Clinical Neurophysiology: New Clinical and Research Applications

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Postscript
It is a pleasure to prepare a foreword for the work by Dr. Yew-Long Lo, whose academic progress I have witnessed for some time. I have seen many notable contributions he has made, covering the central and peripheral nervous systems. This book comprises about 500 pages on new applications of Clinical Neurophysiology methods mostly compiled from his own original papers. Amassing this body of work, he now presents the treatise with added clinical notes and flowcharts to document the bases of electrophysiologic examination.

The recent advent of technology has seen proliferation of new scientific methods ranging from molecular biology to neuroimaging. They have helped answer questions on the human nervous system that researchers have wondered about for a very long period of time. These methods have gradually found their way into clinical medicine, leading to dramatic changes in medical practice. Despite such a shift in landscape, Clinical Neurophysiology has managed to remain relevant to patient care. I welcome Dr. Lo’s effort and enthusiasm to encourage continued developments of this discipline, which I have followed closely during the last twenty years.

The field of Clinical Neurophysiology has also made tremendous progress over the last several decades, and is now a scientific field with far-reaching applications. Its role in evaluating function, monitoring changes, and, of late, therapeutic modulation of the nervous system will certainly be enhanced in the years to come. In many ways, this book depicts the various roles in which Clinical Neurophysiology plays in its contribution to medicine, both within and beyond the Neurosciences. It describes a well-balanced overview so that clinicians understand and appreciate their proper use.

Neurologists consider neurophysiologic analyses as an extension of the physical examination, which, therefore, dictates the overall approach of the study to supplement clinical findings. These techniques contribute in elucidating topographic localisation and grading the degree of functional involvement. The book instructs the principles of electrodiagnosis in a rigorous but unique way, allowing the reader to learn the breadth and depth of its technology to complement the practice of Neurology.
Dr. Lo has successfully covered the topics to discuss the needs of medical practitioners engaged in Clinical Electrophysiology. It provides a comprehensive analysis of many frequently posed questions. I recommend this volume highly to anyone interested in clinical application of electrodiagnostic practice, with the conviction that readers will find many valuable pointers amongst its pages. I hope it will be widely used by Neurologists who are active in the field, adding substantially to the education of young colleagues.

Jun Kimura, MD
Professor of Neurology, University of Iowa
Professor Emeritus, Kyoto University
Past President, World Federation of Neurology
When I was first exposed to basic nerve conduction studies as a Neurology trainee, the ability to record electrical signals in humans fascinated me a great deal. Going through multiple routines of carpal tunnel syndrome or peripheral neuropathy evaluations, it soon occurred to me that very much more value can be added to current capabilities of electrodiagnosis. This book, henceforth, details my journey through Clinical Neurophysiology, primarily with this objective in mind.Secondarily, the field has empowered the Neurologist or Neuroscientist towards a deeper understanding of both central and peripheral nervous system function, pointing them towards clinically relevant research directions.

This book will probably engage more advanced practitioners of the field, but junior colleagues may also benefit from appreciating the workflow and thought processes involved in patient management. I have also taken the liberty to include clinical notes for rationalisation of each technique in the clinical context.

While the book has been divided into collections of materials for each electrodiagnostic technique, it was felt that practical approaches, based on routine patient encounters, would be most apt. To this end, the appendices attempt to fill this gap by integrating the presented material in a logical thought process.

Clinical Neurophysiology is a scientific domain that is highly collaborative, both within Neurology, Neuroscience, as well as other medical subspecialties. I am hopeful that in this way, the efforts invested in this publication will benefit a wider audience.

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The production of this book has taken over 3 years, from conceptualisation to press. I am highly indebted to Ms Quek Shin Yi and the SingHealth Academy for seeing the entire project through. Without the expert editing, art direction, organisation, production and, most of all, encouragement I received, I would have lost faith midway.

I am grateful for the financial support and patience provided by Transmedic Pte Ltd. It is our mutual belief that the project will benefit practitioners of Clinical Neurophysiology at every level.

I am most humbled and inspired by Professor Jun Kimura's encouraging words of support in his Foreword for this publication. Professor Kimura has been a role model, champion and constant source of inspiration for Neurologists and Clinical Neurophysiologists alike. His humility, passion and approachability are qualities that all of us look to emulate, but will unlikely achieve.

