Unusual entrapment neuropathy in a golf player

To the Editor: The article by Hsu et al.[1] provided a very elegant demonstration of the value of the technique of inching in the localization of focal lesions of motor and sensory axons and the ability of this technique to characterize the nature of the lesion as demyelinating. Whether the demyelination is producing focal axonal slowing of conduction, fiber blocking, or both may also be demonstrated and the percentage of total fibers blocked can be estimated. The presence and extent of axonotmesis may also be determined. This information has important prognostic (as the authors point out) and treatment implications and can be obtained in the EMG evaluation of any focal nerve lesion when stimulation proximal and distal to the lesion is possible (e.g., carpal tunnel syndrome [CTS]). The authors feel that the lesion location in their patient (between 2 and 3 cm distal to the distal wrist crease) is "unusual" and speculate on the mechanism of its production.

In our study of 122 patients with a clinical diagnosis of CTS (which was bilateral in 79) the lesion was between 2 and 3 cm distal to the distal wrist crease in 44.5% of the sensory studies and 21.3% of the motor studies.[2] It is a common experience among hand surgeons and electromyographers that patients with long-standing minimal CTS often experience a marked increase in symptoms after unaccustomed heavy hand usage of different types and for varying periods. Sometimes the extent of this usage is less than the reported patient experienced. Patients with no previous symptoms of CTS may also experience such symptoms with comparable increased hand usage. The symptoms of the patient Hsu et al.[1] describe are compatible with CTS. We believe that it is likely that this patient's median nerve lesion resulted from the usual factors producing CTS.

James C. White, MD, Richard K. Johnson, MD, *Los Gatos, CA*

Reply from the Authors: We appreciate the interest in and comments on our report by Drs. White and Johnson. They have two comments: the entrapment site is not unusual, and they speculate that there could have been a pre-existing minimal carpal tunnel syndrome (CTS) that contributed to our patient having median nerve compression.

We agree that compression of the median nerve between 2 and 3 cm distal to the wrist crease is not unusual in patients with CTS, as shown by their study.[2] However, median nerve neuropathy in the palm is uncommon in golf players,[3] more so compression by the first metacarpal bone. The association of median neuropathy and golf practice is clear in two aspects: the temporal relationship and conduction block on the nerve conduction study. This patient developed symptoms after playing golf, which he had not experienced before, and his symptoms remitted after he stopped playing. Further, the clinical consequences of conduction block are weakness and loss of sensation. This patient did not have these symptoms. Therefore, the conduction block shown in our case developed after golfing.

It is difficult to speculate whether this patient had minimal median neuropathy in the carpal tunnel that was aggravated by playing golf or not. This young man did not have any of the well-described risk factors for developing CTS (i.e., obesity, other medical problems, occupation involving repetitive wrist movement, and sex).[4] It remains uncertain how much the transverse carpal ligament contributed to the compression of the median nerve. This is the reason why we preferred median neuropathy in the palm rather than CTS in this case.

What we really wanted to emphasize was the importance of palmar stimulation and that this can distinguish focal demyelination with conduction block, which has a very good prognosis from axonal degeneration. Further, better technique of holding the golf club may prevent this unusual focal neuropathy.

Wei-Chih Hsu, MD, *Taipei, Taiwan*, Agyepong Oware, MRCP, *Bristol, UK*

References

1. Hsu W-C, Chen W-H, Oware A, Chiu H-C. Unusual entrapment neuropathy in a golf player. Neurology 2002;59:646–647.
2. White JC, Hansen SR, Johnson RK. A comparison of EMG procedures in the carpal tunnel syndrome with clinical-EMG correlations. Muscle Nerve 1988;11:1177–1182.
3. Dawson DM, Hallett M, Millender LH. Entrapment neuropathies. Boston: Little, Brown and Co, 1990;351.
4. Atcheson SG, Ward JR, Lowe W. Concurrent medical disease in work-related carpal tunnel syndrome. Arch Intern Med 1998;158:1506–1512.

