Pre-operative Evaluations

Stephane Thobois, MD, PhD[1] Takaomi Taira, MD[2] Cynthia Comella, MD, PhD[3]
Elena Moro, MD, PhD[4] Susan Bressman, MD, PhD[5] Alberto Albanese, MD, PhD[6]

[1] Université Lyon I, Hospices Civils de Lyon, Hôpital Neurologique Pierre Wertheimer and CNRS, UMR 5229, Lyon, France
[2] Department of Neurosurgery, Tokyo Women's Medical University, Tokyo, Japan.
[3] Department of Neurological Sciences, Rush University Medical Center, Chicago, IL, USA
[4] Movement Disorders Center, TWH, UHN, Division of Neurology, University of Toronto, Toronto, Ontario, Canada
[5] Department of Neurology, Beth Israel Medical Center, New York, NY 10003, USA
[6] Fondazione IRCCS Istituto Neurologico Carlo Besta and Università Cattolica del Sacro Cuore, Milan, Italy

Corresponding author:
S. Thobois
Hôpital Neurologique Pierre Wertheimer, Neurologie C, 59 Bd Pinel, 69677 Lyon, France
Tel.: 33 4 72 35 72 18
Fax: 33 4 72 35 73 51
E-mail: stephane.thobois@chu-lyon.fr

Financial Disclosures: the authors of this article have received no compensation for the research covered in this article.

S. Thobois

T. Taira

C. Comella

E. Moro has received honoraria for consulting services and lecturing from Medtronic. She has also received research grant support from CurePSP, St. Jude Medical and Canadian Institute of Health Research.

S. Bressman

A. Albanese

ABSTRACT

The preoperative evaluation in dystonia aims at characterizing the severity and topography of motor symptoms in patients, who have previously been selected for deep brain stimulation (DBS). Commonly used scales for clinical assessment are the Burke Fahn Marsden (BFM) scale for generalized dystonia and the Toronto Western Spasmodic Torticollis Scale (TWSTRS) for cervical dystonia. Motor assessment is completed by quality of life and functional scales, such as the SF-36 or PDQ-39. Validated rating scales for cranial or upper limb dystonia are lacking. In common clinical practice, these outcome measures can be administrated in an open-label fashion since double blind assessment is only required for ascertaining new treatment indications or research purposes. The same measures are to be used postoperatively to revaluate outcome after DBS. Brain MRI is required to confirm diagnosis and assess structural abnormalities. Other imaging techniques, particularly functional imaging are used for research purposes.

INTRODUCTION

The preoperative evaluation is a crucial step in the management of patients with dystonia who are candidate for deep brain stimulation (DBS). Issues related to the inclusion/exclusion criteria for DBS surgery have been detailed in a previous chapter[1] and will not be discussed again. Before entering preoperative workup, each patient should be classified along with the three axes of aetiology, age of onset and spread of dystonia;[2] this will allow identifying the most appropriate tools for assessment. The preoperative evaluation aims at characterizing the severity and topography of motor symptoms and their impact on activities of daily living (ADLs) and social activities, and it provides a baseline to serve as a reference for mid- and long-term postoperative evaluations. The quality and accuracy of the preoperative assessment and the choice of assessment tools is crucial as will affect all subsequent postoperative comparisons. The preoperative phase also includes a number of steps related to the assessment of the surgical risk and the determination of the surgical trajectory. This paper will review the evidence for the application and evaluation of the clinical scales to be used for preoperative and postoperative evaluations of dystonia patients undergoing DBS.

METHODS

Search Strategy

The literature search was performed using PubMed, CINAHL and the Cochrane Collaborative databases initially from 1980 to January 2008 using the terms: dystonia AND deep brain stimulation; pallidal stimulation AND dystonia; subthalamic stimulation AND dystonia; thalamic stimulation AND dystonia; secondary dystonia AND DBS; neurodegenerative diseases AND DBS. The search was combined with the one used for neuropsychology, neuropsychiatry, microelectrode recording, neuroimaging, electrophysiology, surgical techniques, complications and targeting. Only English-language publications involving human subjects' were considered. A total of 235 papers were retrieved. To facilitate the committees' work, the articles were divided in 3 groups, which often overlapped: pre-operative, intra-operative and post-operative. A PDF file was created for each paper obtained from the search and put in a CD that was mailed to the members. During the writing phase additional 71 articles were added to update the search, covering the period from January 2008 to September 2009.

