Transcranial Doppler Assessment of Cerebral Flow Velocity During Cognitive Tasks

Roger E. Kelley, MD; Jen Y. Chang, MS; Nancy J. Scheinman, PhD; Bonnie E. Levin, PhD; Robert C. Duncan, PhD; and Shih-Chang Lee, PhD

Background and Purpose: The purpose of this study was to assess the ability of transcranial Doppler ultrasonography to detect selective circulatory changes during cognitive activity.

Methods: We measured cerebral artery flow velocity in 21 normal volunteers by transcranial Doppler ultrasonography during rest followed by cerebral activation. Mean and peak systolic flow velocities of the anterior, middle, and posterior cerebral arteries were measured during the performance of a commercial video game. We also measured flow velocity of the anterior cerebral arteries in 18 subjects during a mental arithmetic task. Serial measurements of the right and left sides were made with a headband with two probes.

Results: We observed a global increase in the flow velocity above baseline measurements during task performance. During the video game, both middle cerebral arteries (f=2.6, p=0.02 for the left; f=3.3, p=0.004 for the right) and the left posterior cerebral artery (f=2.2, p=0.004) had selective increase in mean flow velocity compared with the ipsilateral anterior cerebral artery. This selective activation was most prominent in the right middle cerebral artery, which had a greater degree of activation than the right posterior cerebral artery (f=2.8, p=0.013). We did not observe a statistically significant difference between the right and left middle cerebral arteries, but there was a trend toward a greater activation on the right for both the mean velocity (t=1.7, p=0.098) and the peak velocity (f=1.9, p=0.079).

Conclusions: Our preliminary investigation suggests that this noninvasive technique has the potential to correlate selective cerebral artery flow dynamics with cognitive activity. (Stroke 1992^23:9-14)

Transcranial Doppler ultrasonography (TCD) is a noninvasive means of assessing the flow velocity and pulsatility of the intracranial arteries.1-2 Changes in the middle cerebral artery (MCA) flow velocity have been found to reliably correlate with changes in cerebral blood flow, but the absolute velocity cannot be used as an indicator of cerebral blood flow.3 The validity of deriving cerebral blood flow information from TCD measurements is subject to question, but useful approximations in steady-state conditions are still possible.4

We report the results of measurement of the flow velocities of the basal cerebral arteries (MCA, anterior cerebral artery [ACA], and posterior cerebral artery [PCA]) in 21 normal volunteers. We used a dual-probe system that allowed alternating serial measurement of a particular homologous vessel pair at rest and during activation. The present study represents an attempt to correlate change in the flow pattern of a particular vascular distribution with mental tasks that would be expected to result in selective cognitive activity.

Subjects and Methods

The normal volunteers consisted of 13 males and 8 females 17-48 (mean±SD, 31.4±7.8) years of age. Fifteen of the controls were right-handed, five were ambidextrous, and one was left-handed. Handedness was determined by detailed questioning in reference to visual aiming, writing, throwing, and kicking. The subjects were all medication-free, with no active medical problems. All subjects abstained from caffeine-containing beverages and smoking for at least 6 hours prior to the study. Baseline studies were performed in a dark, quiet room with the subjects’ eyes kept closed. Blood pressure reading, pulse rate, and an anxiety scale score5 were obtained at the beginning and the end of the study to ensure that significant variations in these measurements did not occur.

We used a commercially available Doppler unit (Transpect, MedaSonics Corp., Mountain View, Cal-
This unit allows continuous-wave Doppler recording of the intracranial artery of interest with on-line calculation of mean velocity ($V_{\text{mean}}$) and peak systolic velocity ($V_{\text{pea}}$). For this particular Doppler unit, flow velocity is calculated over one cardiac cycle, and $V_{\text{mean}}$ is derived from averaging the peak systolic and peak diastolic components of the Doppler waveform envelope. To obtain consistent values in each subject, that is, steady state, we did not record for the first 3–5 minutes of each study. We used a dual 2-MHz transducer probe system fitted on a headband. Because of potential interference, simultaneous velocity measurement was not feasible. We therefore did serial alternating recordings, with the use of a switchbox, for homologous vessels, that is, ACA, MCA, and PCA.

The MCA was initially insonated. We assessed for a strong Doppler signal, with flow toward the probe, at the temporal bone window. The signal was optimized for each artery by adjustment of the insonation angle. The ACA signal was located by aiming the probe toward the MCA signal at a progressively greater depth, through gating of the transducer signal, until an adequate reproducible signal was obtained for flow away from the probe. The localization of the PCA was made by angling the probe in a more posterior direction from the MCA and at a greater depth. A Doppler signal toward the probe in this region was presumed to represent the PCA. In two subjects, an adequate and reliable Doppler signal could not be obtained in the vascular territory of the PCA.

All subjects had serial measurements every 30 seconds over 8 minutes for each baseline study, on each side, as well as for each activation procedure. We uniformly began with an MCA or PCA study in order to protect against possible initial anxiety effect in the frontal lobe region that could, presumably, affect the ACA study. All subjects had ACA, MCA, and PCA studies at rest and during the playing of a video game (Super Breakout, Atari, Sunnyvale, Calif.), except for the two subjects in whom the PCA signal toward the probe in this region was presumed to represent the PCA. In two subjects, an adequate and reliable Doppler signal could not be obtained in the vascular territory of the PCA.