Effects of subthalamic nucleus (STN) stimulation on motor cortex excitability

To the Editor: We agree with Däuper et al.,[1] that STN stimulation may modulate cortical excitability.[2] However, the study by Däuper et al.[1] raises several concerns related to methodology, results, and discussion.

Regarding the methodology, information on the age of the control group is not provided—age, however, is a crucial factor for motor evoked potentials. For a valid comparison the age group of the controls should be matched with the age of the patients. Besides, the reproducibility of the total voltage time integral may be questionable, considering the intertrial variability (see figure 1 in their article) and considering that only a few trials were averaged (possibly preselected from more trials by an unblinded observer). Movement of coil position and angle against the individual's vertex may also have increased data variability. Moreover, patients with predominantly akinetic-rigid PD are not able to cooperate as well as controls in silent period (SP) studies requiring maintenance of a constant muscle tone.[3] Consequently, the SP is frequently interrupted by small amounts of EMG in patients with PD.[4]

Regarding the results, previous studies suggest that STN stimulation restores intracortical inhibition (ICI), similar to the effect of dopaminergic drugs[3,5] and has no effect on the SP.[3] In contrast to these results, Däuper et al. did not report restoration of ICI by dopaminergic drugs alone, but ICI was reduced with stimulation "on"/medication "on" in the same amount as with stimulation "off"/medication "off" (see figure 2 in their article).[1] Different stimulation paradigms only partially explain these inconsistent results.

Finally, in the discussion of their results the authors raise the question, "How can the increase of the SP during stimulator "on" be explained?"[1] Modulation of other indirect connections not mentioned in Däuper et al.'s article,[1] like disinhibition of the dorsal midbrain anticonvulsant zone via the substantia nigra, may also influence motor excitability.[2] Furthermore, high-frequency stimulation does not only inhibit STN neurons but simultaneously excites axons within the STN.[2] Antidromic activation of corticosubthalamic collaterals of the pyramidal tract may lead to cortical modulation (for example via retrograde activation of collaterals to cortical GABAergic basket cells) as well as spinal modulation (via nigrospinal pathways or via collaterals to spinal alpha-motoneurons and activation of Renshaw cells). This could also explain a modulation of intracortical and spinal inhibitory mechanisms by STN stimulation.

Tobias Loddenkemper, MD, Christoph Kellinghaus, MD, Hans O. Lüders, MD, PhD, *Cleveland, OH*

Reply from the Authors: We appreciate the critical comments on our paper "Effects of subthalamic nucleus (STN) stimulation on motor cortex excitability."[1] The authors of the letter have several concerns that we would like to address.

Regarding methodology, we agree that age has a substantial influence on motor cortex excitability. We will publish a paper focusing on this issue in the near future.[6] We have examined two different age groups in this study using paired-pulse transcranial magnetic stimulation (3 vs 13 ms interstimulus interval) and found that intracortical inhibition was significantly greater in older subjects.[6] This result, however, is different from previous reports[7] suggesting a decrease of intracortical inhibition with on-

going age. This might be explained by different stimulation techniques. While our group has administered monophasic magnetic stimuli, Peinemann et al.[7] used biphasic stimulation.

Thus, it is not questionable that age has an impact on motor cortex excitability. Although the main focus of our paper[1] was a comparison of different stimulation/medication conditions among PD patients (and not a comparison of PD and healthy subjects), the control group in our study was of comparable age (mean age 56 years).

Most clinical neurophysiologists would agree that motor evoked potentials are subject to considerable data variation, regardless of efforts to keep coil position and angle constant. As described in our paper,[1] we have performed five trials for each condition (3 ms vs 13 ms, stimulation/medication "on" vs "off") and calculated mean values. This procedure has been used in other publications as well.[6,8]

The problem of poor cooperation in PD patients has been addressed in our paper extensively.[1] However, we found that EMG activity among akinetic-rigid PD patients (only little tremor) was moderate and did not differ significantly from healthy controls. Further, another study confirmed that the extensor carpi radialis and flexor carpi radialis muscles can be fairly well relaxed in PD patients.[9] As far as L-dopa effects on intracortical inhibition are concerned, the authors also found a reduced ICI in patients while on dopaminergic medication.[9]

Regarding our results, this issue has been addressed in the discussion section of our paper in detail.[1] We just would like to point out the fact that our experimental protocol and the sample of PD patients were different from previous studies,[3] possibly accounting for different findings.

