An AUPN/ANA survey of department leader opinions on the health of US academic neurology

To the Editor: It was déjà vu when I read the article by Rizzo and Mobley.[1]

The authors state that the health is not good and the reason is, understandably, "financial pressures." "Academic departments find themselves in the position of 'feeding' neurosurgery and neuroradiology, activities for which they may or may not be adequately compensated."

In the "American Academy of Neurology: The First 50 Years,"[2] I described the difficulties practicing neurologists had in trying to convince academic neurologists (other than Oldendorf, Toole, and Gilroy) that imaging is our field. To this day, the small group of neurologist-imagers ("neuroimagers") remain practicing neurologists while academic departments, where research should be done, are poverty stricken. Magnetic resonance spectroscopy (MRS, neurochemistry), fMRI (neurophysiology and behavioral neurology), and the rest of neuroimaging are in the hands of radiologists who make astronomical salaries while basic research in these fields suffers.

It is not too late for academic neurology departments to obtain their own scanners (even if they have to work with the private sector) and hire their own neuroradiologists (and train their own neuroimagers) who should be in the neurology department and may secretly desire to be.

Jack O. Greenberg, MD, *Philadelphia, PA*

Reply from the Authors: Dr. Greenberg raises concerns about a timely issue facing academic and clinical neurologists. MRS, fMRI, and other emerging imaging techniques may be highly relevant to neurologic research and practice. Progress in neurology patient care, research, teaching, faculty development, clinical service, and program operations will require intense vigilance over the coming years on many key issues. Academy members may keep abreast of these issues by checking the American Academy of Neurology's Federal Advocacy Web site (http://www.aan.com/advocacy/federal/index.cfm).

Matthew Rizzo, MD, *Iowa City, IA;* William C. Mobley, MD, *Stanford, CA*

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Does acute occlusion of the carotid T invariably have a poor outcome?

To the Editor: Georgiadis et al.[1] report that carotid T occlusion may have a better clinical outcome than previously thought, especially after IV thrombolysis.[2,3] In their series of 42 consecutive patients, 17% achieved a modified Rankin score (mRS) of 2 6 months poststroke and the mortality rate was only 31%. Furthermore, complete or partial middle cerebral artery (MCA) recanalization was observed in 12 of 18 patients treated with thrombolysis. This is interesting because intracranial carotid occlusion is often considered as a contraindication of IV and even intraarterial thrombolysis because of very low recanalization rate.

The results obtained in our stroke center confirm and extend the findings of Georgiadis et al. In a consecutive series of 100 patients treated with recombinant tissue plasminogen activator IV within a 5-hour time period,[4] 30 had intracranial carotid occlusion as assessed by pre-thrombolysis magnetic resonance (19 with T occlusion and 11 with intracavernous carotid and ipsilateral MCA occlusions). Three of them were subsequently treated by hemicraniectomy. Median NIH Stroke Scale was 18.5 (range, 7 to 30) and 20 (range, 7 to 30) in the T occlusion subgroup. At 3 months, 20% had Rankin score 1, 70% Rankin 0 to 3, and mortality rate was only 10%. The percentages were 16, 74, and 16 in the T occlusion subgroup. Complete MCA recanalization was documented on a 24 to 48 hours MRA control in 43% of the 30 patients and 42% of the T occlusion subgroup.

Surprisingly, none of the patients developed symptomatic hemorrhage. Thus outcome was even better than in Georgiadis report,[1] perhaps because our patients were younger: 49 (44 to 54) vs 66 (56 to 74) years (median [interquartile range]). Both reports suggest that intracranial carotid occlusion should not be considered as a contraindication to IV thrombolysis, although we obviously need new therapeutic approach since MCA recanalization is only achieved in less than half of the patients.

Y. Samson, MD, S. Crozier, MD, S. Deltour, MD, M. Obadia, MD, M. Bruandet, MD, A. Leger, MD, *Paris, France*

Reply from the Authors: We thank Drs. Samson et al. for the letter concerning our article.[1] The presented results together with those of our study, confirm that IV thrombolysis is a safe treatment in acute stroke patients with carotid T occlusions, as symptomatic intracerebral hemorrhage was only observed in 2/72 cases.