Although 3 years seem short for a scientific publication, much of the content reflects some 2 decades of work in this field. The dedication of my collaborators from the Neurodiagnostic Unit, and my colleagues from the Neurology Department, Singapore General Hospital has humbled me greatly. Specifically, I thank previous co-authors Drs Kerry Mills, Pavanni Ratnagopal, Siew Ju See, Prakash Kumar, Eng King Tan, Simon Ting, David Lau, Stephanie Fook-Chong, Wei Yi Ong, Ling Ling Chan, Sitaram Raman, Jane George, Yew Meng Chan, Cun Tai Guan and the spine surgery team from the Singapore General Hospital for their valuable contributions. Obviously, many of my previous publications would not have materialised without the generous support from the National Medical Research Council and Ministry of Health, Singapore.

Mostly, I would like to express my sincere gratitude to the patients and healthy control subjects from which we obtained valuable clinical data. You have contributed greatly towards the understanding of human nervous system function, which will eventually lead to better treatment of neurological disorders.
If I had omitted any esteemed acquaintance from this seemingly endless list, rest assured it is purely unintentional. Most certainly, it is consequential of an ever expanding network of collaborators often encountered in the specialty of Clinical Neurophysiology. The valuable experiences derived from learning and working together cannot be matched in any other way.

YL Lo
16.1 CERVICAL MYELOPATHY AND MRI

INTRODUCTION

Cervical spondylotic myelopathy (CSM) is a progressive, degenerative mechanical compression of the cervical cord, with impingement by osteo-cartilaginous elements within the spinal canal\(^1,2\). It is mostly a slow and gradual process\(^3\) in which patients present at various clinical stages of severity\(^4\). Most studies, largely using plain radiography and myelography, have correlated clinical signs with electrophysiological findings\(^5-7\). Conflicting results have been reported in studies relating electrophysiological changes and levels of cord compression\(^8,9\). Conversely, it has been reported that corticospinal abnormalities can exist in asymptomatic patients with radiological cord compression on myelography, CT myelography and MRI\(^10,11\).

Transcranial magnetic stimulation (TMS) is a quick, safe, and painless technique to study conduction in the descending corticospinal pathways\(^12-15\). It involves motor cortex stimulation by means of magnetic flux. The conduction time from the motor cortex to the anterior horn cell (central motor conduction time (CMCT)) is a measure of the integrity of corticospinal pathways. TMS has been effectively used to assess corticospinal abnormalities in multiple sclerosis\(^16,17\), motor neuron disease\(^18,19\) and degenerative ataxias\(^20\). It has also contributed to the evaluation of dynamic subclinical corticospinal abnormalities in the Miller Fisher syndrome\(^21\).
There are no large studies addressing systematic correlation between TMS findings and MRI abnormalities in patients with various degrees of CSM. This study aims to critically analyse the actual correlation of TMS findings with the degree of cord compression on MRI scans in patients presenting with symptoms and signs suggestive of CSM. Secondarily, this study aims to determine if TMS can be potentially used to screen warranted cases for early MRI, with view to surgery, hence saving health costs by reducing or delaying the need for an expensive imaging technique.

**METHODS**

**Participants**
One hundred and forty-one patients (46 females) with a mean age of 51 years (range: 36 to 78) were prospectively entered into the study over a 3.5-year period. They were referred with a clinical diagnosis of CSM after consultation with an experienced orthopaedic surgeon. Presenting symptoms included bilateral hand or feet numbness, difficulty walking, clumsiness or weakness of limbs, neck pain, radicular symptoms and cramps. A detailed history, physical examination by a neurologist and relevant investigation were included to rule out other conditions which may confound the study. Patients who were not fit for TMS study or did not undergo MRI within the allocated time frame of eight weeks were excluded.

Twenty-five healthy volunteers (nine females) with an age range of 20 to 75 years were also entered into the study with informed consent. Controls were screened strictly to exclude cervical disease and other neurological problems by the authors.

