Long-term follow-up of aneurysms developed during extracranial internal carotid artery dissection

To the Editor: We thank Guillon et al.1 for their valuable study on the long-term follow-up of aneurysms resulting from extracranial internal carotid artery dissections. In particular, the study shows that medical management with antiplatelet therapy alone is generally sufficient for this condition. Guillon et al. used angiography, MRA/MRI, or both for follow-up of dissecting aneurysms. Although the efficacy of MRA/MRI for diagnosis of carotid artery dissection is well known, the results of this investigation provide good evidence for its use in detection and follow-up of associated aneurysms.

Angiography and MRA/MRI can also be complemented by ultrasonographic follow-up of carotid aneurysms. Recent developments in ultrasound technology, in particular broad band transducers with improved axial resolution and depth penetration, have led to new neurosonologic applications for evaluation of cerebrovascular disease, including evaluation of carotid artery dissection and carotid aneurysms. Our general approach in patients with MRA/MRI-verified carotid aneurysms developing during carotid artery dissections is now a follow-up examination with color Doppler flow imaging and power Doppler imaging every 6 months. Stable ultrasonographic findings require no additional imaging procedure. In cases of aneurysms located in close proximity to the skull base, special transducers may be necessary that are not commonly used in routine evaluation of the carotid arteries. Ultrasonographic techniques not only offer excellent visualization of dissecting aneurysms of the carotid artery (figure), but also allow hemodynamic Doppler evaluation of both the aneurysm and the adjacent carotid artery. This noninvasive approach to follow-up of carotid aneurysms is both cost effective and efficient and should be considered in all patients presenting with aneurysms after carotid artery dissection. The results of the study by Guillon et al. documenting the general long-term efficacy of medical treatment of extracranial dissecting aneurysms provide additional support for follow-up with ultrasonography.

Stephen Meairs, MD, Michael Hennerici, MD, Mannheim, Germany

Reference

Tongue and limb myokymia in amyotrophic lateral sclerosis

To the Editor: We agree with Sander et al.1 that myokymia may be observed in anterior horn cell disease more often than previously suspected. Continuous myokymic discharges in one or more affected muscles were a remarkable EMG finding in 4 of 43 patients with syringomyelia, another disease affecting the lower motor neuron.2 In one of the four patients, myokymia was limited to paraspinal muscles, whereas in the other three cases limb myokymia was associated with continuous motor unit activity and minipolymyoclonus. Furthermore, we found myokymic-like discharges synchronous with inspiration (respiratory synkinesis) in another four patients from the same series. These discharges were similar to myokymic discharges in the number of potentials per burst and the average number of bursts per minute. It has been suggested that electrotonic spread of discharges from rhythmic generators within the CNS to hyperexcitable anterior horn cells may be responsible for the appearance of myokymic discharges in such cases.3 Increased anterior horn excitability has been demonstrated by H-reflex studies in patients with syringomyelia.4

The use of multichannel EMG, surface electrodes, and a slow sweep speed may be more useful than conventional concentric needle EMG to detect abnormal spontaneous activity other than fibrillations and positive sharp waves, including myokymia and respiratory synkinesis.5,6 Currently, we sample several muscles with surface electrodes and a slow sweep speed to search for these abnormal spontaneous discharges. A high level of suspicion is required to record myokymic-like discharges associated with breathing, the so-called respiratory synkinesis.

Martin Nogués, MD, Erik Stalberg, MD, Buenos Aires, Argentina

Reply from the Authors: We thank Drs. Nogués and Stalberg for their comments. We agree that myokymia and respiratory synkinesis are likely to be under-recognized. If there is a sufficiently high index of suspicion, their technique of surface recording with a slow sweep speed could be helpful in screening multiple muscles for the presence of these discharges.

