Letters to the Editor

Secular Trends in Stroke Incidence and Mortality

In their recent article, Wolf et al note a decrease in the severity of stroke over the three decades beginning 1953, 1963, and 1973, sequentially. It is of interest that most of this difference was seen between decades two (i.e., 1963–1973) and three (i.e., 1973–1983). This third decade was also the time when aspirin first became widely used for stroke prevention and the first trials demonstrating its efficacy were reported. We have previously questioned whether platelet antiaggregant therapy lessens the severity of stroke, but subsequent placebo controlled platelet antiaggregant trials have either not settled the issue or unfortunately not even addressed it. Is there any way that Dr. Wolf and colleagues can look back at their data to see whether the use of aspirin was an important variable distinguishing patients having strokes in decade two versus decade three of this study?

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References

Response

Dr. Grotta questions if increased use of aspirin explains the decreased severity of stroke in the third decade of our study of secular trends in stroke in the Framingham cohort. Unfortunately, we are unable to answer this question for two reasons. First, aspirin use was collected systematically for the first time on biennial examination 13 in 1973, at the start of the third decade. Since aspirin use was not documented during the first two decades, no comparisons can be made.

Second, although aspirin use was ascertained in 1973 and on every examination since 1981 (and we can evaluate stroke severity in persons according to aspirin usage), aspirin use was not assigned randomly to Framingham cohort participants and may well have been related to the presence of coexisting cardiovascular diseases or risk factors. Thus, persons selected by their treating physicians to use aspirin might sustain more or less severe strokes than those not taking aspirin. The results of an analysis might be misleading since the impact of aspirin might be obscured by coexisting disease or risk factors. An observational study is not suited to answer the question Dr. Grotta raises; only a random allocation clinical trial can do that.

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Simultaneous Bihemispherical Assessment of Cerebral Blood Flow Velocity Changes During a Mental Arithmetic Task

In the January issue of Stroke, Kelley and coworkers reported changes of cerebral blood flow velocity (CBFV) during a mental arithmetic task assessed by transcranial Doppler ultrasonography (TCD) applied serially to the left and right anterior cerebral artery (ACA). Measurements were performed at 30-second intervals. With their task, consisting of writing down seven subtractions, the authors found a significant increase of mean blood flow velocities (Vmean) but failed to detect any hemispheric differences. The mean difference between the baseline and activation condition was as small as 2 cm/sec. On the basis of an earlier study of regional cerebral blood flow, the authors proposed that crucial areas for arithmetic processing are supplied by the ACA. This finding contrasts sharply with the clinical experience with acalculia syndromes occurring mostly after ischemic lesions in the territory of the middle cerebral artery (MCA). To address the question of the cerebral localization of arithmetic processes, we measured CBFV in the anterior and middle cerebral arteries of 20 healthy, right-handed volunteers during mental arithmetic processing (addition, subtraction, and multiplication of three-digit numbers) using the recently developed technique of simultaneous bilateral TCD (sbTCD) (DWL-HemoDop, Sipplingen, Germany) that allows continuous insonation of homologous cerebral arteries simultaneously. In our calculation paradigm, we recorded five trials of 120 seconds, each consisting of a 60-second calculation period and a resting period of equal length for each artery pair. Trials were averaged individually, and maximum increase of Vmean within the 10 seconds following the stimulus in relation to the resting period was evaluated from the average trials. To avoid artifacts from motor activation caused by writing or speaking, our task had to be performed mentally. Results were communicated orally after the trial.

Figure 1 shows the differences in individual maximum increase of Vmean in ACA compared with MCA, depicted for the right (Figure 1A) and the left (Figure 1B) hemispheres separately. A significant increase in cognitive evoked flow velocity (p<0.001 by Wilcoxon test) compared to baseline could be detected in all four arteries, but the increase of CBFV in the MCA exceeded that of the ACA at a significance level of p<0.001 (by paired Wilcoxon test).

Thus, in contrast to the opinion of Kelley et al., cortical areas most important for mathematical reasoning are located in the MCA territory. CBFV increases were found to be bilateral in the MCAs, as reported in the rCBF study, and reflect the numerous cognitive processes involved in the completion of a calculation task. These processes include verbal encoding, perception and recognition of number symbol representation, algorithmic reasoning, and sustained attention.

In an attempt to exclude fatigue or habituation factors, Kelley and coworkers restricted their measurements to the ACA. We did not find any significant effect of the sequence of insonation of the different arteries. Insonation sequence was reversed in the second series of volunteers; the results are depicted in Figure 1. Thus, habituation effects seem to be far less strong than expected.

With the advantage of a very high temporal resolution at the expense of spatial resolution, sbTCD provides a valuable tool for
We clearly recognize that calculation ability is primarily localized to the dominant hemisphere MCA territory. However, this localization principle traditionally applies to rote calculation tasks, such as the one used by Thomas and Harer. We would argue that the serial seven task extends beyond rote abilities and involves organization, monitoring, mental thinking, and sequencing, which are skills well known to rely on the integrity of the frontal lobes. The bilateral MCA activation reported by Drs. Thomas and Harer is difficult to interpret, as no apparent lateralization was observed. According to their letter, they observed a flow velocity increase, during calculation, in both ACAs and both MCAs. The rise above baseline, on average, was greater for the MCAs than for the ACAs but certainly this finding is subject to interpretation.