During the period of study, two patients with motor neuron disease, two with demyelinating disease, three with stroke and one with syringomyelia were incidentally encountered. TMS, MRI and electrophysiological studies were performed on them as well.

**Materials and Procedure**

**MRI**
All patients had MRI of the cervical spine on either a 1.0 T or 1.5 T superconducting unit, using the tailored cervical spine phased-array coil. The following pulse sequences were used with a 3 mm section thickness and a 0.3 mm gap: (a) sagittal turbo spin-echo T1-weighted (600–660 ms/12 ms/2 [TR/TE/excitations]), (b) sagittal turbo spin-echo T2-
CERVICAL DISORDERS

weighted (4500 ms/112 ms/3, echo train length 15) and (c) axial gradient-echo (500–660 ms/22 ms/2, flip angle 30 degrees) sequences. The sagittal sequences were obtained using a 188 x 250 mm field of view (FOV) and a 180–240 x 256 matrix; and the axial sequences, a 175 x 200 mm FOV and 192–256 x 256 matrix.

The patients were separated into four groups according to the degree of cord compression by degenerative osteo-cartilaginous elements at the most significant level on MRI:

Group 1: Cervical spondylosis with or without contact with the cord, but cord deformity is absent
Group 2: Mild indentation or flattening of the cord with resultant anterior-posterior (AP) cord diameters not less than two-thirds of the original (mild cord compression)
Group 3: Significant cord indentation by osteo-cartilaginous elements with resultant AP cord diameters less than two-thirds of its original, but not associated with hyperintense T2 signal within the cord (moderate cord compression)
Group 4: Significant cord indentation by osteo-cartilaginous elements with resultant AP cord diameters less than two-thirds of its original, and associated with hyperintense T2 signal within the cord (severe cord compression)

The original AP cord diameter was the average of the AP diameter of the spinal cord at the mid-vertebral body levels directly above and below the disc level assessed, based on actual measurements on MRI images.

All MRI studies were reviewed by two experienced radiologists. In the event of discordance, findings were based on a consensus opinion. For further standardisation, all patients included in the study had MRI performed within eight weeks of the TMS study.

TMS
All patients had informed consent before TMS was performed. Patients with a past history of seizures, heart disease and intracranial operations were excluded.

Magnetic stimulation was performed with a Dantec Mag 2 Stimulator (Dantec, Skovlunde, Denmark) by means of a Dantec S100 circular 10 cm diameter coil generating up to
1.9 T in output. Motor evoked potential (MEP) recordings were made with adhesive surface electrodes on the FDI for upper limb (UL) and AH for lower limb (LL) muscles. The coil was positioned over the scalp vertex to obtain consistent MEPs of maximum amplitude with the relevant muscle in slight contraction. For AH recordings, the site of stimulation was 2 cm anterior from the vertex. Patients received multiple cortical stimulations, up to 10 for each muscle, to obtain distinctly recordable MEPs of consistent morphology. The average latency of the shortest of three most consistent responses was analysed. The minimum latency of 20 F responses was obtained.

CMCT was calculated with the formula: MEP latency – (F latency + M latency − 1)/2 in ms. MEP responses were considered absent if 10 consecutive TMSs up to 100% stimulator output consistently failed to elicit a reproducible MEP. For most patients, stimulator output of 80% was adequate to elicit consistent MEPs of similar morphology.

CMCT measurements were also performed on the controls for comparison.

Electrophysiological Studies
NCSs of the median, ulnar, sural, tibial and peroneal nerves with relevant late responses were performed according to previously described methodology (see Section 1 "Nerve Conduction Study"). Needle EMG of UL muscles comprising C5 to T1 root levels were performed as part of the neurodiagnostic workup. Additional tests, including evoked response studies, were performed if clinically indicated.

Statistical Analysis
In this study, we focused on actual clinical scenarios in which patients were referred for neurophysiological assessments, followed by MRI. All patients who did not have contraindications had TMS regardless of clinical features or the presence of root abnormalities. TMS data were finally collated and only excluded after MRI studies, according to the exclusion criteria set above.