Howard W. Sander, MD, Donald C. Aberfeld, MD, Sudhansu Chokroverty, MD, New York, NY

References

Suppression of pendular nystagmus by smoking cannabis in a patient with multiple sclerosis

To the Editor: I read with interest the article by Schon et al.1 In the early 1960s, I observed an individual with congenital nystagmus whose nystagmus dampened after smoking cannabis; the damping was obvious and it was evident to others. Unfortunately, the

Figure. (A) Arteriography of an extracranial aneurysm of the internal carotid artery at the skull base resulting from carotid dissection in a 34-year-old man. Corresponding power Doppler image of the aneurysm (B; white arrow) using a 4–7 MHz dynamic range linear transducer on an ATL HDI 5000 ultrasound machine (Advanced Technology Laboratories, Bothel, WA) is also shown.
setting precluded ocular motor recording and the date preceded preclinical techniques to accomplish such recording. However, the subject was able to read small print on a poster across the room on the wall opposite to where he was seated, which was not possible before smoking the cannabis. Over the ensuing years, that observation has been supported by unsolicited, first-hand reports of similar effects by several patients with congenital nystagmus referred to our laboratory for ocular motor recording; the most recent report came from a participant of the inaugural meeting of the American Nystagmus Network, held in Cleveland, OH, July 30–31, 1999.

Research into the therapeutic benefits of cannabis is discouraged in the United States so I have not properly recorded or studied these effects in a controlled setting. Nevertheless, the damping effect was great enough to be observed visually and to increase visual acuity. To a lesser extent, alcohol has a similar damping effect on congenital nystagmus (personal observation).

Schon et al. noted that only by smoking the cannabis was the pendular nystagmus of MS dampened; that, itself, is worthy of further study. Even more interesting is that cannabis damped an acquired form of nystagmus. Although the beneficial effects of cannabis on congenital nystagmus have been recognized for many years by a small number of people with congenital nystagmus, this latter observation raises the possibility that this drug can be used in different types of acquired nystagmus (horizontal and vertical) where damping the oscillations can have the beneficial effect of reducing or eliminating the debilitating effects of oscillopsia. I encourage these authors to continue their work in this area.

Louis F. Dell’Osso, PhD, Cleveland, OH

Reply from the Authors: We read with interest Dr. Dell’Osso’s observation of a further patient with cannabis-responsive nystagmus. He raises four important issues.

The first is the possibility of widespread benefits of cannabis in patients with different types of nystagmus. We suspect that cannabis may benefit only a subgroup of patients with acquired nystagmus because our patient’s acquired pendular nystagmus (APN) was also dramatically suppressed, and his visual acuity improved, by drinking 2 to 3 glasses of red wine. We observed this in the eye movement laboratory on three occasions and on the third recorded his eye movements and measured blood ethanol levels (figure). The maximum blood ethanol level was 61 mg/dL, which is the same level as that shown to suppress benign essential tremor.

There is only one previous report documenting two patients with APN who responded to alcohol, suggesting that this is very unusual.

The second point concerns whether ethanol and cannabis act in similar situations. This is strongly suggested by our observation on this single patient and needs to be examined further.

The third question is why we were only able to demonstrate the effect with smoked cannabis and not the cannabis-containing capsules. Clearly it is important to find nonsmoked alternative cannabis preparations that are active in our patient and of wider therapeutic potential.

Finally, Dr. Dell’Osso raises the issue of the political climate needed to allow research into the possible therapeutic benefits of cannabis. In Britain, a large multicenter trial of cannabis on spasticity in MS is about to start, reflecting the current interest that also allowed our study to take place.

Fred Schon, FRCP, Paul Hart, MRCP, Tim Hodgson, PhD, Alyth Pambakian, MRCP, PhD, Christopher Kennard, FRCP, PhD, London, UK

Copyright © 2000 by the American Academy of Neurology

References


Defective slow inactivation of sodium channels contributes to familial periodic paralysis

To the Editor: I applaud the elegant work of Hayward et al.,1 which delineates a role for slow inactivation in familial hyperkalemic periodic paralysis (HyperPP) and cold-induced weakness. Disrupted slow inactivation facilitates depolarization-induced weakness. The authors argue that in the two HyperPP Na+ channel mutations in which slow inactivation was not disrupted, A1156T and M1360V, the pathologic depolarizing Na+ current produced by the mutant channels could persist for clinically relevant periods of time because, based on the behavior of slow inactivation shown in their figure 3, 20% to 25% of A1156T, M1360V, or wild type Na+ channels will not enter the nonconducting slow inactivated state during prolonged depolarization to −50 to −40 mV.

