	Femoral R	1
	18	64	M	Trauma	Femoral L	2
	22	80	F	Trauma	Tibial L	36
	14	58	M	Tumor	Femoral L	2
	6	47	F	Trauma	Tibial R	28
	24	28	M	Trauma	Tibial L	2
2 (control)	16	52	M	Trauma	Tibial L	2
	17	56	M	Vasc	Tibial L	1
	20	59	M	Vasc	Tibial R	1
	27	53	M	Trauma	Femoral L	0.5
	30	38	M	Trauma	Forearm R	1
	31	58	M	Vasc	Tibial L	3
	28	48	F	Vasc	Tibial L	0.5
	32	37	M	Trauma	Tibial R	7
	33	61	M	Vasc	Tibial L	12
	34	29	F	Trauma	Femoral R	3

Abbreviations: F, female; L, left; M, male; R, right; Trauma, traumatic; Vasc, vascular.

paroxysmal manifestations experienced spontaneously (n=10) or evoked by percussion (n=12). At examination, pain was strictly focal (n=3) or irradiated (n=9).

One or several neuromas were identified in 11 of the 12 patients with a positive TMS test result. Persistence of the clinical manifestations led to an indication for surgical resection, which was performed in 9 patients. Two patients declined surgery. The clinical manifestations resolved totally in all patients after removal of the neuroma (n=9), and their postoperative TMS result was negative. In 1 patient, MRI did not show any sign of neuroma, and the pain disappeared progressively. TMS performed after resolution of pain and the response to it was negative.

Four patients had undergone prior neuroma resection, and 2 experienced a recurrence during the study period. In 1 patient, residual limb pain that began 4 months after resection was highly suggestive of neuroma recurrence. TMS again elicited abnormal phenomena, and a second resection was performed. Removing the neuroma led to total regression of both the spontaneous and TMS-induced manifestations.

Group 1 patients with negative TMS responses. TMS failed to elicit abnormal reaction in 14 patients in group 1. In these 14 TMS-negative patients, MRI showed bursitis or soft tissue inflammation (n=6), bone anomalies (n=2), and a lipoma. Their residual limb symptoms resolved with symptomatic treatment of inflammation and pain. In addition to the possible revision of the prosthesis, if necessary, this symptomatic treatment comprises successively stimulation-induced analgesia (transcutaneous electric stimulation) and local application of steroids and medications (conventional analgesics, opiates if pain persists). MRI also showed a neuroma (alone or in association with the preceding lesions) in 7 of these patients. The clinical course was favorable, with spontaneous resolution of the symptoms without resection of these "silent" neuromas.

Analysis with the Fisher exact test of the 2-way contingency tables, in which we compared the number of TMS-positive and TMS-negative patients with or without residual limb symptoms, with or without resolution of symptoms with symptomatic treatment, and with or without MRI-identified neuromas, showed highly significant *P* values. *P* was equal to .0001 for the first 2 conditions and *P* was equal to .0006 for the third condition. The row-by-column association was statistically significant. The sensitivity and specificity of TMS for the diagnosis of pathologic neuroma were excellent (value=1.000; 95% confidence interval [CI] for sensitivity; 0.6197–1.000; 95% CI for specificity, 0.5409–1.000).

DISCUSSION

In certain amputees, TMS elicits pain, abnormal movement, or vasomotor skin reactions. Analysis of this phenomenon