A total of 18 subjects performed a resting (baseline) study followed by a mental arithmetic task during monitoring of the ACA flow velocity. The mental arithmetic task consisted of writing down serial seven subtractions, starting with the number 1,000, with the right hand while the eyes were kept closed. All 18 subjects were right-hand dominant in terms of writing. To avoid a fatigue factor, we restricted measurements to the ACAs during the math task. This type of task has been reported to be associated with a prominent rise in cerebral blood flow in the ACA-supplied cortex.

Each subject had continuous end-tidal CO$_2$ monitoring during the testing period. We used an oxygen face mask connected to a CO$_2$ analyzer (model LB-1, Beckman Instruments, Palo Alto, Calif.) and recorded the readings every 30 seconds. This was well tolerated by all subjects and allowed us to ensure that alterations in flow velocity during the study were not related to a possible effect of changing Pco$_2$ on vessel diameter.

The data for analysis consisted of the mean of 16 measurements for each artery for each 8-minute baseline period and each 8-minute activation period. To assess the global response to the stimuli, the statistical model used was a 2 (activation versus no activation) x 2 (right versus left hemisphere) x 3 (ACA, MCA, and PCA) repeated-measures analysis of variance. This model allows comparison of activation values to baseline values averaged over all arteries as well as the global assessment of left–right differences. Because the repeated-measures model requires complete observations on all subjects included in the analysis, only 19 subjects were used to make comparisons between hemispheres, between homologous vessel pairs, and between arteries of the same hemisphere with the video game task. The analyses were made on absolute change in velocity instead of relative change because relative change would introduce inhomogeneity of error in the analysis. Post hoc analyses were carried out using paired t tests to assess the effects of activation within and between arteries as well as within and between hemispheres. Similar analyses were made on the 18 subjects who had baseline measurements compared to math task activation.

### Results

The 21 subjects were observed to be physiologically stable throughout the testing period. We did not observe significant differences between beginning of study and end of study pulse rates, blood pressures, or anxiety scores. Furthermore, the Pco$_2$ was observed to remain stable throughout each recording. Table 1 summarizes the baseline and activation mean scores for all 21 subjects who performed the video game. On average, there was an increase in both the $V_{\text{mean}}$ and $V_{\text{pea}}$ for all vessels insonated during the video game.

The baseline and activation $V_{\text{mean}}$ values for the 19 subjects who had all pertinent vessels insonated during the video game and for the 18 subjects who performed the math task are summarized in Table 2. If we average all six arteries together at baseline for all subjects and compare this value to the averaged
TABLE 1. Baseline and Activation Values for the Mean Velocity and Peak Systolic Velocity During Performance of Video Game

<table>
<thead>
<tr>
<th></th>
<th>Anterior cerebral artery (n=21)</th>
<th>Middle cerebral artery (n=21)</th>
<th>Posterior cerebral artery (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>V_mean   Baseline</td>
<td>47±12</td>
<td>49±13</td>
<td>60±14</td>
</tr>
<tr>
<td>Activation</td>
<td>48±12</td>
<td>52±13</td>
<td>65±17</td>
</tr>
<tr>
<td>V_peak  Baseline</td>
<td>80±13</td>
<td>82±17</td>
<td>99±20</td>
</tr>
<tr>
<td>Activation</td>
<td>83±14</td>
<td>85±16</td>
<td>104±24</td>
</tr>
</tbody>
</table>

All flow velocities are in units of centimeters per second; values are mean±SD. V_mean, mean velocity; V_peak, peak systolic velocity.

measurements during the video game for all subjects, there is a global significant increase in both the V_mean (F=36, p<0.0001) and the V_peak (F=25, p<0.0001). On the other hand, no significant side-to-side difference, that is, specific hemisphere, difference was noted for either the V_mean (F=0.5, p=0.5) or V_peak (F=0.2, p=0.7). In other words, the increase was global without a specific hemisphere localization.

For the math task, we observed an increase in the V_mean for both ACAs, taken together, compared with baseline (F=17, p<0.001), but we did not observe a similar increase in the V_peak (F=2, p=0.2). In addition, we did not observe a left–right difference for either the V_mean (F=0.3, p=0.6) or the V_peak (F=0, p=0.9).

The evaluation of selective arterial activation is summarized in Table 3. We observed a pattern in which the V_mean of each MCA had greater activation than did the ipsilateral ACA. We also observed that the increase in the V_mean of the right MCA was greater than that of the right PCA. In addition, the V_mean of the left PCA was significantly activated compared with the left ACA, but we did not observe this on the right. The activation of the V_peak of the right MCA was greater than that of the right ACA, but no other selective activation was observed with the V_peak.

The assessment of possible side-to-side differences between arteries is summarized in Table 4. There was a trend toward greater activation of the right compared with the left MCA during the video game, and this trend was observed for both the V_mean (t=1.7, p=0.098) and the V_peak (t=1.9, p=0.079).