The stated purpose of our study was to “assess the ability of transcranial Doppler ultrasonography to detect selective circulatory changes during cognitive activity.” We approached our data in a statistically rigorous fashion, and we hope that we have contributed to the evolution of the use of TCD in the noninvasive assessment of cognitive function. We are not yet able to make a statement that this technique “provides a valuable tool for the assessment of cognitive evoked flow velocity changes in healthy volunteers and patients with cerebrovascular diseases.”

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References

Middle Cerebral Artery Embolism and Unilateral Visual Loss After Autologous Fat Injection Into the Glabellar Area

Autologous fat injection is a plastic surgery technique with few complications, apart from pain at the puncture site. After liposuction, a semiliquid fat graft is injected subcutaneously for soft-tissue augmentation. We report a case of unilateral visual loss and left-sided hemiplegia following autologous fat injection into the glabellar area. A 47-year-old, right-handed woman underwent autologous fat injection into her forehead area to correct glabellar frown lines. The procedure was performed under local anesthesia. While she was receiving the injection, the patient felt a sudden, severe periorcular pain and suffered complete visual loss in her right eye. Simultaneously, her left limbs became paralyzed. The patient was admitted to our hospital 2 hours after symptom onset. There was no history of cardiovascular risk factors.

Upon examination, she was oriented but inattentive. Blood pressure was 130/80 mm Hg. There was an erythematous lesion on her right eye and periorcular pain and suffered complete visual loss in her right eye. There was anosognosia and left unilateral spatial neglect. Speech was normal. She had a complete left hemiplegia involving her lower face. Plantar response was absent on the left side. Sensory examination showed tactile extinction and impaired two-point discrimination on the left.

There was no light perception in her right eye. The right pupil was nonreactive to light, but consensual reflex was present. The right eye could not be abducted and showed conjunctival injection. Ophthalmoscopically, the right eye showed a pale optic disc, with several retinal arteries segmentally occluded.

Routine laboratory tests were all normal. Antinuclear antibodies and serological test for syphilis were negative. Electrocardiography and transthoracic echocardiography results were normal. Contrast echocardiography failed in showing right-to-left flow.

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Response
I am happy to see that our recent article in Stroke has stimulated interest in the use of TCD in the assessment of cognitive activity. Several points in the letter from Drs. Thomas and Harer require clarification, however. Nowhere in our article do we state that “crucial areas for arithmetic processing are supplied by the ACA.” We do make note of a study which contributed to the evolution of the use of TCD in the noninvasive assessment of cognitive function. We are not yet able to make a statement that this technique “provides a valuable tool for the assessment of cognitive evoked flow velocity changes in healthy volunteers and patients with cerebrovascular diseases.”

We clearly recognize that calculation ability is primarily localized to the dominant hemisphere MCA territory. However, this localization principle traditionally applies to rote calculation tasks, such as the one used by Thomas and Harer. We would argue that the serial seven task extends beyond rote abilities and involves organization, monitoring, mental thinking, and sequencing, which are skills well known to rely on the integrity of the frontal lobes. The bilateral MCA activation reported by Drs. Thomas and Harer is difficult to interpret, as no apparent lateralization was observed. According to their letter, they observed a flow velocity increase, during calculation, in both ACAs and both MCAs. The rise above baseline, on average, was greater for the MCAs than for the ACAs but certainly this finding is subject to interpretation.

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Computed tomography was performed at the time and was normal. Eight days later, brain CT scan showed infarction involving the frontal and parietal right lobes. Digital subtraction arteriography, performed 48 hours after the onset of symptoms, was normal.

On discharge, after 3 weeks, she was able to raise her left leg against minimal resistance, her left arm remained plegic, there was no anosognosia, and the left spatial neglect had improved. Her right eye remained blind.

The clinical features were consistent with fat embolism to the branches of the middle cerebral artery and ophthalmic artery, leading to monocular blindness and left hemiplegia. The skin lesion and ocular motility indicated that distal branches supplying orbita and glabellar area were occluded.

Two cases of visual loss after fat injection into the glabellar area have been reported, and retinal emboli following periocular injection of corticosteroids has been documented. Interestingly, none of these presented hemispheric symptoms.

We think that the foreign material was injected into a distal branch of the ophthalmic artery, such as the supratrochlear artery. Under injection pressure, the fat material could reach choroidal and retinal circulation and send emboli into the upper division of the middle cerebral artery. This unusual cause of stroke should be counted among the complications of periocular injections.

References

Correction
I would like to clarify my editorial comment concerning the manuscript by Ueda et al entitled, “Changes in Extracellular Glutamate Concentration Produced in the Rat Striatum by Repeated Ischemia” (Stroke 1992;23:1125–1131). During the editing of this editorial comment in my office, some material was inadvertently omitted from the text. As a result, the comment could be misleading.

To clarify this comment, I would like to add the following: The conclusion of this paper was that there was no cumulative effect of brief repeated episodes of ischemia on glutamate concentration despite an effect of this treatment on progressive deterioration of ionic homeostasis. The authors of this article demonstrate that cumulative excitotoxicity of minor ischemic events does not produce prolonged glutamate elevation under conditions that still can produce a significant ischemic injury. These results underscore the importance of looking at the molecular mechanisms involved in regulating ischemic injury.

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