Table 2: Group 1 Clinical Data

No.	MRI*	Clinical Data†			TMS Initial	Treatment	Clinical Course‡	TMS Course
		Pain	Myoclonus	Vasomotor				
10 a	N(20*12)	+	+	–	P/M	Surgery	0	0
10 b	N(25)	+	+		P/M	Surgery	0	0
13 a	2*N(15)	+	+	–	P/M	Surgery	0	0
13 b	N(10) B	+	–		0	Prosthetic	0	*
15	N(10*15)	+	–	–	P	Surgery	0	0
12	N(10)	+	+	+	P/V/M	Surgery	0	0
2	N(2*15)	+	+	+	P/V	Surgery	0	0
29	N(15)	+	+	+	P/V/M	Surgery	0	0
23	ND	+	+	–	P	Surgery	<	0
3	N(12)	+	+	–	M	Prosthetic	>	ND
9	N(10)	+	+	–	0	Prosthetic	=	0
5	N(15)	–	+	+	M	Medical	>	M
19	N(3*10)	+	–	–	P	Prosthetic	0	0
4	N(12) B	+	–	–	0	Prosthetic	0	ND
8	N(10 B)	+	–	–	0	Prosthetic	0	ND
7	N(15*12)	+	–	–	0	Prosthetic	0	ND
11	N(10) infarct osseous	+	+	–	0	Prosthetic	<	ND
25	N(10) STI	+	–	–	0	Surgery	0	0
1	ND	+	–	–	P	Surgery denied	=	ND
21	ND	+	+	–	0	Prosthetic	>	P/M/V
26	STI	+	–	–	0	Prosthetic	0	ND
18	STI	+	–	–	0	Prosthetic	<	ND
22	0	+	–	–	0	Prosthetic	0	ND
14	0	+	–	–	0	Medical	0	ND
6	Fatigue fracture	+	–	–	0	Medical	0	ND
24	0	+	–	–	0	Prosthetic	<	ND

Abbreviations: B, bursitis; M, myoclonus spasm; N, neuroma; ND, no documentation; P, pain; STI, soft tissue inflammation; V, vasomotor skin reaction.
*Neuroma size in millimeters.
†+, intolerable pain (requires treatment); –, absent or tolerable pain (does not require treatment).
‡0, normalization; =, no change; <, decrease; >, increase.

showed the potential of TMS as a diagnostic tool for pathologic neuromas and provided insight into its underlying mechanism.

Diagnostic TMS

Evidence that the clinical phenomenon observed during TMS is the expression of a cause-and-effect relationship is provided by the fact that symptoms occurred during TMS in patients who experience spontaneous and evoked residual limb symptoms, and that these TMS-induced symptoms were equivalent to the spontaneous and evoked symptoms. Furthermore, TMS never induced symptoms in "control" amputees who did not experience spontaneous and evoked symptoms (Fisher exact test, $P=.0001$).

A positive TMS test was significantly linked with the presence of a neuroma. A neuroma was identified in 11 of the 12 amputees who exhibited abnormal responses to TMS (Fisher exact test, $P=.0006$). Furthermore, removing the neuroma stopped residual limb symptoms and inverted the TMS effect (9/9). As well, although the reappearance of clinical manifestations coinciding with a newly positive TMS test in the 2 subjects with recurrent neuroma is not formal proof of the relationship, it is in full agreement. TMS causes symptoms in patients who have residual limb symptoms when the symptoms result from a neuroma.

Nevertheless, the response to TMS was not positive in all amputees with neuromas. It was negative in 7 amputees with an MRI-proven neuroma. In all 7 of these patients, symptoms resolved totally with symptomatic treatment (notably, refitting the prosthesis). Because the symptoms responded to removal of the mechanical stress, the neuromas (which remained in situ) were not the causal agents and could be considered silent neuromas. A stump neuroma must be pathologic (suspected ephaptic transmission) for TMS to induce stump symptoms.

After correcting the fit of poorly adapted prostheses, the clinical course of residual limb symptoms was well correlated with the TMS results. Total regression of clinical manifestations correlated with a negative response to TMS, and their persistence correlated with a positive response to TMS (Fisher exact test, $P=.0006$). The response to TMS was always negative in all group 2 patients with no stump symptoms and in all group 1 patients whose manifestations were caused by mechanisms other than the neuroma (soft tissue inflammation, bony anomalies), which resolved after conservative treatment. Furthermore, in this series, the response to TMS was always negative in patients with no clinical symptoms and no MRI evidence of neuroma. It was also negative in patients with residual limb symptoms that were not due to ephaptic transmission in neuromas and that responded to conservative treatment.

A larger series would be necessary to obtain a perfectly valid assessment of TMS sensitivity and specificity, which appear to be excellent based on the results obtained here (value=1.00; 95% CI for sensitivity, 0.6917–1.000; 95% CI for specificity, 0.5409–1.000).