Process of Generating Clinical Recommendations

The Consensus Committee members of the Task Force included neurologists, neurosurgeons, neurophysiologists, psychiatrists, neuropsychologists, nurses and mid-level practitioners with expertise and experience in DBS. The experts were also chosen from different countries in Asia, Europe, North and South America, to provide a more comprehensive contribution to the Task Force. The authors of each chapter were selected taking into account their specific expertise in the field. The steering committee prepared a list of questions related to pre-operative, intra-operative and post-operative issues and established two chairs responsible for each of these 3 areas (subcommittees). These chairs then assigned a few questions to be addressed by each member of the subcommittees. The answers to the questions had to be formulated after reviewing the available literature (provided on CD) and combining their expertise. Since the level of evidence for most of the DBS studies was low, the responses were organized following the template previously used for the Special Supplement on DBS for Parkinson's disease (PD): 1) available data, 2) conclusions, 3) pragmatic recommendations, and 4) points to be addressed.[3] A first document was prepared from this

initial work and was reviewed and discussed by the entire Task Force group during a one-day meeting. During this meeting the Task Force members provided further feedback and agreed on additional refinements of the whole document adding the comments and remarks collected during the meeting. Special attention was paid to formulate pragmatic recommendations in absence of available studies. A second version of the project was sent to the entire working committee for final approval. The Executive Committee then met again to refine the Special Issue document before submission.

SECTION 1

Methods of Assessments

a. Descriptions and interest of the different scales for dystonia

Available Data

Motor scales

Generalized/segmental dystonia

The Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS)[4] was introduced to assess generalized dystonia patients. It is composed of a motor part assessing the dystonic movements and a part assessing the consequent disability. The motor subscale evaluates two clinical features of dystonia (severity and provoking factors) in eight body regions (eyes, mouth, neck and the four limbs) and one functional area (speech and swallowing). Severity ranges from 0 (no dystonia) to 4 (severe dystonia). The provoking factors assess the situation under which dystonia occurs and range from 0 (no dystonia) to 4 (dystonia at rest). These two features, severity and provoking factors, are multiplied and then scores are summed, except for the eyes mouth and neck which are halved prior to summing as they are considered regions of "lower weight". The resulting maximum total score on the BFM severity is 120.[4] The BFMDRS was clearly designed to assess patients with severe generalized dystonia, and has limitations when applied to milder or non-generalized cases. These limitations include the fact that arms and legs are given one rating each, without distinguishing proximal and distal components, the combination of functional features (such as speech and swallowing) with the inspection of dystonia in other body regions, and the arbitrary reduction of the weight in the cranial/cervical region.

The BMFDRS clinimetric properties were assessed in a study of 10 patients with dystonia rated by 4 different examiners: the overall reliability, inter-rater agreement and concurrent validity were demonstrated for the BMFDRS total score but not analyzed for each different body regions and area of function.[4] After the first encouraging effort, the BFMDRS was not further systematically developed and tested as a multicenter instrument.

The BFMDRS section on disability assesses the consequences induced by the dystonia in ADL (speech, handwriting, feeding, eating/swallowing, hygiene, dressing and walking), and the total maximum score is 30.

The Unified Dystonia Rating Scale (UDRS) was designed to overcome limitations of the BFMDRS. It includes a more detailed assessment of separate body areas with specific ratings for proximal and distal limbs, and does not mix bodily inspection with functional variables, such as speech and swallowing.[5] In addition, the UDRS rates duration similarly to the duration factor previously validated for the Toronto Western Spasmodic Torticollis Scale

(TWSTRS).[5] Furthermore, the UDRS weights the different body regions equally. Fourteen body areas are evaluated: eyes and upper face, lower face, jaw and tongue, larynx, neck, trunk, shoulder/proximal arm (right and left), distal arm/hand (right and left), proximal leg (right and left), distal leg/foot (right and left). For each of these, the UDRS requires rating the severity and duration. Severity rating is specific for each body region and varies from 0 (no dystonia) to 4 (extreme dystonia); duration also ranges from 0 to 4 and assesses whether dystonia occurs at rest or with action, and whether it is predominantly of maximal or sub maximal intensity. The total UDRS score is the sum of the severity and duration factors, with a maximum total of 112. The severity score is expressed as a percentage of the maximum amplitude of the physiological movement, which indicates that this scale is more appropriate to rate "mobile" versus "fixed" dystonia.

The Global Dystonia Rating Scale (GDS) evaluates the severity of dystonia in the same 14 body areas as the UDRS.[4] The GDS is a Likert-type scale with ratings of 0-10 (from 0, no dystonia, to 10, severe dystonia). There are no modifying factors in the GDS, and the total score is the sum of all the body area scores with a maximum of 140. The GDS is a very simple scale that allows a quick rating of dystonia but does not give precise indications about its clinical aspects (mobile vs. fixed ; disability...). On the other hand each body part has a similar weight, which has the advantage not to minimize any features of dystonia. The other advantage of this scale is its ease of use.