The explanation provided by Hayward et al.1 is parsimonious; however, I contend that the incompleteness of slow inactivation and the voltage dependence of slow inactivation shown in figure 3 for wild type Na+ channels is controversial. In figure 3, slow inactivation could eliminate about 90% of Na+ current for wild type channels. In support of figure 3, some studies of Na+ channels expressed in nonmuscle cell lines found slow inactivation was incomplete, with approximately 10% to 20% of INa not affected by slow inactivation.2,3 Further, it has been shown that Na+ channels with unaltered slow inactivation would be slow inactivated at membrane potentials that were hyperpolarized compared with the operating ranges for fast inactivation.2,3,8 In contrast, Cummins and Sigworth6 reported that slow inactivation reversibly eliminated Na+ current for rat skeletal muscle Na+ channels expressed in HEK cells. In addition, studies of slow inactivation of Na+ current in mammalian skeletal muscle fibers from rabbits, cats,9,10 and humans9,11–13 showed that slow inactivation could eliminate INa. Furthermore, Na+ channels were completely slow inactivated at membrane potentials that were hyperpolarized compared with the operating ranges for fast inactivation.7,11,12 Slow inactivation also developed at hyperpolarized potentials compared with fast inactivation for in vitro studies of frog twitch muscle fibers9,12 and crayfish giant axons.13 Consequently, one study of Na+ channels expressed in HEK cells and several in vitro studies of Na+ channels in intact skeletal muscle or nerve tissue suggest that slow inactivation can eliminate Na+ current.

Figure 3 indicates that slow inactivation required large membrane depolarizations to reduce Na+ currents. The operating voltage ranges of slow inactivation were similar to the operating range for fast inactivation. Several other studies of skeletal muscle Na+ channels expressed in non-native cells found that the operating voltage ranges of fast and slow inactivation overlapped.2,4,9 In contrast, in vitro studies on intact rat and human fast twitch skeletal muscle fibers found that slow inactivation developed at membrane potentials that were hyperpolarized compared with the operating ranges for fast inactivation.7,11,12 Slow inactivation also developed at hyperpolarized potentials compared with fast inactivation for in vitro studies of frog twitch skeletal muscle fibers9,12 and crayfish giant axons.13 Consequently, in vitro studies of skeletal muscle and nerve suggest that slow inactivation may develop at hyperpolarized potentials compared with the voltage operating range shown in figure 3.

The argument provided by Hayward et al.1 that only 75% to 80% of Na+ channels with unaltered slow inactivation would be slow inactivated at membrane potentials of −50 to −40 mV may not be valid if in vitro studies provide a more accurate representation of Na+ channel behavior compared with studies of Na+ channels in heterologous expression systems.

Robert L. Ruff, MD, PhD, Cleveland, OH

June (1 of 2) 2000 NEUROLOGY 54 2191

Figure. Eye movements and blood ethanol levels.
Reply from the Authors: We agree with Dr. Ruff that there are unresolved discrepancies among published reports on slow inactivation of sodium channels. Moreover, these areas of contention have critical implications for the pathophysiologic basis of depolarization-induced weakness during attacks of periodic paralysis.

One such issue is the maximal extent of slow inactivation. This is not a trivial matter to resolve experimentally because fast and slow inactivation cannot be separated unequivocally. The variability in the reported extent of slow inactivation is due in part to differences in the pulse protocols used by different laboratories. Despite these technical obstacles, most studies have reported a residual fraction of channels not slow inactivated even after strong depolarization, including the study by Cummins and Sigworth, who found that 3% of channels remained available and were thus not "reversibly eliminated" as claimed by Dr. Ruff. In vitro studies on nerve and muscle fibers generally show more complete slow inactivation than is observed for channels heterologously expressed in HEK cells. Even in these native preparations, however, a measurable fraction of sodium current resists slow inactivation (e.g., ~5% in Almers et al. figure 5).

