Transcranial Doppler Ultrasonographic Assessment of Intermittent Light Stimulation at Different Frequencies

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Seven normal adult volunteers underwent intermittent photic stimulation at frequencies of 5–60 Hz while their posterior cerebral arteries were monitored using transcranial Doppler ultrasound. Baseline measurements were obtained under conditions of total darkness, and sampling was also done during continuous illumination. Overall variation in mean flow velocity between complete darkness and continuous illumination was 9.8%, but the maximal change (expressed as percentage deviation from baseline) occurred consistently when stimulation was undertaken at frequencies of 10 (21%) and 20 (19%) Hz (p = 0.05). Frequencies higher than 20 Hz resulted in mean flow velocity variations that were not significantly different from that found during continuous illumination. The optimal frequency of intermittent visual stimulation required to induce measurable changes in posterior cerebral artery Doppler characteristics appears to be in the range 10–20 Hz. *(Stroke 1990;21:1746–1748)*

Transcranial Doppler ultrasonography (TCD) is a relatively new technique useful in the evaluation of the cerebral circulation. TCD allows the study of hemodynamic characteristics of the basal cerebral arteries. Preliminary data suggest that using TCD it is possible to observe changes in the blood flow dynamics of the posterior cerebral artery (PCA) when illumination of the environment changes. In fact, the effect of opening and closing the eyes upon the Doppler characteristics of the PCA has been introduced as a criterion for the identification of this vessel during TCD studies. To assess the effect of variations in the temporal distribution of visual stimuli on the Doppler characteristics of the PCA, we studied seven normal individuals by changing the frequency of intermittent light stimuli while monitoring their PCAs with TCD. We hypothesized that, by progressively increasing the frequency of stimulation, we could demonstrate a correlative and progressive increase in mean blood flow velocity in the PCA due to temporal summation of the stimuli. The present report summarizes our findings.

**Subjects and Methods**

We studied seven healthy adult volunteers, four women and three men, ages ranging from 27 to 36 years. All underwent TCD studies using a 2-MHz pulsed Doppler ultrasound transducer affixed to a headband. The latter is set in place, allowing extended monitoring and preventing motion interference. The transducer is connected to a TCD-dedicated spectral analyzer (Transpect, Medasonics, Mountain View, Calif.) that calculates mean flow velocity automatically using a fast Fourier transform. End-tidal carbon dioxide pressure was measured throughout the procedure using a capnograph (223 CO₂ Monitor, Datex Instrumentation Corp., Helsinki, Finland). Intermittent light stimulation was carried out using a stroboscopic photic stimulator (Grass Instruments, Quincy, Mass.).

The PCA of either side was identified following conventional criteria. After identification of the bifurcation of the internal carotid artery, the transducer is angled posteriorly and slightly inferiorly while maintaining the depth of the sample volume unchanged; proper identification of the signal as the PCA is accomplished by following it deeper, to the origin of the vessel at the top of the basilar artery. Measurements were recorded under conditions of total environmental darkness and while the subject's eyes were closed. Each subject was then asked to open his/her eyes, and repetitive light stimulation was carried out at frequencies of 5, 10, 20, 30, and 60 Hz. Finally, measurements under conditions of continuous illumination were performed. For each of the
seven conditions (darkness, five light frequencies, and continuous illumination), measurements were done over 5 minutes, with resting darkness periods of 15 minutes in between. During the measurements end-tidal carbon dioxide pressure varied only slightly (±2 torr), following the respiratory cycle. Five measurements of PCA mean flow velocity were obtained for each condition in each subject. For each subject, all measurements were performed when the end-tidal carbon dioxide pressures were exactly the same. The measurements were then repeated in every subject while monitoring the contralateral PCA. Intensity of the light source was kept constant throughout all measurements. Auditory stimulation of the subject was avoided by having the technologist wear earphones to listen to the Doppler signals.

A total of 490 mean flow velocity measurements were obtained, 70 for each condition. The measurements obtained under conditions of total darkness were considered to be the baseline. Mean flow velocity during each condition of illumination was expressed as a percentage change from baseline, using each subject as his/her own control. The percentages were entered into a database. Taking the frequency of light stimulation as the grouping variable, the data were examined by computerized analysis of variance using the Newman-Keuls multiple comparison test; p<0.05 was considered significant.