A comparison of the internal consistency and reliability of the BFMDRS, UDRS and GDS was performed by 25 dystonia experts using a standardized videotape protocol.[5] All 3 scales showed excellent internal consistency and good correlation among raters. The inter-rater agreement was excellent being lowest for eyes, jaw, face, and larynx. There was higher inter-rater consistency for motor severity than for the ratings of modifying factors (duration in the UDRS and provoking factors in the BFM). Seventy-four percent of the raters found the GDS the easiest to apply against 38% for the BFM and only 5 % for the UDRS.[5]

The Global Outcome Scale (GOS) scores the global improvement of the dystonia after a therapeutic intervention. The improvement is rated from 4 (marked) to 0 (no effect).[6] The GOS is a very simple but imprecise scale that does not differentiate the improvement of each body part. Because of these limitations the scale is rarely employed.[6]

For tardive dyskinesia, which encompasses dystonia and other movement disorders (particularly chorea, myoclonus and tremor), composite scales appear more appropriate, such as the Abnormal Involuntary Movement Scale (AIMS) or the Extrapyramidal Symptoms Rating Scale (ESRS).[7-8] The ESRS is divided into four subscales and four clinical global impression severity subscales. These consist in a questionnaire of drug-induced extrapyramidal symptoms, an examination of parkinsonism and akathisia, an examination of dystonia, an examination of dyskinesia and a clinical global impression severity scales for tardive dyskinesia, parkinsonism, dystonia and akathisia.[8] The AIMS contains 7 items assessing the severity of abnormal movements in different body locations. This scale also includes a global judgment of the severity, consequences and patient's awareness of abnormal movements. It has been observed that the ESRS and the AIMS have a high degree of concordance.[9]

Cervical dystonia

The Tsui Torticollis Rating Scale was the first rating scale specifically designed for cervical dystonia (CD).[10] It contains six items and is designed for video assessment. This scale evaluates the amplitude and duration of neck involuntary movements in the neck, elevation of shoulder and head tremor.

The TWSTRS[5] was developed to provide clinical investigators with a better instrument to assess the severity and disability of CD, which is the most common form of focal or segmental dystonia. The TWSTRS was developed in 1990 and consists of 22 items. The total TWSTRS is comprised of 3 separate subscales: motor severity, disability and pain due to CD. The motor severity scale consists of 10 items assessing the severity of head posture in several axes of movement (turning, tilting, anterocollis, retrocollis, shoulder elevation), the effect of sensory tricks, range of motion, and duration of dystonia. The score for motor severity subscale ranges from 0 (no symptoms) to 35 (severe CD). The TWSTRS subsection for motor severity has been validated for inter-rater reliability and validity and a teaching tape has been developed to ensure consistency across raters for multi-center trials.[11-12] The disability subscale consists of 7 items assessing the effect of CD on work performance, activities of daily living, driving, reading, watching television, conducting activities outside home, and social embarrassment. The maximal score for the disability subscale is 32. The pain subscale consists of 5 items to assess CD related pain at its maximal, minimal and usual level, and to indicate the duration of pain during a day, and disability due to pain. The maximum score for the pain subscale is 20. The total TWSTRS is the sum of the three subscale scores, with a maximum value of 87. The total TWSTRS has been used extensively as an outcome variable in clinical trials of pharmacological and surgical interventions.[13-20]

It has been shown that there is a good correlation between the scores obtained with the TWSTRS and the Tsui scale.[21] The metric properties of the total TWSTRS and of severity subscales were investigated. Factor analysis showed that 18 of the 22 items of the total TWSTRS fall into three clinically distinct and relevant factors, (1) motor severity, (2) disability and (3) pain.[11] These domains correspond to the three subscales of the total TWSTRS, and each measures a separate aspect of CD. The item for social embarrassment did not load on any factor.[12] Three additional items (sensory trick, lateral shift and sagittal shift) did not load on one factor. There are two possible explanations for this inconsistency. First, the range of scores available for these items is limited to absence/presence (lateral and sagittal shift) or to 0-2 (sensory tricks). Second, it has been observed that the observation of sensory tricks is a clinical feature relevant to the diagnosis rather than to clinical signs. Furthermore, the TWSTRS does not clearly assess dystonic tremor, as well as complex combination of phasic and tonic dystonic features.

Focal dystonias

The clinical evaluation of focal dystonias is often difficult.

A scale of 0 (normal) to 4 (worst) has been proposed to rate the severity of blepharospasm and oromandibular dystonia, but the inter-rater reproducibility was poor.[22-23] In a recent study the metric properties of the Jankovic Rating Scale (JRS) and a self-rating patient response outcome scale (the Blepharospasm Disability Index, BSDI) have been compared in blepharospasm patients.[24] The internal consistency, and retest reliability of the BSDI were good and the scores obtained using both scales were well correlated. Therefore, these authors suggest that JRS and BSDI can be both used to reliably assess blepharospasm in treatment trials.

For task-specific dystonias, the Writer's Cramp Rating Scale (WCRS) was developed for patients with writer's cramp.[25] The WCRS is divided into 3 subscales, respectively studying the dystonic posture, the latency for dystonia to occur and the presence of writing tremor.[25] Although this scale is easy to use and has sufficient inter-rater reliability it remains largely unused.

