interpretation of TCD velocities in patients harboring an intracranial AVM. We agree that some portion of the variance that accounted for the less-than-perfect correlations may have been attributable to errors related to the angle of insonation.

We would point out the following considerations regarding AVMs. Distortion of the proximal conductance vessels is most likely to occur with mass lesion effects, as Finn et al have described for hydrocephalus; bowing of vessels may cause an underestimation of the true velocity of the blood column. True AVMs present with mass effect only in the rarest of cases. However, because AVMs sometimes result in bizarre changes even in proximal vessels, the authors' point is well taken and should be borne in mind in future studies or the interpretation of values from an individual patient. On an individual basis, this may be especially pertinent because feeding artery pressure, when considered in context with other factors, may influence the incidence of spontaneous intracranial hemorrhage from AVMs and therefore may affect the decision of whether or not to treat a particular lesion.

It is worth noting that Manchola et al performed a study of AVM feeding arteries that was in some respects similar to ours (without pressure measurements). As a part of that study, they described a very careful inspection of the angiograms to optimize the best angle of insonation to minimize this source of error. Of their 40 patients, however, they did not describe any with the remarkable deviations suggested by Martin and Gaunt (ie, angle of insonation of > 30°).

A possible pitfall in trying to determine the actual angle of insonation should also be considered. Unless one performs the TCD during fluoroscopy (which is almost never the case), the exact relationship of probe angulation to the insonated vessel can only be approximated.

William L. Young, MD
Lauren H. Fleischer, MD
Department of Anesthesiology
Buckley terPenning, MD
John Pile-Spellman, MD
Department of Radiology
J.P. Mohr, MD
Department of Neurology
College of Physicians and Surgeons
Columbia University
New York, NY

References

Effect of Nitric Oxide Synthase Inhibition on Cerebral Blood Flow and Injury Volume

We commend Nishikawa et al for the care they exercised in their study of middle cerebral artery (MCA) occlusion-induced focal cerebral ischemia in cats, in which they investigated the effects of nitric oxide (NO) synthase inhibition on cerebral blood flow, sensory evoked potentials, and extent of acute cerebral "injury." They tightly controlled relevant variables--a merit of using this large animal model. Their finding of significantly reduced volumes of acutely "injured" caudate nucleus but not of cerebral cortex with no differences in sensory evoked potentials or reductions of cerebral blood flow in the treated versus the control groups contributes new information regarding the mechanisms involved in ischemic brain injury.

The authors assessed tissue "injury" after 4 hours of MCA occlusion using visual evidence of the lack of reduction of 2,3,5-triphenyltetrazolium chloride (TTC) by tissue mitochondrial enzymes and the morphometric quantitation of such nonreactive brain volumes. The authors indicate their awareness that this method's "injury" volume may not necessarily represent actual tissue infarction and that the comparison group's eventual verifiable tissue injury extent might be similar. Because we have carried out studies using the same animal model, our data can provide an estimate of how their acute "injury" volume may compare with permanent tissue infarction volume. We assessed infarct size morphometrically after 2 weeks' survival following 4 hours of temporary, normoglycemic MCA occlusion in 12 cats. Eleven survived and one died acutely from hemispheric edema, cerebral tissue herniation, and brain stem compression. The 11 survivors showed infarction of only 0.6±0.6% of the ipsilateral hemisphere (de Courten-Myers et al, 1989). In comparison, the cats of Nishikawa et al, showed a mean volume of acute "injury" in control animals of 32% of the hemisphere.

Thus, it appears that only a small fraction of the acutely "injured" tissue as measured by the TTC reduction technique evolves into permanent infarcts. Differences in the model can account for only part of this large difference, because both studies were closely controlled and are similar regarding glycemia levels (mean serum glucose concentrations during 4 hours of MCA occlusion in the study of Nishikawa et al versus ours, 163 vs 144 mg/dl, respectively), brain temperature, blood respiratory gases, and other monitored parameters. The two studies did, however, use different anesthetics (halothane versus pentobarbital).

Readers may be tempted to extrapolate the early changes in mitochondrial dysfunction to permanent damage to the brain. However, the data presented suggest that the extent of acute metabolic alterations grossly overestimate the extent of actual brain tissue infarction. Notwithstanding the value of establishing the therapeutic effects of pharmacologic interventions during exposure, follow-up studies determining the extent of permanent tissue injury remain a necessary step in evaluating the effects of drug therapy.