Regarding the discussion, we are thankful for their additional suggestions. However, at this stage all explanations are rather hypothetical; an open discussion on this matter would be appreciated.

J. Däuper, C. Schrader, J.D. Rollnik, *Hannover, Germany*

References

1. Däuper J, Peschel T, Schrader C, Kohlmetz C, Joppich G, Nager W, et al. Effects of subthalamic nucleus (STN) stimulation on motor cortex excitability. Neurology 2002;59:700–706.
2. Loddenkemper T, Pan A, Neme S, Baker KB, Rezai AR, Dinner DS, et al. Deep brain stimulation in epilepsy. J Clin Neurophysiol 2001;18:514–532.
3. Cunic D, Roshan L, Khan FI, Lozano AM, Lang AE, Chen R. Effects of subthalamic nucleus stimulation on motor cortex excitability in Parkinson's disease. Neurology 2002;58:1665–1672.
4. Cantello R, Gianelli M, Bettucci D, Civardi C, De Angelis MS, Mutani R. Parkinson's disease rigidity: magnetic motor evoked potentials in a small hand muscle. Neurology 1991;41:1449–1456.
5. Pierantozzi M, Palmieri MG, Mazzone P, Marciani MG, Rossini PM, Stefani A, et al. Deep brain stimulation of both subthalamic nucleus and internal globus pallidus restores intracortical inhibition in Parkinson's disease paralleling apomorphine effects: a paired magnetic stimulation study. Clin Neurophysiol 2002;113:108–113.
6. Kossev AR, Schrader C, Däuper J, Dengler R, Rollnik JD. Increased intracortical inhibition in middle-aged humans: a study using paired-pulse transcranial magnetic stimulation. Neurosci Lett 2002;333:83–86.
7. Peinemann A, Lehner C, Conrad B, Siebner HR. Age-related decrease in paired-pulse intracortical inhibition in the human primary motor cortex. Neurosci Lett 2001;313:33–36.
8. Siggelkow S, Kossev A, Moll C, Dengler R, Rollnik JD. Impaired sensorimotor integration in cervical dystonia: a study using TMS and muscle vibration. J Clin Neurophysiol 2002;19:232–239.
9. Lewis GN, Byblow WD. Altered sensorimotor integration in Parkinson's disease. Brain 2002;125:2089–2099.

Predictors of effective bilateral subthalamic nucleus stimulation for PD

To the Editor: Charles et al. make an important contribution with their article describing possible predictors of deep brain stimulation (DBS) of the subthalamic nucleus efficacy for PD.[1] While DBS is highly effective and FDA approved, the procedure has considerable risks. Effective predictors could favorably shift the risk-to-benefit ratio. Unfortunately, the analysis performed is of limited value and potentially misleading.

A more appropriate analysis would be to report the area under the receiver–operator characteristic curve, which relates the specificity and sensitivity of the tests to age and levodopa responsiveness. The goal of any predictive task not only is to avoid surgery for those patients not likely to benefit but also to avoid withholding surgery from those that would. Visual inspection of the data represented in the graphs provides little confidence that either age or levodopa responsiveness will have sufficient specificity and sensitivity to be an effective predictor that can be used for patient selection.

In addition, the study of predictors was limited to a retrospective correlational analysis. Correlation is a mathematically optimizing procedure that will find a correlation, even if spurious.[2] Thus, it remains unclear how generalized are the regression analyses performed. That is why it is so important to apply the predictive regression equations in a prospective manner. Often, dividing the sample population into two groups, the first to develop the regression equations and the second to prospectively test those equations, can do this. The large majority of times, the specificity and sensitivity of predictors protectors fall when tested prospectively.