Quality of life scales

The assessment of quality of life is crucial to determine the impact of the surgery on ADL. Most of the studies assessing this outcome measure have used the Short-Form Health Survey (SF-36) or the Parkinson's Disease Questionnaire 39 (PDQ-39).[26-33] The SF-36 scale assesses the general and mental health, the physical and social functioning, the physical and emotional roles, the pain and vitality.[34] The scores on each subscale are comprised between 0 (worst) to 100 (best). The PDQ-39 scale was originally designed for Parkinson's disease[35] but has also been employed for dystonia. It is divided into 7 sections: mobility, activities of daily living, emotional wellbeing, stigma, cognition, communication and bodily discomfort.

The Cervical Dystonia Impact Profile (CDIP-58) has been developed for CD. It measures the health impact of the disease from patient's perceptions.[36] This scale is divided into 8 sections (head and neck symptoms, pain and discomfort, upper limb activities, walking, sleep, annoyance, mood and psychosocial functioning). This composite scale appears more sensitive than the SF-36 or TWSTRS to measure the functional outcome of a treatment such as botulinum toxin.[37] However, its use remains rare compared to the SF 36 for example.

Conclusions

For generalized and cervical dystonia, the two most accepted and used rating scales are the BFMDRS and TWSTRS, respectively. For other focal dystonias, there are no generally agreed upon scales. The currently available rating scales have several limitations. The BFMDRS scale uses weighting factors that can minimize the real impact of eyes, mouth and neck dystonia. In addition, other associated movement disorders, such as tremor or myoclonus, are not considered in most of the available dystonia scales. Moreover, the available current scales do not sufficiently discriminate more mobile (phasic) dystonic movements from more fixed (tonic) dystonic postures.

Pragmatic Recommendations

The features of dystonia should be monitored before DBS using the most appropriate among the available dystonia scales. The choice of which scale to use should depend upon the dystonia type, according to the topography rather than the etiology of dystonia. For generalized dystonia, the total BFMDRS is recommended. For focal dystonias, the BFMDRS may not always be appropriate. As an alternative, the GDS provides a rapid assessment; although this scale has been less used than the BFMDRS, it can be easily applied in the clinical setting. The UDRS may also be used although its implementation is more difficult. For cervical dystonia, the TWSTRS, including subscales for severity, disability and pain, is recommended. The available scales have been designed to assess patients with primary dystonia and do not always capture complex dystonia phenotypes, such as those observed in dystonia-plus or in secondary dystonias.

Given these limitations, it is recommended that a limited number of expert evaluators is charged to rate patients with dystonia and that standardized videos are performed during each assessment.[4]

The impact of surgery on quality of life is a crucial outcome issue that may provide results divergent from the motor assessment.

Points to be addressed

New more comprehensive scales should be developed: they should also accurately measure tonic postures and phasic movements. Finally, there is a need for uniform training for the BFMDRS and UDRS. Uniform training is available for the TWSTRS, although it has not been shown whether such training improves inter-rater reliability. For other focal dystonias,

although several scales exist, their internal consistency and reliability have been poorly studied and their use remains incidental. Thus there is a clear need for specific scales that objectively quantify the effect of DBS in focal dystonias.

b. Clinical use of the scales for dystonia

1. Should standardized evaluation be performed pre-operatively and post-operatively? How? When?

Available data

Motor assessment

Post-operative objective and subjective assessments have been compared to the preoperative condition in a number of publications, encompassing clinical series, case control studies, cohort studies and single case reports.[20,26,28-33,38-75] There are only 6 controlled trials that evaluate the effects of GPi DBS in a blinded fashion.[28-29,31-32,38,77] One of these studies[31] reach a Class I level of evidence while the 5 others reach a Class II/III level of evidence in the classification proposed by the American Academy of Neurology (Table 1).[76] These trials provide a clear demonstration of the benefit of DBS for the primary generalized and tardive dystonias and also for CD.[28-29,31-32,38] Favorable outcome has also been reported for PKAN.[39] In these studies a videotaped assessments scored by independent blinded raters allowed controlled evaluations of the effects of the surgery.[28-29,31-32,38-39] It is notable that data on the benefit of DBS in dystonia reported by open studies are in keeping with the findings reported by controlled studies.