Gabrielle M. de Courten-Myers, MD
Department of Neuropathology
Ronald E. Myers, MD, PhD
Department of Neurology
University of Cincinnati Medical Center
Cincinnati, Ohio

References

Response

We appreciate the generous comments by Drs de Courten-Myers and Myers. We agree that it would be improper to extrapolate the early changes in mitochondrial dysfunction observed in our study to indicate the volume of actual brain tissue infarction. This question has been directly evaluated by Cole et al,1 who demonstrated that the histochemical abnormality revealed by TTC staining may not necessarily represent inevitable infarction when used for paradigms of short ischemic periods (3 hours in
References


5. Warner DS, Zhou J, Ramani R, Todd MM. Reversible focal ischemia is difficult to predict on the basis of the study by de Courten-Myers et al because the anesthetic techniques in the two studies were different. In the study by de Courten-Myers et al, the anesthetic used was pentobarbital, a barbiturate that decreases brain injury in animals exposed to focal ischemia. In contrast, halothane is an inhalational anesthetic that at high concentrations decreases cerebral metabolism but does not appear to decrease brain injury after focal cerebral ischemia. Furthermore, we excluded the cats in which somatosensory evoked potentials were not immediately reduced to ensure a more reproducible insult.

In addition, caution must be taken when comparing results among laboratories. For example, Kolluri et al observed TTC-determined infarct volumes of about 24% in cats subjected to 2 hours of MCA occlusion under ketamine-pentobarbital anesthe sia followed by 1 week of reperfusion. Comparison of this study with our results would suggest little further change in injury volume after 4 hours of ischemia. In the absence of anesthesia, infarct volumes of 12.8±8.5% have been reported in cats subjected to 4 hours of transient MCA occlusion. This value is greater than that observed by de Courten-Myers et al. Therefore, one cannot conclude that the TTC determined injury volume of 30% that we observed at 4 hours of occlusion would eventually shrink to the 0.6% infarct volume observed by de Courten-Myers et al.

Our data demonstrate that the amount of early brain injury produced by 4 hours of MCA occlusion is reduced by inhibition of NO synthase. If treatment with L-NAM decreases injury volume at 4 hours, our data would suggest that inhibition of NO synthase decreases the rate at which brain injury occurs in this experimental model. An alteration in rate of injury may have important clinical implications as it may increase the window of opportunity for use of other therapeutic agents. We believe that it will be important to extend our experiments to evaluate the therapeutic role of NO synthase inhibitors on permanent tissue injury resulting from permanent and transient focal ischemia.

Toshiaki Nishikawa, MD
Jeffrey R. Kirsch, MD
Raymond C. Koehler, PhD
Richard J. Traystman, PhD

Department of Anesthesiology and Critical Care Medicine
The Johns Hopkins Hospital
Baltimore, Md

References


Frontal Headache in Vertebobasilar Stroke

To date, little is known about the clinical features of headache in acute stroke. Headache is more frequent in hemorrhagic stroke when the topography is verteobasilar. Supratentorial lesions are usually accompanied by headache in the front half of the head, and infratentorial lesions are usually accompanied by headache in the rear half of the head. Very rarely, frontal headache has been described in cases of basilar thrombosis or cerebellar hemorrhage. However, in their recent Stroke article, Vestergaard et al claim that there is an equal distribution between frontal and occipital headache in carotid and verteobasilar stroke.

To contribute to the study of headache topography in verteobasilar acute stroke, we carried out a prospective clinical study in 81 consecutive patients (59 with cerebral infarction and 22 with hemorrhagic stroke) who had intact expressive function. Computed tomography and/or magnetic resonance imaging was performed in all cases immediately after admission. The mean±SD age of the patients was 64±12.6 years; 52 patients (64%) were men. The main cerebrovascular risk disorders were arterial hypertension in 45 patients (55%), heart disease in 7 (9%), and diabetes in 4 (5%). The frequency of headache was 59% (n=48), occurring in 34 patients (57.5%) in the cerebral infarction group and 14 (63.5%) in the hemorrhagic stroke group. The mean±SD duration of the headaches was 34±33 hours. Frontal headache was detected in 24 (50%) of the patients with headache: in 20 patients (50%) in the cerebral infarction group and 4 (28.5%) in the hemorrhagic stroke group. The other 24 patients with headache had diffuse or occipital headache.

There is a general consensus in the literature that frontal headache and/or eye pain is frequent in carotid artery distribution stroke and is uncommon in posterior cerebral circulation stroke. However, our findings agree with those of Vestergaard et al: frontal headache occurred in 50% of verteobasilar stroke, a percentage greater than reported in previous studies on headache in stroke. Our results indicate that there are exceptions to the pattern of referred pain on headache in stroke patients. Dual trigeminal and cervical neurovascular system implication in headache genesis in verteobasilar stroke may explain the difficulty to follow the classical "rules of referral."
Effect of nitric oxide syntase inhibition on cerebral blood flow and injury volume.

G M de Courten-Myers and R E Myers

Stroke. 1994;25:1082-1083
doi: 10.1161/01.STR.25.5.1082

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1994 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/25/5/1082.citation