The CMCT data were analysed with SPSS for Windows software. Mann-Whitney test for non-parametric statistical data was employed, with a p-value of significance set at 0.05. For sensitivity and specificity calculations, absent MEPs, abnormal CMCT in any limb or abnormal side-to-side CMCT comparisons were regarded as pathological for each patient.
RESULTS

Clinical
71% of the patients presented with sensory symptoms. 75% had hyperreflexia and upper or lower limb weakness. 25% had gait abnormalities of which 5% needed walking aids. None complained of bowel or bladder disturbance.

NCS and EMG showed changes supportive of radiculopathy in 72% of patients.

MRI
Twenty-eight, 49, 28 and 36 patients were classified into Groups 1 to 4 respectively. The concordance rate of the two radiologists reviewing MRI films was 97%. The most significant level of cord impingement or compression in all 141 patients were localised to C3/4 in 23% of patients, C4/5 in 26%, C5/6 in 43% of patients and C6/7 in 8% of patients. Amongst the patients in Group 4, 34%, 29%, 29% and 8% of patients had increased T2 signal changes at C3/4, C4/5, C5/6 and C6/7 levels respectively. Therefore, the level of hyperintense T2 signals did not always correlate with the most significant levels of cord indentation or compression on MRI.

Figure 16.1 shows examples of MRI and TMS tracings of patients in Groups 1 to 4.

TMS (Controls)
Mean (SD) for UL and LL CMCTs in normal controls were 5.5 (1.11) ms and 12.26 (1.88) ms respectively. The upper limit of normality at 2 SDs were 7.72 and 16.02 ms. For all control subjects, upper and lower limb MEPs were easily obtainable and reproducible with stimulator outputs of between 70% to 80%.

Mean right and left CMCT differences (RLD) were 0.84 (0.88) ms and 1.27 (1.12) ms for UL and LL respectively. The upper limits of normality at 2 SDs were thus 2.57 ms and 3.51 ms.

TMS (Patients)

CMCT
The mean (SD) UL CMCTs for Groups 1 to 4 were 5.14 (1.07) ms, 6.82 (1.88) ms, 12.09 (3.69) ms and 12.91 (3.14) ms respectively. For the LL, they were 12.51 (1.54) ms, 15.32 (2.46) ms, 21.29 (4.63) ms and 21.48 (4.59) ms respectively.
Mean UL and LL CMCTs were seen to increase with severity of MRI cord compression. UL and LL CMCTs both correlated significantly with MRI groups (Spearman's correlation coefficient: 0.75 and 0.73 respectively; \( p < 0.01 \)).

There was no significant difference in mean CMCTs between Group 1 and the control group. Comparison between groups revealed significant differences \( (p < 0.0005) \) in mean UL and LL CMCTs for all pairs of groups, with the exception of Groups 3 and 4 for both UL \( (p = 0.38) \) and LL \( (p = 0.99) \).

In Group 1, there were no patients with absent MEPs or abnormal CMCTs in the ULs and LLs.

In Group 2, one patient (2%) had absent MEP in the right LL and 39 patients (79%) had at least one limb with abnormal CMCT. This includes nine with UL, 24 with LL and six with both UL and LL abnormalities.

In Group 3, nine patients (32%) had absent MEPs, including three in the ULs and six in the LLs. 28 patients (100%) had at least one limb with abnormal CMCT. This includes two with UL, two with LL and 24 with both UL and LL abnormalities.

In Group 4, 24 patients (67%) had absent MEPs, including two in the ULs, 17 in the LLs and five in both ULs and LLs. 36 patients (100%) had at least one limb with abnormal CMCT. This included none with UL, one with LL and 35 with both UL and LL abnormalities.

**Side-to-side CMCT Comparison**

Mean UL RLDs were 0.8 (0.65) ms, 1.53 (1.59) ms, 2.72 (3.51) ms, and 2.03 (2.19) ms for Groups 1 to 4 respectively.

Mean LL RLDs were 1.01 (0.8) ms, 2.26 (1.91) ms, 2.45 (3.35) ms and 2.69 (2.51) ms for Groups 1 to 4 respectively.