A number of practical issues have been addressed by the available studies. Preoperatively the assessment is most often performed between within the last month and the last week preceding the surgery.[20,26,28-33,38-75] The time interval between surgery and the first post-operative evaluation is usually comprised between 3 and 12 months.[20,26,28-33,38-75] Management of the patients does not require more frequent controls and the first preoperative evaluation is aimed at assessing any acute effects of stimulation on dystonia and threshold for stimulation-induced side effects. Most of the studies have clearly shown that the improvement starts within the first hours or days after beginning the stimulation, and then progresses. Most of the benefit is usually obtained after 3 to 6 months.[20,26,28-33,38-75] The improvement first affects the phasic signs and later the tonic ones.[28] Some additional improvement can occur later but, usually, to a less extent and slower. Some studies however have shown an additional 10-30 % improvement of the dystonia between 1 year and 1.5 year.[41,73-74] The post-operative outcomes will be discussed in detail in another paper on this same issue.[78]

Quality of life assessment

The quality of life (QoL) assessment is usually performed when the patients have the pre-operative motor assessment, i.e. from 1 month to one week before surgery.[26-33] The interval between surgery and the post-operative evaluation of QoL is generally between 3 and 18 months.[26-33] QoL usually improves significantly after GPi DBS in generalized and segmental dystonia, and CD.[26-33]

Conclusions

Validated motor and disability scales are widely used to assess patients before surgery in all the published studies. Most of the time evaluations have been done in open label fashion.

Pragmatic recommendations

Validated scales (see previous section) should be used to assess patients with dystonia within few weeks before surgery. The benefit should be evaluated at 3-6 month after surgery and further evaluations should be scheduled at yearly intervals. Videotaped assessments are recommended.

Points to be addressed

The ideal time-frame to assess the efficacy of DBS in different forms of dystonia needs to be better defined. It remains also to be specified if this should differ for primary generalized or focal forms or for secondary dystonias.

2. Should evaluation in the OFF stimulation condition be performed in routine or research protocol? How long and when?

Available data

Evaluations are rarely performed in OFF stimulation condition.[28-29,38,49,51,59,64,75] However, assessments without stimulation may provide important information on the immediate effect of stimulation, the delay of reoccurrence of the clinical signs and possibly further worsening of pre-operative motor conditions. OFF stimulation studies thus allow better comparison with the preoperative motor condition and may show evidence of underlying disease progression.

The duration of the stimulation wash-out period preceding assessment may be variable. This has been specifically studied by Grips et al.,[51] who showed that most of the phasic motor symptoms in patients with segmental dystonia reoccurred within 4 hours after switching off bilateral GPi DBS, while the tonic signs may take much longer to worsen. In the Vidailhet's et al.[28] study of generalized dystonia patients the maximum tolerated duration of the OFF stimulation period was 7 hours. In a single case study in Lesch-Nyhan dystonia the stimulator could be switched off for 1 month.[64] By contrast, tardive dystonia and cervical dystonia may worsen very quickly after the stimulator is switched off.[38,75] This indicates that the effects observed after switching off stimulation may depend on the etiology of dystonia. Furthermore, it has to be taken into account that severe worsening of dystonia may be life threatening in severe generalized cases; this can be prevented by careful observation of patients during this period.

Conclusions

Evaluations in the OFF stimulation condition have been performed in few studies, which provide interesting data concerning the post-effect duration of DBS in dystonia.

Pragmatic recommendations

A reasonable duration of the OFF period may be of around 3 to 4 hours although this does not lead to the worst off condition. In routine clinical setting, OFF stimulation evaluation is not acceptable because of the risk of reoccurrence of severe dystonia manifestations.

Points to be addressed

It is unclear whether the time course of motor signs reoccurrence after DBS switch-off depends on the etiology of dystonia. This needs to be addressed by specific studies.

SECTION 2

Role of Imaging

Is there any role for pre-operative imaging (brain MRI, PET)?

a. Morphological imaging

Available Data

Conventional MR Imaging

Brain imaging is mandatory in order to determine the aetiology of dystonia and should be performed before considering any patient for surgical treatment.[1] In primary dystonia there are no major structural abnormalities as seen with brain CT or MRI. However, some detailed MRI studies indicate changes of gray mater density in the motor circuit or changes of basal ganglia volume.[2,79-81] One study with conventional MRI showed T2 bilateral abnormalities in the lentiform nucleus in primary cervical dystonia.[82] However, the abnormalities were only detected on calculated T2 values; no obvious signal changes could be recognized on visual inspection of T2-weighted images.[82] Recently, structural abnormalities were shown in the cerebellum and sensorimotor circuit in writer's cramp.[83] Using voxel-based morphometry, gray matter decrease was found in the hand area of the left primary sensorimotor cortex, bilateral thalamus and cerebellum. However, such changes were not visualized on conventional images. The main aim of conventional structural MR images of the brain in surgical candidates is to determine the feasibility of surgical implantation and the technical approach independently of the search for the cause of the dystonia. Surgeons will use this brain MRI to rule out major surgical contra-indications such as brain tumors, severe vascular changes or malformations and to visualize the target structures. Some secondary dystonias such as PKAN, post-stroke dystonia, neuroacanthocytosis or inborn errors of metabolism are associated with severe basal ganglia damage that can have an impact on the choice of the target of implantation and on the expected results.[84-87] In most of the published series the brain MRI sequences are not described.