Although recanalization rate was higher in our study (66% vs 42%), outcome was worse (mRS 0 to 3 in 22% vs 74%). This marked difference could be due to age differences between the two groups, as noted by Dr. Samson. We concur that the presented results add weight to the hypothesis that IV thrombolysis should not be withheld in acute stroke patients with carotid T occlusion, although more potent therapeutic approach would certainly be needed in this specific patient group.

D. Georgiadis, MD, S. Schwarz, MD, S. Schwab, MD, *Zürich, Switzerland*

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Ulnar neuropathy at the elbow: Follow-up and prognostic factors determining outcome

To the Editor: I read the article by Beekman et al.[1] with great interest and want to make the following comments. The conservative treatment is very minimal. A correct way of treating patients conservatively is described by Dellon.[2] It does include instructing the patient, modification of work and home environment, and splinting the arm during the night. Even periodic changes of work were suggested, as were nonsteroidal antiinflammatory drugs in selected cases.

They do not discuss what impact the loss of 18% (15/84) of the patients might have on the results. The number of patients included in this study is of concern. Within this group, 15 subsamples were created without any statistical correction. The probability of obtaining significance by change is increased with every subanalysis, and is, therefore, substantial in this study. While evaluating the predefined factors, they do not discriminate between not-treated and surgically treated patients, except for the sonographic results. This is not correct. Globally, surgically treated patients have a good outcome 61% of the time whereas those of the not-treated group only 35% and in the worse case 26%.

In table 4,[1] the authors represent the data on the sonographic results. In the surgical group differences were found. However, recalculation shows a 95% CI of −0.05 to 0.64 for the mean difference between pre- and postoperatively for all arms, and a 95% CI of −0.15 to 0.55 for the remission group. Considering the preoperative situation, a significant difference is found comparing the remission and the stable group (95% CI: 0.18 to 0.82). However, postoperatively no difference was found (95% CI: −0.10 to 0.50). In conclusion, the preoperative sonographic findings do not to predict any outcome.

The authors pay attention to the finding of a thickened asymptomatic ulnar nerve at the contralateral side. They calculated a relative risk of 3.7. However, they fail to report the estimated 95% CI: 0.35 to 37.8, indicating that there is absolutely no relation. They state that there is much debate about the efficacy and type of operation. Generally, a success rate of 70% is reported.[3] Therefore, the resistance against surgery is not correct.

This study does not disclose that sonography is a valuable tool in the management of patients with ulnar neuropathy. Furthermore, the claim of the authors to be the first to show the role of electrodiagnostic data should be questioned.

Ronald H.M.A. Bartels, MD, *Nijmegen, The Netherlands*

Reply from the Authors: We appreciate the interest of Dr. Bartels for our work,[1] but disagree with most of the points that were raised.

There are no prospective randomized studies for the subsequent conservative treatment measures mentioned.[2] However, we advised patients to incorporate the instructions described in our paper in home and work environment.

The result section describes that the 15 patients lost to follow-up were clinically not different from the others. Therefore this will not have much impact on the results.

The primary conclusions of the study concerning the two patient groups (surgery vs conservative treatment) were based on the full 69 patients for which follow-up was available. Secondary analyses were performed on patient subgroups and because of the nature of these evaluations, no statistical adjustments were considered necessary. Furthermore, prognostic factors were evaluated in a full multivariate model (simultaneous analysis) after initial univariate analyses.

The primary clinical outcome was, of course, compared between the study arms and emphasized in the paper. However, a partial objective of this paper was to demonstrate the factors that predict outcome other than treatment approach.

The analysis suggested here is overly simplistic. If the goal is to consider the relationship between pre- and posttreatment sonographic results across treatment arms, then the more meaningful approach is to use an analysis of covariance with terms for treatment arm and pretreatment results, as well as a term for treatment-by-time interaction. We did not perform this analysis, since our interest was simply to evaluate each study arm.

We did not claim any statistical meaningfulness for this relative risk. The paper quotes a sizable p value (0.55). This is tantamount to indicating a wide CI.

We disagree that there is substantial evidence to decide when and how to operate in ulnar neuropathy at the elbow (UNE). The study mentioned here is an overview of the literature that contains no prospective randomized studies and mainly deals with different surgical techniques for UNE, not with the topic to operate or not to operate.[3]

Only Eisen and Danon[4] found that slowing of motor conduction below 41 m/s across the elbow predicted a greater likelihood of progression to motor deficits, but this was not found by Dellon et al.[2] No other electrodiagnostic parameters were evaluated in a prospective study in UNE.

