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.1 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.2 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.3 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.3 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 mea-
surements 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. In-
tensity 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 measure-
ments obtained under conditions of total darkness
were considered to be the baseline. Mean flow veloc-
ity during each condition of illumination was ex-
pressed 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 depolar-
ization of neurons located in the occipital cortex.\(^5\)
These neurons are the final link in a chain of cellular
networks that experience a series of electrophysio-
logic 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.\(^6\)
The most common example of our ability to record
the electrophysiologic effects of visual stimuli on the
occipital cortex is the electroencephalographic driv-
ing response produced by stroboscopic light stimula-
tion. 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).\(^7\)
Previous experience using positron emission tomog-
raphy (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.\(^7\)

The ability of retinal receptors to resolve stimuli
separated in time depends on the critical fusion
frequency.\(^8\) This value varies depending on the loca-
tion 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.\(^9\)\(^12\)
Regardless of their locations, neurons in the visual
pathway have a resting discharge rate independent of
retinal stimulation.\(^9\)\(^10\) Superimposed on this back-
ground 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.\(^6\) 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.\(^6\) These patterns of en-
hanced electrical activity have a direct effect on
metabolic demands of the occipital cortex and, there-
fore, on rCBF. The rCBF is regulated by changes in
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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