Non conventional MR imaging

Brain MR spectroscopy revealed no abnormal N-acetylaspartate/creatine (NAA/Cr) and lactate/creatine ratios in patients with focal hand dystonia, while it has been shown that NAA/Cho and NAA/Cr were significantly lower in patients with spasmodic torticollis.[88-89]

There are some reports on diffusion tensor images (DTI) indicating abnormal fractional anisotropy and mean diffusivity in cervical dystonia and idiopathic dystonia.[90-91]

Conclusions

Brain MRI is required for the aetiological diagnosis of dystonia. At the preoperative evaluation stage brain MRI is used to ensure that no focal lesions may interfere with the implantation. Other imaging modalities such as fMRI, MR spectroscopy and DTI are used only for research purpose, and thus not useful for routine preoperative evaluation.

Pragmatic Recommendations

Brain MRI should be performed in every patient considered for DBS in order to ascertain if there are structural lesions that may be causative of dystonia or interfere with the surgical procedure. Functional MRI, MR spectroscopy and DTI are not necessary in general clinical

practice of DBS and do not influence surgical procedure or outcome. Therefore they should be done in specialized centers for research on movement disorders.

Points To Be Addressed

Morphological brain MRI is required before DBS in dystonia for every patient. However, the sequences to be used may differ from a center to another. It would be useful to define a common protocol that could be applied in every center aiming at implanting patients with dystonia. The contribution of new MRI sequences also needs to be clarified.

b. Functional imaging

Available Data

The pathophysiology of dystonia is complex and not fully understood. Electrophysiological and functional imaging studies have shown an excess of brain activation, a loss of cortico-cortical inhibition and a lack of the selectivity of brain activation.[92] More precisely, functional imaging studies have shown overactivity of the dorsolateral prefrontal cortex, premotor and anterior cingulate cortex, cerebellum and putamen in patients with primary and secondary dystonia.[92-95] In primary dystonia (generalized or focal) a decrease of rCBF is usually seen in the primary motor cortex.[93-97] On the other hand, in secondary dystonia rCBF is often increased in the primary motor cortex.[98] fMRI studies performed in writer's cramp and Meige's syndrome have demonstrated an altered somatotopic representation, which contributes to the loss of functional selectivity of muscle activity.[99] In tardive dystonia an increase in regional cerebral blood flow has been found in the prefrontal cortex (areas 8 and 11), the anterior cingulate and the lateral premotor cortex.[100] Other PET or SPECT studies in tardive dystonia patients have looked at the modifications of the post-synaptic dopaminergic system. In patients studied after long-term neuroleptic treatment withdrawal, an upregulation of dopaminergic D2 receptors has been observed using PET and [11C]-Raclopride, a D2 receptor ligand.[101] Notably, these studies concerned patients with severe tardive dystonia, and they are in agreement with the suspected role of dopamine receptor trafficking in the occurrence of this pathology.[101] In contrast, other studies showed normal dopamine D2 receptor density and / or affinity in TD.[102]

Conclusions

PET functional imaging has clearly demonstrated that the abnormal movements and postures in dystonia are related to a widespread excess of brain activation, whatever is the cause of the dystonia.

Pragmatic Recommendations

Despite their important application elucidating the pathophysiology of dystonia, functional imaging studies have no clear role at present in routine clinical practice.

Points to be addressed

None.

Acknowledgments

The authors thank Dr. R. Kaji for his initial participation to the Task Force.

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Clinical Neurophysiology 121 (2010) 1930–1933

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Cortico-conus motor conduction time (CCCT) for leg muscles

Hideyuki Matsumoto [a,*], Ritsuko Hanajima [a], Yuichiro Shirota [a], Masashi Hamada [a], Yasuo Terao [a], Shinya Ohminami [a], Toshiaki Furubayashi [a], Setsu Nakatani-Enomoto [b], Yoshikazu Ugawa [b]

[a] Department of Neurology, Division of Neuroscience, Graduate School of Medicine, The University of Tokyo, Japan
[b] Department of Neurology, School of Medicine, Fukushima Medical University, Japan

ARTICLE INFO

Article history:
Accepted 19 April 2010
Available online 14 May 2010

Keywords:
Magnetic stimulation
Motor evoked potential
Cortico-conus motor conduction time (CCCT)
Central motor conduction time (CMCT)
Pyramidal tract

ABSTRACT

Objective: To measure the conduction time from the motor cortex to the conus medullaris (cortico-conus motor conduction time, CCCT) for leg muscles using magnetic stimulation.
Methods: Motor evoked potentials (MEPs) were recorded from tibialis anterior muscles in 51 healthy volunteers. To activate spinal nerves at the most proximal cauda equina level or at the conus medullaris level, magnetic stimulation was performed using a MATS coil. Transcranial magnetic stimulation of the motor cortex was also conducted to measure the cortical latency for the target muscle. To obtain the CCCT, the latency of MEPs to conus stimulation (conus latency) was subtracted from the cortical latency.
Results: MATS coil stimulation evoked reproducible MEPs in all subjects, yielding CCCT data for all studied tibialis anterior muscles.
Conclusions: MATS coil stimulation provides CCCT data for healthy subjects.
Significance: This novel method is useful for evaluation of corticospinal tract function for leg muscles because no peripheral component affects the CCCT.