RLDs for UL and LL between Groups 1 to 4 were not significantly different except for LLs between Groups 1 and 2 \( (p < 0.001) \) and Groups 1 and 4 \( (p < 0.03) \). In addition, there was no significant difference in RLD between Group 1 and the control group.
Fig. 16.1. MRI and TMS tracings of patients in Groups 1 to 4. 
A and B: MEPs of UL and LL respectively. 
Latency, vertical gain and sweep speeds are as shown on the recordings.
C and D: Sagittal turbo-spin echo T2-weighted (C) and axial gradient echo images of the cervical spine (D), demonstrating osteo-cartilaginous bars causing increasing degrees of cord impingement/compression as defined in text.
The Group 4 patient did not have a recordable MEP in the LL recording.
In Group 1, there were no patients with RLD exceeding normal control values in both UL and LL.

In Group 2, there were nine patients in UL, 10 in LL and one patient in both UL and LL with RLD exceeding normal control values.

In Group 3, there were 10 patients in UL and five in LL with RLD exceeding normal control values.

In Group 4, there were seven patients in UL, three patients in LL and two patients in both UL and LL with RLD exceeding normal control values.

Although RLD for LL between Groups 1 and 4 reached statistical significance, a large proportion of these patients had absent MEPs, in keeping with the severity of cord compromise. Hence, TMS findings were analysed in greater detail in terms of RLDs compared with MRI findings only in Group 2. For UL, only 29% with significant RLD had lateralised disc herniation corresponding to the affected side from CMCT calculations. The other patients had central disc herniations and/or osteophytes on MRI. For LL, only 22% of patients with significant RLD had lateralised disc herniation corresponding to the affected side from CMCT calculations. The other patients again had central disc herniations on MRI.

All patients and controls tolerated the TMS procedure well with no reported complications. Each TMS study, including preparation and explanation, took an average of 12 minutes to perform.

**TMS and MRI Combined Findings**

Based on TMS findings in relation to MRI, all 28 subjects in Group 1 (no MR cord compression) had normal TMS findings. Forty of 49 patients in Group 2 had at least one limb with abnormal CMCT while the other nine had right-left CMCT differences exceeding control values. All 28 and 36 patients in Groups 3 and 4 had at least one limb with abnormal CMCT.

Additionally, of the eight patients incidentally encountered during the study who had other conditions, three patients (two with demyelination, one with syringomyelia) also had abnormal MRI and TMS. The other five patients (two with motor neuron disease,
three with stroke) had normal MRI but abnormal TMS. No patient with normal MRI had abnormal TMS studies. In sum, all eight patients had abnormal CMCTs for ULs, LLs, or both.

Thus, with MRI as the reference standard, the sensitivity and specificity of TMS for cord abnormality was 100% and 84.8% respectively. The findings also corresponded to a positive predictive value of 95.9% and a negative predictive value of 100%.

DISCUSSION

Clinical Aspects
The clinical presentations and levels of MRI abnormalities in this study appeared comparable with smaller series published previously\(^5,10\). Hence, this larger series can be considered representative of a typical group of patients presenting to the neurophysiologist for functional evaluation.

While asymptomatic cord compression may be encountered in individuals, especially in advanced age\(^24,25\), it can be clinically difficult to distinguish symptoms and signs of radiculopathy from myelopathy, particularly if pyramidal signs of spasticity, gait changes and hyperreflexia are equivocal. A previous study\(^6\) comprising 25 patients showed that MEPs and SSEPs were normal in asymptomatic individuals but the correlation of TMS findings with the degree of cord compression on MRI has not been systematically evaluated.

Pathophysiology
The pathogenetic factors of CSM are often multiple and interactive. These include congenital spinal narrowing\(^26\), spondylotic bars, discs, hypertrophic facets, disturbed blood flow and demyelination\(^27\). Pathological studies suggest that the corticospinal tracts are affected early\(^28\). Mouse models of spinal cord compromise have been used to achieve reproducible degrees of spinal compression\(^29\). A separate mouse study showed that 20% occupation rate, a measure of the severity of spinal canal stenosis by ossified lesions, may be the critical level for functional changes in the spinal motor neurons\(^30\). Hence, our MRI grouping criteria (in Groups 1 and 2) of preservation of two-third cord diameter is a reasonable close approximation of this parameter. Posterolateral compression in another mouse model resulted in linear correlation of the reduction in number of motor neurons with the extent of ipsilateral compression\(^31\).
Moreover, spinal motor neurons were shown to translocate immediately rostral to the area of external compression\textsuperscript{32}. A canine model of progressive myelopathy separately revealed grey matter vascular morphology changes in addition to spinal motor neuron loss using histological techniques\textsuperscript{33}.