We sustain our conclusion that sonography is a useful tool in the management of patients with UNE, not only by improving the diagnostic accuracy of UNE,[5] but also by providing prognostic information.[1]

R. Beekman, MD, J.H.J. Wokke, MD, PhD, M.C. Schoemaker, MD, M.L. Lee, PhD, L.H. Visser, MD, PhD

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The occurrence of Guillain–Barré syndrome within families

To the Editor: We read with interest the report by Geleijns et al.[1] describing the occurrence of Guillain–Barré syndrome (GBS) in at least two members in each of 12 Dutch families. In order to perform the study, a letter was sent to patients with known GBS or chronic inflammatory demyelinating polyneuropathy (CIDP), asking them whether they had a relative with GBS or CIDP. Patients with CIDP were eventually excluded from the study. Based on the occurrence of GBS within siblings, and an earlier onset of GBS in successive generations, Geleijns et al. suggest a role for genetic factors in the pathogenesis of GBS. They conclude that GBS is a complex genetic disorder with an outcome determined by environmental and genetic factors.

We reported a father with CIDP and a daughter who developed acute IDP (AIDP) a year later.[2] Several years later, a second daughter also developed CIDP. We then considered that the underlying genetic abnormality in all three members might be the 17p12 deletion responsible for hereditary neuropathy with liability to pressure palsy (HNPP). The mutation was discovered in this family.[3]

Two of our observations may be relevant to Geleijns et al.'s article. The HNPP mutation might be a predilection for the development of GBS and of CIDP. Therefore, when a genetic component is suspected in these conditions, screening for HNPP might be warranted. Including CIDP in this study might have increased the number of families with more than one member affected with an immune demyelinating neuropathy. Many clinical similarities exist between AIDP and CIDP and both may eventually share also some pathogenetic features.[4]

We suggest that all the Dutch patients with familial GBS, including familial CIDP, should be screened for the HNPP deletion. Finding further cases positive for the deletion will clarify the complex relationship of inflammatory and hereditary neuropathies.[5]

Isabelle Korn-Lubetzki, MD, Israel Steiner, MD, *Jerusalem, Israel*

Reply from the Authors: We thank Drs. Korn-Lubetzki and Steiner for their interest in our article.[1] They concluded that the 17p12 deletion responsible for HNPP was also present in a family in which three members had an IDP. Two members fulfilled the criteria for CIDP and the other for AIDP.[3]

This finding may indicate that CIDP and this deletion may also be present in our recently reported Dutch families in which two or more members had GBS.[1] In this study, we excluded two families in which one or more members had a subacute or CIDP in response to the Editor's opinion. In one of these families, a 79-

year-old grandmother developed a subacute IDP after an upper respiratory tract infection and her grandson developed a CIDP at age 20 with a time interval of 5 years.

In the other family, two cousins were affected; one had an acute and the other one a subacute sensomotoric IDP without preceding events and with a time interval of 14 years. None of them reported a recurrent episode, similar to the family reported by Korn-Lubetzki et al.[3] We also know a family in which two brothers have CIDP but lack the 17p12 deletion. Nevertheless, it would be interesting to screen all our families with IDP for the 17p12 deletion to further elucidate the pathogenesis of these disorders.

Screening for the 17p12 duplication or other Schwann-cell related genes like myelin protein zero (P0) or connexin 32 (CX32) that are involved in other hereditary demyelinating neuropathies would further clarify the relationship between inflammatory and hereditary polyneuropathies.[5] In the case of a positive finding within our families, it would be of further interest to screen for these mutations within our larger cohort of non-familial GBS patients.[6]

Karin Geleijns, MD, Bart C. Jacobs, MD, PhD,
Pieter A. van Doorn, MD, PhD, *Rotterdam, The Netherlands*

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Single-fiber EMG in familial hemiplegic migraine

To the Editor: Terwindt et al.[1] stress the importance of methodological factors in single fiber EMG (SFEMG). When we performed the first SFEMG study in migraine,[2] we were aware that adequate training was necessary to avoid technical flaws. The statement by Terwindt et al.[1] that jitter is pronounced before blocking occurs cannot be generalized. It does not apply to botulism for instance, and may also not apply to migraine. Complete blinding seems illusory in patients with rare conditions who undergo multiple investigations. We chose to limit blinding to the migraine subtype,[2] which likely avoided significant bias, as SFEMG abnormalities were found in only 17 out of 62 patients.