Erwin B. Montgomery, Jr., MD, *Cleveland, OH*

Reply from the Authors: We thank Dr. Montgomery for his comments and share his concern about the importance of adequately selecting parkinsonian patients for surgery. Dr. Montgomery's remark deals with the use of regression and correlational analyses to study the predictive factors of outcome from bilateral subthalamic nucleus stimulation. While it is true that the regression analysis of the data is retrospective, the original patient enrollment, treatment, and data collection were performed prospectively. The calculation of the sensitivity, specificity, and confidence intervals would need considerably more patients, hardly compatible with this type of therapeutic procedure. The receiver–operating characteristic curves proposed by Dr. Montgomery are frequently used to assess the usefulness of diagnostic markers, but the method also has some disadvantages.[3] We think that univariate analysis is one of the most appropriate statistical methods for our study. We agree with the necessity of validating our model in another prospective study. We do not know if "the large majority of times, the specificity and sensitivity of protectors fall when tested prospectively," but it has been shown that it is not always true.[4]

Most studies of the surgical treatment of PD found that outcomes from surgery are better in patients with levodopa-responsive motor symptoms. Welter et al.[5] also used regression analysis in their series of parkinsonian patients treated with subthalamic nucleus stimulation. In keeping with our results they found that the outcome of STN stimulation was excellent in levodopa-responsive forms of PD. Our results are consistent with the classic inclusion criteria for subthalamic nucleus stimulation and imply that the decision to operate on the oldest patients and/or patients with levodopa-resistant motor symptoms should be carefully weighed. The other lesson from our experience is that parkinsonian patients with severe levodopa-induced motor complications may still be surgical candidates if a fair levodopa response is maintained, i.e., if their best on-motor score is low. This result is clinically sensible. The relative young age at the time of surgery could have been expected as a good predictor because young-onset PD is characterized by a good response to levodopa with minimal on-period axial or nonmotor symptoms except fluctuations and dyskinesias.[6] Moreover, surgery-related complications are more frequent in an elderly population.

P.D. Charles, MD, *Nashville, TN;* N. Van Blercom, MD, P. Krack, MD, *Grenoble, France;* S.L. Lee, MD, PhD, *Nashville, TN;* J. Xie, MD, PhD, G. Besson, MD, PhD, A.L. Benabid, MD, PhD, P. Pollak, MD, *Grenoble, France*

References

1. Charles PD, Van Blercom N, Krack P, et al. Predictors of effective bilateral subthalamic nucleus stimulation for PD. Neurology 2002;59:932–934.
2. Wasson JH, Sox HC, Neff RK, Goldman L. Clinical prediction rules: applications and methodological standards. N Engl J Med 1985;313:793–799.
3. Feinstein AR. Clinical epidemiology. The architecture of clinical research. Philadelphia: WB Saunders Company, 1985.
4. Besson G, Robert C, Hommel M, Perret J. Is it clinically possible to distinguish non-hemorrhagic infarct from hemorrhagic stroke? Stroke 1995;26:1205–1209.
5. Welter ML, Houeto JL, Tezenas du Montcel S, et al. Clinical predictive factors of subthalamic stimulation in Parkinson's disease. Brain 2002; 125:575–583.
6. Quinn N, Critchley P, Marsden CD. Young onset Parkinson's disease. Mov Disord 1987;2:73–91.

Correction

GDAP1 mutations in CMT4: Axonal and demyelinating phenotypes? The exception "proves the rule"

In the recently published editorial titled "*GDAP1* mutations in CMT4: Axonal and demyelinating phenotypes: The exception "proves the rule," (*Neurology* 2002;59:1835–1836) the authors inadvertently misstated a mutation. The text should have stated "*myotubularin-related protein-2 (MTMR2).*"

GDAP1 mutations in CMT4: Axonal and demyelinating phenotypes? The exception "proves the rule"

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