A second controversy has been the voltage dependence of slow inactivation relative to that of fast inactivation. When skeletal muscle sodium channels are expressed in fibroblasts or oocytes, the operational voltage range of slow and fast inactivation is identical.2,3,4,5 Loose-patch recordings from skeletal muscle fibers have consistently shown a hyperpolarized shift of slow relative to fast inactivation.6,7,8 The basis of this difference remains unknown. Conspicuous explanations include modulating factors in the muscle internal milieu and differences in recording technique (loose-patch versus tight-seal whole cell, or the use of only a 20-msec conditioning pulse) for all of the 20-msec channel studies may have caused an apparent depolarized shift in the voltage dependence of slow inactivation. Yet another uncertainty is the precise membrane potential, in vivo, at which affected fibers become flaccid and inexcitable. It remains possible that this occurs in the operational voltage range of slow inactivation.

Thus, despite several unanswered controversies about slow inactivation behavior of skeletal muscle sodium channels, there are sufficient data to suggest that not all channels would be slow inactivated during an attack of paralysis. If less than 100% of channels are slow inactivated in depolarized muscle, then slow inactivation can never completely compensate for defects in fast inactivation (or activation) that produce the aberrant depolarizing inward sodium current.

Regardless of the mechanistic interpretation, the data on slow inactivation in relation to HyperPP are unequivocal. All three mutations that disrupt slow inactivation (I693T, T704M, and M1592V) always result in episodic weakness as the predominant symptom. Conversely, slow inactivation was intact for two rare HyperPP mutations (A1156T and M1360V) and was enhanced for a new HyperPP mutation (I1458F) reported after our publication.1

Stephen C. Cannon, MD, PhD, Boston, MA

Copyright © 2000 by the American Academy of Neurology

References
8. Ruff RL. The single channel basis of slow inactivation of Na+ channels in rat skeletal muscle. J Physiol (Lond) 1996;525:C1–C17.
9. Ruff RL. Sodium channel slow inactivation and the distribution of sodium channels on skeletal muscle fibres enable the performance of...
trans-RA and 9-cis-RA with the pathogenesis of IIH, the determination of such metabolites is (and—where appropriate—of synthetic retinoid receptor ligands) should be considered in investigations of the pathogenesis of IIH in addition to analysis of plasma retinol and retinyl esters.

Jörn Oliver Sass, Dr rer nat, Innsbruck, Austria; Thomas Arnhold, Dr rer nat, Biberach an der Riss, Germany; Georg Tzimas, Dr rer nat, Thessaloniki, Greece

Reply from the Authors: On behalf of the readership of Neurology, we thank Sass et al. for their review of the potential additional roles and effects of other retinoid metabolites and retinoid receptor ligands in the pathogenesis of IIH. Our exploratory study was limited to investigating the role of serum retinol and retinyl ester concentration in this disorder. As we stated in the concluding paragraph, "Our results provide testable hypotheses for future investigations." We encourage Sass et al., as well as other skilled scientists, to design additional investigations to elucidate the role of these agents in IIH.

Daniel M. Jacobson, MD, Marshfield, WI

Copyright © 2000 by the American Academy of Neurology

References

Correction

In the article “Neurology in the next two decades: report of the Workforce Task Force of the American Academy of Neurology” (Neurology 2000;54:787–789) by Bradley, the dramatic rise in Postgraduate Year 2 residency positions was presented incorrectly. The correct information is that there has been a 338% rise in 38 years. The author apologizes for the error.
Neurology in the next two decades: report of the Workforce Task Force of the American Academy of Neurology

Neurology 2000;54;2193
DOI 10.1212/WNL.54.11.2193

This information is current as of June 13, 2000

Updated Information & Services
including high resolution figures, can be found at:
http://www.neurology.org/content/54/11/2193.full.html

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
http://www.neurology.org/misc/about.xhtml#permissions

Reprints
Information about ordering reprints can be found online:
http://www.neurology.org/misc/addir.xhtml#reprintsus