1. Introduction

Magnetic stimulation enables us to evaluate the corticospinal tract function non-invasively by measuring the central motor conduction time (CMCT) (Rossini et al., 1994; Chen et al., 2008). The CMCT is usually obtained by subtracting the motor evoked potential (MEP) latency to magnetic stimulation over the spinal enlargement (spinal latency) from that to magnetic stimulation over the primary motor cortex (cortical latency). Magnetic stimulation over the spinal enlargement activates the spinal nerve at the neuro-foramina level (Ugawa et al., 1989b). Therefore, the CMCT described above includes the conduction time through the spinal nerves running in the spinal canal (Rossini et al., 1994; Chen et al., 2008).

Maccabee et al. reported that an 8-shaped coil can activate the most proximal cauda equina at around the conus medullaris (Maccabee et al., 1996). They proposed the possibility that this stimulation method might enable us to measure the conduction time from the motor cortex to the conus medullaris [cortico-conus motor conduction time (CCCT)]. The CCCT necessarily reflects the corticospinal tract function more correctly than the conventional CMCT because peripheral components (some conduction time within the cauda equina) do not contribute to CCCT, especially in patients with peripheral neuropathy. The CCCT, however, has not been widely used yet.

A few alternative methods can be used to measure the proximal spinal nerve conduction time, such as F-wave measurement and high-voltage electrical stimulation (Ugawa et al., 1988a,b, 1989a, 1995; Claus, 1990; Eisen and Shtybel, 1990). However, F-wave measurement provides no information about the lesion sites, and high-voltage electrical stimulation is often associated with severe pain. Especially, high-voltage electrical stimulation is not tolerated by patients with skin problems (Matsumoto et al., 2005, in press).

We have developed a new method to activate the most proximal cauda equina at around the conus medullaris level using a specially devised coil [magnetic augmented translumbosacral stimulation (MATS) coil] (Matsumoto et al., 2009a,b).

The aim of this paper is to apply the MATS coil to CCCT measurement. The relation between MEP latency and body height was also studied.

2. Materials and methods

2.1. Subjects

Subjects were 51 healthy volunteers (25 men and 26 women). Their mean age and body height were 42.1 ± 15.5 (mean ± standard deviation (SD); range 24–78) years and 163.9 ± 9.3 (144–185) cm.

* Corresponding author. Address: Department of Neurology, Division of Neuroscience, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan. Tel.: +81 3 5800 8672; fax: +81 3 5800 6548.
E-mail address: hideyukimatsumoto@mail.goo.ne.jp (H. Matsumoto).

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doi:10.1016/j.clinph.2010.04.014

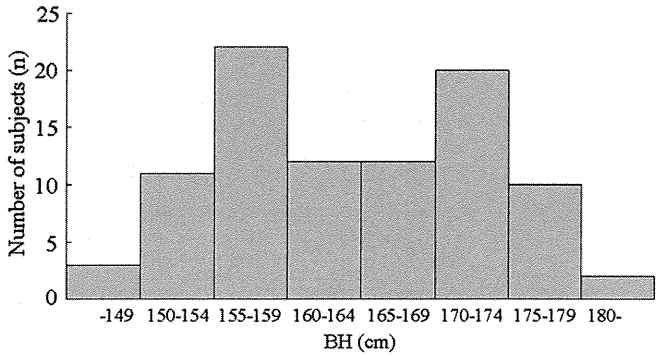

Fig. 1. Histogram of body height. There is no extremely skewed distribution of body height in our study.

The histogram of body height is shown in Fig. 1. No extremely skewed distribution of body height was observed.

Informed consent to participate in this study was obtained from all subjects. The protocol was approved by the Ethics Committee of the University of Tokyo. The experiments were conducted in accordance with the ethical standards of the Declaration of Helsinki.

2.2. Stimulation, recording and analysis

During the examination, MEPs were recorded from the tibialis anterior muscle (TA) as subjects sat comfortably on a bed. The TA muscle was selected because this muscle could be easily contracted and recorded compared to other leg muscles. Disposable silver–silver chloride disc electrodes of 9 mm diameter were placed in a belly tendon montage over TA. Signals were amplified with filters set at 20 Hz and 3 kHz and recorded using a computer (Neuropack MEB-9100; Nihon Kohden Corp., Japan).

Magnetic stimulation was conducted using a monophasic stimulator (Magstim 200; The Magstim Co. Ltd., UK). For cortical magnetic stimulation, a double-cone coil (The Magstim Co. Ltd., UK) was placed over the Cz (international 10–20 system), with induced currents flowing mediolaterally over the contralateral leg motor area (Terao et al., 1994, 2000). The MEP onset latency was measured in the active condition (cortical latency).