Discussion

The present study illustrates the potential ability to correlate the physiological information provided by TCD with specific cognitive activity. Transcranial Doppler ultrasonography has been found to detect flow velocity increase in the PCA in response to visual stimulation in 10 normal subjects.10 The average increase observed was 16.4% in this study. In a study of 70 subjects who had TCD of the MCAs performed at rest and during mental activity,11 during stimulation there was a bilateral increase in flow velocity of 1.6–10.6%. A study of the effect of inter-
Table 3. Comparison of Degrees of Activation Between Different Arteries During Video Game

<table>
<thead>
<tr>
<th>Vessel comparison*</th>
<th>Left</th>
<th>Right</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>t</td>
<td>p</td>
</tr>
<tr>
<td>$V_{\text{mean}}$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCA (5.8±1.4) vs. ACA (2.0±1.2)</td>
<td>2.6</td>
<td>0.020</td>
</tr>
<tr>
<td>MCA (5.8±1.4) vs. PCA (5.1±1.0)</td>
<td>0.5</td>
<td>0.593</td>
</tr>
<tr>
<td>PCA (5.1±1.0) vs. ACA (2.0±1.2)</td>
<td>2.2</td>
<td>0.044</td>
</tr>
</tbody>
</table>

*Mean absolute difference above baseline±SE by paired t test.

Table 4. Mean Side-to-Side (Right Minus Left) Difference in Change From Baseline During Activation

<table>
<thead>
<tr>
<th>V$_{\text{mean}}$</th>
<th>V$_{\text{peak}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean difference±SE</td>
<td>t*</td>
</tr>
<tr>
<td>Video game</td>
<td></td>
</tr>
<tr>
<td>ACA</td>
<td>0.3±0.6</td>
</tr>
<tr>
<td>MCA</td>
<td>1.4±0.6</td>
</tr>
<tr>
<td>PCA</td>
<td>-0.7±0.7</td>
</tr>
<tr>
<td>Math task</td>
<td>0.5±1.7</td>
</tr>
</tbody>
</table>

*By paired t test.
closed during the baseline study, had an activating effect on the occipital cortex. This would not necessarily explain the selective activation seen within the left but not the right PCA, however. The trend toward a greater increase in flow velocity of the right compared with the left MCA suggests that attention and visuospatial orientation, primarily right hemispheric functions, were of greater significance, from the standpoint of localization, than motor activity. The math task did result in an activation of both ACAs above baseline values, but we did not observe a hemispheric localization.

Physiological monitoring is pertinent in health and disease, and a number of techniques have evolved to noninvasively assess cortical function. Positron emission tomography scanning, as mentioned above, allows quantitative assessment of normal physiological function. Such studies have also determined that one must take into account normal regional asymmetries when assessing brain lateralization.

Xenon-133 cerebral blood flow measurements have been used to noninvasively assess cognitive activity. Thinking tasks have been found to be routinely associated with increased rCBF, and auditory discrimination is associated with a selective increase in rCBF in the right hemisphere. Verbal tasks, on the other hand, tend to lateralize to the left hemisphere. Mental activity with a digit-span-backward task was associated with augmentation of rCBF of a diffuse nature, which was attributed to an arousal mechanism, as well as with a more selective increase in the suprasylvian regions. Speech and reading, not unexpectedly, are associated with an increase in rCBF in the dominant hemisphere. Learning has been associated with increased flow in the left frontal and parietal regions while recall of the same material is associated with an rCBF increase restricted to the left parietal lobe. A visual memory task, on the other hand, has been associated with greater activation in the right hemisphere.

Motivational factors, as well as anxiety and anticipation, can have an effect on mental task performance and rCBF in normal volunteers. Gur et al, noting that handedness has an effect on cognitive function, with left-handed subjects having a lesser degree of hemispheric specialization, found that both gender and handedness were associated with differences in rCBF during rest. In addition, asymmetric cerebral somatosensory metabolic response of right-versus left-handed stimulation has been found with positron emission tomography scanning.

Despite possible variation among individuals, in terms of flow velocity response to mental tasks, we can conclude that this technique has potential for completely noninvasive, sequential correlation of cerebral hemodynamics with cognitive activity. The limitations of the technique must be understood and it must be established, with larger series of subjects, whether consistent patterns of flow velocity activation can be expected in normal subjects before comparisons can be made with individuals with central nervous system disease. The major attractive features of this technique are that it is completely noninvasive, quite well tolerated, and provides a quantitative index of cerebral blood flow velocity that can be correlated with rCBF.

Acknowledgments

The authors would like to express their appreciation to Neil Schneiderman, PhD, for the use of his behavioral psychology laboratory where the studies were performed. We would also like to thank Myron D. Ginsberg, MD, for critical review of this manuscript.

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**KEY WORDS** • blood flow velocity • cognition • ultrasonics
Transcranial Doppler assessment of cerebral flow velocity during cognitive tasks.
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Stroke. 1992;23:9-14
doi: 10.1161/01.STR.23.1.9

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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