It is well known in human CSM that the lateral corticospinal tracts are first to be affected in minor compression\textsuperscript{10,34}. Moreover, it is known from the somatotopic arrangement of the spinal cord that fibres to the LLs are located more laterally than those to the ULs\textsuperscript{35}. These facts are most relevant in the explanation of TMS and MRI findings of this study as described below.

**MRI**

Most patients in the study were eventually classified as Group 2 after MRI, suggesting that in the actual clinical setting, mild CSM is most commonly encountered.

Simultaneous use of both T1 and T2-weighted MR sequences are well shown to be of value in evaluating CSM\textsuperscript{36,37}.

The levels of high T2 signals in the spinal cord did not correlate directly with the most significant levels of cord compromise in many patients, suggesting that other factors, including oedema, gliosis, ischaemia or disturbed blood flow may play a role in addition to mechanical factors\textsuperscript{38–42}. In addition, the presence of T2 signal change in the cord may not always be directly related to the degree of cord compression. A mild disc herniation may occasionally cause intramedullary cord T2 signal change if this was complicated by direct trauma or cord contusion against the disc\textsuperscript{43}. As the cervical spine is a dynamic structure, significant mechanical tension has also been shown to occur within the cervical cord during neck flexion, which may be clinically relevant for patients with CSM\textsuperscript{44}.

It is, however, evident that patients in Group 4 with T2 signal changes had the most severe TMS abnormalities, including 67\% with absent MEPs and 100\% with at least one limb showing abnormal CMCT.

**TMS**

The use of TMS in the evaluation of CSM is well-described\textsuperscript{7,45}. MEP amplitudes have not been shown to be of value for CSM\textsuperscript{10}, although one small study\textsuperscript{46} found lower MEP amplitudes in patients with multilevel lesions compared with those with single level
lesions. Hence, central motor conduction latencies were employed as a measurement, as in previous studies. CMCT reflects function in the fast conducting pyramidal fibres\textsuperscript{15,47,48} and prolonged CMCT reflects desynchronisation, temporal dispersion, conduction block or even axonal degeneration in the fastest conducting fibres\textsuperscript{16}. Intraoperative electrophysiological studies have documented prolonged CMCT with only a minor degree of conduction slowing in the corticospinal tract in compressive CSM, likely contributed by impaired summation of multiple descending potentials after TMS\textsuperscript{49}. CSM is also more likely to produce corticospinal tract rather than dorsal column compression. Hence, SSEPs, which are known to be less sensitive than MEPs in CSM\textsuperscript{50,51}, were not included as a study parameter. The FDI was suitable as a recording site as CMCT abnormalities are more likely to be found in muscles below the site of the spinal lesion\textsuperscript{5}. Additionally, LL recording made from the AH muscle was utilised as the lateral corticospinal tract is known to be involved early in extramedullary compression\textsuperscript{10,34}. LL MEPs are more sensitive to cervical cord compression as descending volleys in the motor tracts traverse the entire cervical cord before reaching the lumbar segments\textsuperscript{6}. The F wave method has been shown to be ideal for measurement of CMCT in the presence of a peripheral nerve lesion\textsuperscript{52}.

In this study, the mean CMCTs were positively correlated with the severity of cord compression from Groups 1 to 4. Inter-group testing also revealed statistical significance with the exception of Groups 3 and 4. This finding supports the reliability of CMCT as a tool for functional evaluation of the different degrees of corticospinal tract dysfunction. Of the 141 patients enrolled in this study, TMS reliably selected 28 (20\%) of patients into Group 1, all with normal CMCTs to ULs and LLs and no RLDs exceeding controls. These patients could have had an expensive MRI of the cervical spine deferred or be managed medically. On the other hand, absent MEPs in one or more limbs suggest significant cord compression (Groups 3 and 4) and further MR imaging was then warranted with a view to surgical intervention.