It surprised us that Terwindt et al.[1] found that "the contrast" between our SFEMG report and their normal findings in familial hemiplegic migraine (FHM) patients with a proven mutation in the CACNA1A gene "remarkable." First, there is no disagreement between the two studies. Average mean value of consecutive differences (MCD) was within normal limits in all our subgroups of migraineurs.[2] When we reclassified patients according to the 2nd edition of the International Classification of Headache Disorders, three fulfilled the criteria for familial hemiplegic migraine, five others for sporadic hemiplegic migraine. Only one patient in each group had an increased mean MCD, which is comparable to Terwindt et al.'s results.

Second, as recommended in SFEMG guidelines[3] and contrary to Terwindt et al., we took into account single muscle fiber MCD which was increased in 10 to 15% of fibers in four patients, but in at least one fiber in nine others.

Third, although our studies were initiated by the finding of CACNA1A mutations in FHM and the known crucial role of P/Q Ca2+ channels in neuromuscular transmission, we concentrated on the common forms of migraine following the hypothesis that CACNA1A could be involved in other migraine types than FHM. The latter hypothesis, however, has not been confirmed by genetic studies[4] and in migraineurs with abnormal SFEMG our screening for 14 known FHM1 mutations was negative (unpublished results). It seems unlikely that the neuromuscular transmission abnormalities reported by us[2] and by others in subtypes of migraine and in cluster headache[5] are related to dysfunctioning P/Q Ca2+ channels.

Although our analysis may have been more sensitive, we think that the contrast between Terwindt et al. and our results is not due to methodological factors, but to the study of different migraine types.

Jean E. Schoenen, MD, PhD, Anna Ambrosini, MD, PhD,
Alain Maertens de Noordhout, MD, PhD, *Liége, Belgium*

Reply from the Authors: Schoenen et al. address the implications of our findings as well as methodologic matters. We reported normal mean jitter in FHM[1] as customary.[3] We also investigated abnormality on the level of single fibers, but the normal results were omitted due to length limitations set by editorial policy.

Schoenen's group[2] reported abnormal SFEMG results in common forms of migraine. A possible dysfunction of P/Q Ca2+ channels was mentioned as the rationale for the study as well as the explanation of the abnormal findings. There was no proof for a mutation affecting this channel in these patients. We felt that the contrast with normal results in FHM patients in whom such a mutation had been proven was remarkable. Schoenen et al. seek to resolve the contrast by concluding that their findings in common forms of migraine were not due to a dysfunctioning P/Q Ca2+ channel, which leaves the mechanism unclear.

We feel justified in stressing that blocking without a high jitter is odd. Past reports on botulism mentioned that blocking can occur in fibers with only mildly abnormal jitter, but there were always fibers with markedly abnormal jitter in these patients[6] not reported in the migraine patients. This observation has not been repeated in more recent papers on botulism. Blocking clearly increased with jitter.[7] Near-liminal stimulation causes axonal blocking, which has nothing to do with the neuromuscular synapse; even then blocks are usually accompanied by high jitter. The only well-documented instance of blocking with normal jitter concerns blocking in abnormal axons in Guillain–Barré syndrome.[8]

We consider complete blinding a necessity rather than illusory, as recommended by the American Association of Neuromuscular and Electrodiagnostic Medicine[9] and the Standards for Reporting of Diagnostic Accuracy initiative.[10]

We do not think methodologic explanations for the contrast can be ignored. Differences between groups are possible, even though the P/Q Ca2+ channel rationale to presume SFEMG abnormalities in migraine has been disproved. We await confirmation SFEMG studies in common forms of migraine that follow the above-mentioned guidelines.

J. Gert van Dijk, MD, PhD, G.M. Terwindt, MD, PhD, E.E. Kors, MD, A.A Vein, MD, PhD, M.D. Ferrari, MD, PhD, *Leiden, The Netherlands*

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