Neuromas were not identified on the MRI study in only 1 patient with a positive TMS test. With the MRI detection level

being less than 10mm, a small-sized neuroma may not have been recognized, which raises concern as to whether a positive TMS response might reveal neuritis or a mechanical process that increases the sensitivity of the neuroma membrane,[20] which could be reversible with regression of the process.[18] Further work is necessary to answer this question.

Underlying Mechanism (Ephaptic Transmission)

Our data provide clear evidence that the neuroma is the causal factor that leads to the residual limb symptoms that occur spontaneously or are induced by percussion and reproduced by TMS, but the actual ephaptic transmission within the neuroma is more difficult to show. Intermodal crosstalk is the only logical explanation of sensorial, painful, or autonomic response to motor stimulation. The fact that these phenomena are eliminated with removal of the neuroma (and thus any intraneuroma shunts) is indirect proof that ephaptic transmission occurs within the neuroma. The myoclonic movements we observed had exactly the same clinical features as the spinal myoclonic movements described in amputees.[21,22] This suggests that spinal mediation would also be involved, but it does not contradict the fact that the neuroma is necessary to trigger the phenomenon. Structural changes in the central and peripheral nervous system that occur after limb amputation are well described and include modifications in the residual limb, spinal ganglions, the posterior horn of the spinal cord, the somatosensory cortex, and the basal nuclei.[9,23-25] These changes appear to have a facilitating role.

It is well known that the plasticity of the nervous system leads to functional remodeling after amputation. Such functional remodeling is especially well demonstrated in the motor and sensory cortex[23,26,27] and could have a facilitating effect on the observed phenomenon. However, functional remodeling cannot be considered as the causal mechanism, because it is a common feature found in all amputees and not just in certain amputees as shown here. The same would hold for dynamic reorganization of the cortex secondary to the repeated stress placed on the stump from walking.[28]

Limitations

Undoubtedly, certain neuromas devoid of ephaptic transmission involving motor fibers would escape detection by diagnostic TMS.

Practical Implications: Diagnostic TMS in Amputees

TMS appears to be a good diagnostic tool for identifying pathologic neuromas in amputation stumps that should be removed surgically. A TMS test should be performed in amputees with pain, abnormal movements, or autonomic manifestations of the residual limb that persist after adequate adaptation of the prosthesis. If the TMS test result is positive, an MRI study should be obtained to search for a neuroma.

CONCLUSIONS

TMS with recording of MEPs can be indicated for amputees to show the presence of ephaptic transmission and, indirectly, the presence of a residual limb neuroma. Eliciting sensory, painful, and/or autonomic reactions reproducing the disorders experienced by such patients is a simple and rapid way to distinguish pathologic neuromas from silent neuromas and to confirm that a neuroma detected by MRI is implicated in the generation of the clinical symptoms. A positive TMS test result is a strong argument for surgical removal of the neuroma in these patients.