**Results**

Percentage change in PCA mean flow velocity according to the frequency of light stimulation is shown in Figure 1. The highest values were obtained at 10 (21±5%) and 20 (19±5%) Hz. These values were significantly different from those obtained at other frequencies. Frequencies of stimulation greater than 20 Hz resulted in percentage change values that were not significantly different from that found upon continuous illumination.

**Discussion**

Stimulation of the visual system results in depolarization of neurons located in the occipital cortex. These neurons are the final link in a chain of cellular networks that experience a series of electrophysiologic phenomena beginning with the excitation of photoreceptors of the retina. The responses of all cells of the visual system follow a highly complex pattern that depends on the spatial and temporal distribution as well as on the intensity of the stimuli. The most common example of our ability to record the electrophysiologic effects of visual stimuli on the occipital cortex is the electroencephalographic driving response produced by stroboscopic light stimulation. The net effect of stimulation of the visual pathway is also represented by increased metabolic demands in the occipital cortex, coupled with an increase in its regional cerebral blood flow (rCBF). Previous experience using positron emission tomography (PET) confirms that it is possible to analyze the metabolic response to visual stimulation of the occipital cortex and to record the effects of increased metabolism on rCBF.

The ability of retinal receptors to resolve stimuli separated in time depends on the critical fusion frequency. This value varies depending on the location of the cell in the retina and the intensity of the stimulus; it is partly representative of the threshold of stimulation and the refractory period of cells of the retina. The number of cells stimulated by a flash of light depends on its location in the environment, its intensity, and the frequency at which it occurs. Regardless of their locations, neurons in the visual pathway have a resting discharge rate independent of retinal stimulation. Superimposed on this background of resting activity, changes in illumination of the retinal surface modify the frequency and pattern of firing of visual neurons or result in their complete suppression. Visual responses may therefore be grouped as those that are excitatory and those that are inhibitory. These are also known as "on" or "off," depending on whether the neurons respond to the transition from dark to light or to the transition from light to dark.

In general, stimulation of the retinal receptors results in more complex patterns of firing of the occipital cortex neurons. These patterns of enhanced electrical activity have a direct effect on metabolic demands of the occipital cortex and, therefore, on rCBF. The rCBF is regulated by changes in

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**FIGURE 1.** Bar graph showing mean±SEM percentage change from baseline (mean flow velocity in posterior cerebral artery during darkness). Only changes at 10 and 20 Hz were significantly different from that during continuous illumination (p=0.05 by one-way analysis of variance followed by Newman-Keuls multiple comparison test).
the precapillary resistance vessels. These changes respond quite extensively to metabolic alterations of the area in question. There is a significant amount of information to support the concept that alterations in neuronal activity and metabolic rate can be quite localized, and this has been interpreted as requiring an equally localized regulation of rCBF. It is now accepted that the mechanism of blood flow regulation based on metabolic demands involves not only a closed-loop system but also open-loop systems.

In vivo changes in rCBF secondary to metabolic variations have been quantified using different physiologic imaging techniques, the most sophisticated being PET. These studies have clearly disclosed increases in the occipital metabolic rate for glucose and rCBF during stimulation with either white light or complex scenes. However, PET is a relatively complicated technique that is at present available only in research institutions. For this reason, alternative methods of measuring rCBF changes secondary to cerebral metabolic variations are of interest for both physiologic and clinical studies. This background of ideas represents the basis of our study.

The occipital cortex receives its blood mainly from the PCA, a vessel that can be easily studied using TCD. Contrary to our original hypothesis, our data indicate that there is an optimal frequency of intermittent light stimulation required to induce metabolic changes in the occipital cortex of sufficient magnitude to change mean flow velocity in the PCA. Provided that the intensity used remains constant, this optimal frequency approximates 10–20 Hz. The maximal change of mean flow velocity demonstrated at these frequencies represents the distal precapillary vasodilation responsible for the increase in rCBF during visual stimulation. The pattern observed suggests that the optimal frequency of stimulation creates an overall balance in the excitation of both "on" and "off" neuronal populations. This balance may depend on matching the average refractory periods of all these neurons so that the largest number of them fire at any time.

References

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