The findings of significant RLD between Groups 1 and 2 in the LLs corroborates mild early cervical cord indentation in Group 2. This can be useful in the clinical setting to screen patients with mild CSM for more vigilant follow-up and eventual imaging. The high proportion of LL RLD in Group 2 as compared with Groups 3 and 4 can be explained by early involvement of lateral corticospinal tracts and length traversed by motor tracts before reaching the AH (as discussed above). In addition, there is also the possibility of asymmetric disc herniation in early CSM, progressing to centralisation as the disc
herniation enlarges. Thus, the collective TMS findings pointing to Group 2 from this study were universal presence of MEPs, abnormal CMCT to one limb, particularly the LL, and significant RLDs.

The side correlation of TMS and MRI findings were low for patients with significant UL and LL RLD in Group 2. This can be partly explained in relation to the dynamic state of herniated discs in CSM and lumbar disc herniation. A previous study of 38 patients with serial MRI over several months demonstrated reduction in cervical disc herniation in 40% of patients, especially in the early stages of disease. It was also shown that the lateral type of herniation regresses more frequently. Vascular factors, resorption of hematoma by macrophages and dehydration of nucleus pulposus have been cited as possible mechanisms. This is in contrast to large central disc herniations causing significant myelopathy which are not resorbable. It is also well known that the cervical cord is a dynamic structure during neck flexion and extension. A small central disc seen on MRI in many cases in Group 2 may impinge on the left or right side of the cord in relation to dynamic neck movements. The presence of these factors may account for the lack of side correlation between TMS and MRI features in Group 2.

The lack of differences in mean CMCTs between Groups 3 and 4 suggest that the disease has reached a severe plateau stage of corticospinal tract dysfunction. However, Group 4 has a distinctly larger proportion of patients (67% vs. 32%) with absent MEPs, which may reflect the underlying mechanisms leading to increased T2 MRI changes mentioned above.

Finally, during the course of study, eight patients with incidental diagnoses other than CSM were screened out successfully for further management, suggesting further utility of TMS as a clinical adjunct.

**Practical Implications**
There are implications of the findings in this study with respect to the pathogenesis, clinical management and health costs of CSM.

CSM is an almost universal consequence of human aging, and prevalence is increased concomitant with age. This study has examined a cross-section of patients presenting at various stages of severity. From MRI classification, Groups 1 to 4 can be regarded as Stages 1 to 4 of the disease. The findings of significant LL RLD in Group 2
suggests that the condition progresses from minimal spondylosis and root changes, to small potentially resorbable disc herniation with lateral cord impingement, to overt cord compression and eventual intramedullary changes detected with MRI.

The evidence for surgical management of CSM is not plentiful. In the Cochrane Review, only two randomised trials comprising 130 patients were noted, both of which did not show any significant difference between conservative and surgical treatment.

Our results point to the high sensitivity and specificity of TMS in differentiating patients with and without cervical cord abnormalities. Furthermore, with the high cost of MRI compared to TMS, and the evidence of excellent correlation between TMS findings and MRI outcomes from this large study, TMS can be recommended as a non-invasive, less costly and less time-consuming technique for screening and serial evaluation of CSM. Only patients with TMS evidence pointing to more severe disease can then be imaged, with a view to possible surgical intervention.

Finally, all patients had initial clinical diagnoses of significant CSM despite careful examination by an experienced doctor. Much of the difficulty arises in view of the large number of mild cases (Group 2), as well as the coexistence of myelopathy with root pathology, which form a large group highlighted in our series. This renders clinical examination difficult and signs equivocal due to the combination of upper and lower motor neuron features. Here, TMS adds considerable information to the functional evaluation of upper motor neuron corticospinal pathways in CSM.

CLINICAL NOTES

This chapter outlines our standard technique to determine CMCT for cervical spine disorders. It should be cautioned, however, that while the role of TMS as a screening tool to MRI in CSM is highly promising, an MRI should not be deferred in clinically doubtful cases of CSM, since it can demonstrate other non-spondylotic causes of myelopathy.

REFERENCES

CERVICAL DISORDERS

CERVICAL DISORDERS