References

1. Curra A, Modugno N, Inghilleri M, Manfredi M, Hallett M, Berardelli A. Transcranial magnetic stimulation techniques in clinical investigation. Neurology 2002;59:1851-9.
2. Cohen LG, Bandinelli S, Findley TW, Hallett M. Motor reorganization after upper limb amputation in man. A study with focal magnetic stimulation. Brain 1991;114:615-27.
3. Mills KR. Magnetic brain stimulation: a review after 10 years experience. Electroencephalogr Clin Neurophysiol 1999; 49(Suppl):239-44.
4. Amassian VE, Somasundaram M, Rothwell JC, et al. Paraesthesias are elicited by single pulse, magnetic coil stimulation of motor cortex in susceptible humans. Brain 1991;114(Pt 6):2505-20.
5. Sugishita M, Takayama Y. Paraesthesia elicited by repetitive magnetic stimulation of the postcentral gyrus. Neuroreport 1993; 4:569-70.
6. Cajal S. Mecanismo de la regeneraciòn de los nervios. Trab Lab Invest Biol 1905;4:119-210.
7. Granit R, Skoglund C. Facilitation, inhibition, and depression at the "artificial synapse" formed by the cut end of the mammalian nerve. J Physiol (Lond) 1945;103:435-48.
8. Tinel J. Affections traumatiques des nerfs. In: Roger G, Widal F, Teissier P, editors. Nouveau traité de médecine. Paris: Masson; 1927. p 1-98.
9. Sunderland S. Nerves and nerves injuries. 2nd ed. Edinburgh: Churchill Livingstone; 1978.
10. Roth G, Magistris MR, Pinelli P, Rilliet B. Cryptogenic hemifacial spasm. A neurophysiological study. Electromyogr Clin Neurophysiol 1990;30:361-70.
11. Fried K, Govrin-Lippmann R, Devor M. Close apposition among neighbouring axonal endings in a neuroma. J Neurocytol 1993; 22:663-81.
12. Glocker FX, Krauss JK, Deuschl G, Seeger W, Lucking CH. Hemifacial spasm due to posterior fossa tumors: the impact of tumor location on electrophysiological findings. Clin Neurol Neurosurg 1998;100:104-11.
13. Seltzer Z, Devor M. Ephaptic transmission in chronically damaged peripheral nerves. Neurology 1979;29:1061-4.
14. Sebag J, Sadun AA. Aberrant regeneration of the third nerve following orbital trauma. Synkinesis of the iris sphincter. Arch Neurol 1983;40:762-4.
15. Schwartzman RJ, McLellan TL. Reflex sympathetic dystrophy. A review. Arch Neurol 1987;44:555-61.
16. Dachy B, Denis L, Deltenre P. Usefulness of transcranial magnetic stimulation to predict the development of reflex sympathetic dystrophy poststroke: a pilot study. Arch Phys Med Rehabil 2002;83:730-2.
17. Pover CM, Lisney SJ. An electrophysiological and histological study of myelinated axon regeneration after peripheral nerve injury and repair in the cat. J Neurol Sci 1988;85:281-91.
18. Martinet N, Foisneau-Lottin A, Henrot P, Paysant J, Blum A, André JM. [MRI and leg stump neuroma] [French]. Ann Readapt Med Phys 2001;44:600-7.
19. Foisneau-Lottin A, Martinet N, Henrot P, Paysant J, Blum A, André JM. Bursitis, bursae adventitiae, localized soft tissue inflammation and bone marrow edema in tibial stumps: MRI contribution to diagnosis and management of mechanical stress complications. Arch Phys Med Rehabil 2003;84:770-7.
20. Kretschmer T, England JD, Happel LT, et al. Ankyrin G and voltage gated sodium channels colocalize in human neuroma—key proteins of membrane remodeling after axonal injury. Neurosci Lett 2002;323:151-5.
21. Marion MH, Gledhill RF, Thompson PD. Spasms of amputation stumps: a report of 2 cases. Mov Disord 1989;4:354-8.
22. De Mattos JP, Rosso AL, Carneiro AJ, Novis S. Spinal myoclonus: report of four cases. Arq Neuropsiquiatr 1993;51:498-501.
23. Schwenkreis P, Witscher K, Janssen F, et al. Changes of cortical excitability in patients with upper limb amputation. Neurosci Lett 2000;293:143-6.
24. Hamzei F, Liepert J, Dettmers C, et al. Structural and functional cortical abnormalities after upper limb amputation during childhood. Neuroreport 2001;12:957-62.

25. Chen R, Corwell B, Yaseen Z, Hallett M, Cohen LG. Mechanisms of cortical reorganization in lower-limb amputees. J Neurosci 1998;18:3443-50.
26. Borsook D, Becerra L, Fishman S, et al. Acute plasticity in the human somatosensory cortex following amputation. Neuroreport 1998;20:1013-7.
27. Elbert T, Flor H, Birbaumer N, et al. Extensive reorganization of the somatosensory cortex in adult humans after nervous system injury. Neuroreport 1994;5:2593-7.
28. Braun C, Heinz U, Schweizer R, Wiech K, Birbaumer N, Topka H. Dynamic organization of the somatosensory cortex induced by motor activity. Brain 2001;124:2259-67.

Suppliers

a. Dantec Dynamics A/S, Tonsbakken 16-18, PO Box 121, DK-2740 Skovlunde, Denmark.
b. Version 3.0a; GraphPad Software, 5755 Oberlin Dr, Ste 110, San Diego, CA 92121.