Fig. 2 portrays the placement of MATS coil (diameter 20 cm, 0.98 T; The Magstim Co. Ltd., UK) when recording MEPs from the right TA. The MATS coil was always placed from the midline to the contralateral side of the body (the opposite side from the recorded muscle) to prevent some non-target parts of the coil from activating distal peripheral nerves for the target TA. The most proximal cauda equina at around the conus medullaris was activated using the MATS coil, whose edge was positioned over the first lumbar (L1) spinous process for inducing currents to flow upward in the body (Matsumoto et al., 2009b). For the neuro-foramina level stimulation, the edge of MATS coil was positioned over the fifth lumbar (L5) spinous process for inducing currents to flow 45° downward from horizontal direction (Matsumoto et al., 2009a). This direction of induced currents (45°) was optimal to elicit MEPs because the induced currents should flow along the anatomical course of spinal nerves (Ugawa et al., 1989b; Epstein et al., 1991; Mills et al., 1993; Maccabee et al., 1996; Ruohonen et al., 1996; Matsumoto et al., 2009a). In L1 and L5 level stimulation, the onset latencies of MEPs were measured in the relaxed condition (L1 and L5 level latencies).

To obtain the minimal and reproducible MEP latency, the stimulus intensity was increased gradually and several MEPs evoked by stimulation at several different intensities were superimposed. The CCCT, conventional CMCT, and cauda equina conduction time (CECT) were obtained (92 sides). The CCCT was obtained by subtracting the L1 level latency from the cortical latency, the conventional CMCT by subtracting the L5 level latency from the cortical latency, and the CECT by subtracting L5 level latency from L1 level latency. Linear regression analysis was conducted to investigate the relation between each conduction time and body height.

The MEP sizes were compared between the simulation positions (60 sides). The base-to-peak amplitude of MEP was mea-

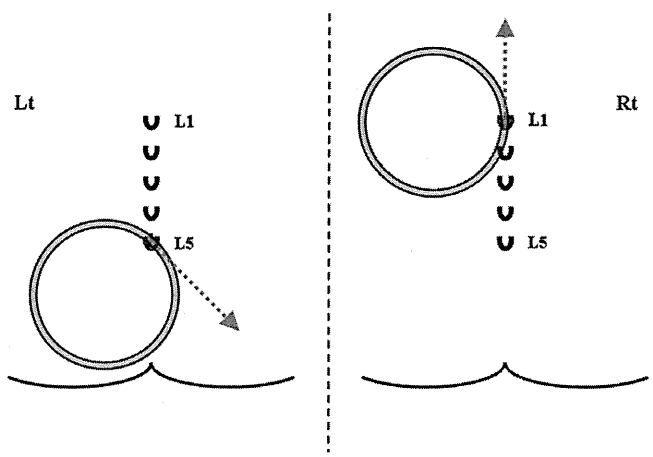

Fig. 2. MATS coil stimulation method. This figure shows positions of MATS coil when MEPs are recorded from right TA. For the most proximal cauda equina stimulation, the edge of MATS coil is positioned over the first lumbar spinous process for inducing currents to flow upward. For neuro-foramina level stimulation, the edge of the MATS coil is positioned over the fifth lumbar spinous process for inducing currents to flow 45° downward from a horizontal direction.

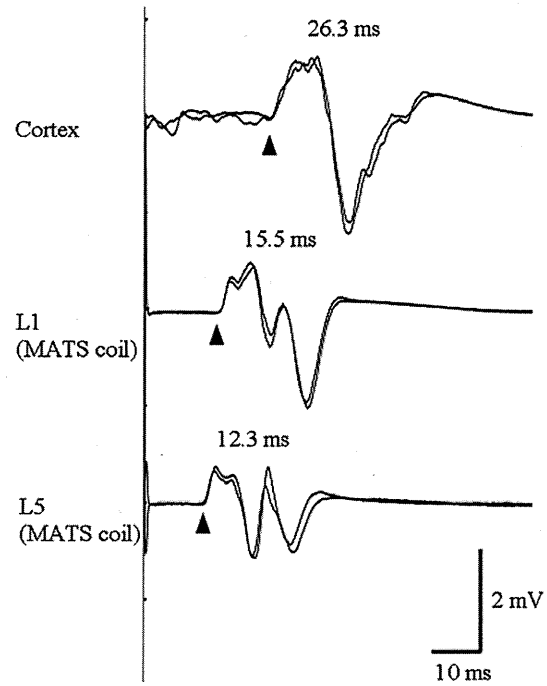

Fig. 3. Representative MEPs in a normal subject. The conventional CMCT is obtained by calculating the latency difference between MEPs to cortical and L5 level stimulation. Similarly, the CCCT is obtained by calculating the latency difference between MEPs to cortical and L1 level stimulation.