Ethnic Influences on Neurovascular Coupling
A Pilot Study in Whites and Asians

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Background and Purpose—An ethnic extraintracranial difference in atherosclerosis has been well reported, whereas the potential mechanism remains unclear. We aimed to investigate neurovascular coupling in healthy whites and Asians.

Methods—Twenty volunteers of each ethnicity were recruited to perform a functional transcranial Doppler examination with standardized checkerboard patterns as visual stimulation (3×4, 6×8, and 12×16 checks subtending a visual field section of 18°×24°, flicker rate 1 Hz). Hemodynamic responses in both posterior cerebral arteries were evaluated with a control system approach.

Results—The rate time, that is, the initial speed of flow velocity adaptation, was significantly lower in Asians leading to an approximately 2-second delayed hemodynamic adaptation. The other hemodynamic parameters and the dependency of hemodynamic responses in regard to the complexity degree of the stimulus were similar between groups.

Conclusion—The constellation suggests a greater initial mismatch between functionally increased metabolic demand of neurons and adjusted cerebral blood flow in Asians. (Stroke. 2010;41:383-384.)

Key Words: cerebral blood flow ■ ethnicity ■ metabolic activity ■ neurovascular coupling

The extraintracranial difference of arterial stenosis with a predominantly intracranial location in Asians and an extracranial in whites is commonly explained by ethnic factors pointing to a weaker compensation of the intracranial vessels against cerebrovascular risk factors in Asians.1,2 The neurovascular coupling denotes a brain-intrinsic regulative mechanism that adjusts local blood flow in accordance with the underlying cortical activity.3 To investigate a possible ethnic difference in functional parameters, we compared the neurovascular coupling as an indicator of the intracranial small vessel function in healthy young whites and Asians with a standardized functional transcranial Doppler test.

Materials and Methods
The study was approved by both Institutional Review Committees. Twenty healthy students of each white and Asian ethnicity were included in the study. All volunteers were nonsmokers, did not take regular medication, and had no family or personal history of migraine, premature vascular disease, hypertension, diabetes mellitus, or hyperlipidemia. The arterial blood pressure was measured noninvasively and the arterial blood pressure was measured noninvasively and the functional transcranial Doppler test was performed in all subjects after sitting for 10 minutes. One stimulation experiment lasted 10 minutes and each minute consisted of a 40-second visual stimulation period alternating with a 20-second resting period to increase the signal-to-noise ratio.4 The volunteers were asked to fix their eyes on a small spot presented in the center of the computer screen (CRT screen, 21") during the stimulation phase and to close their eyes during the resting phase. Three different “checkerboard” patterns (contrast≈92%; 1-Hz reversal; n=10 rest–stimulation cycles) were applied in random order: 3×4 checks on the screen (vertical×horizontal; check size in angles: 6°×6°); 6×8 checks (check size: 3°×3°), and 12×16 checks (check size: 1.5°×1.5°). Peak systolic (versus) blood flow velocity responses were recorded in the P2 segment of both posterior cerebral arteries with 2-MHz probes by Multidop T2 Doppler (DWL). Data were averaged and transformed to relative data in relation to the resting flow velocity level setting the baseline to zero. The method and algorithm for analyzing the data sets in terms of a control system are described in detail in an earlier work.4 The following parameters were specified. The gain (K) indicates the evoked flow velocity level above baseline under stabilized hemodynamics. The rate time (Tv) specifies the steepness of initial increase in flow velocity. The undampened natural angular frequency (natural frequency [ω]) describes the oscillatory features of the neurovascular coupling mechanism, whereas the attenuation parameter (ε) specifies the dampening of the vascular system.

Statistical comparisons of resting flow velocity levels and control system parameters for both sides were performed using an analysis of variance with Fisher post hoc test. Statistical significance was inferred at P<0.05.

Results
All volunteers (whites: 25.7±3.6 years, 12 male; Asians: 22.6±1.4 years, 7 male) completed the study. Blood pressure changes did not occur during the test experiments and was similar between ethnic groups (whites: 110±8 mm Hg systolic, 77±8 mm Hg diastolic; Asians: 107±9 mm Hg systolic, 70±7 mm Hg diastolic; P=nonsignificant).

With increasing number of checks (ie, complexity), the gain parameter showed a statistically significant increase. The resting flow velocity levels and the other control system parameters did not show a significant task-related effect (Table).
Regarding ethnic influences, we found only a significant lower rate time parameter in Asians (Figure) leading to a more delayed hemodynamic adaptation.

Discussion
Our study showed ethnic differences in functionally evoked hemodynamic responses in the posterior cerebral arteries comparing young healthy white and Asian students. Differences occurred in the rate time parameter that describes the initial upstroke in flow velocity regulation: Asians had a slower initial hemodynamic response to visual activation tasks than whites, whereas the stabilized flow velocity levels under rest and activation as well as the dependence from the stimulus complexity were similar between groups.

According to the animal experiment, the slower initial responses might be related to a deficit in the nitric oxide system.6 This is supported by a study finding a 27-bp repeat polymorphism in intron 4 of the endothelial constitutive nitric oxide synthase (ecNOS) gene in Chinese patients with stroke, which could decrease the synthesis of nitric oxide.7 Further evidence comes from another study performing electric forepaw stimulation in rats.8 With the beginning of stimulation, a peaking nitric oxide release in the brain microcirculation was found with an exponential decrease during succeeding stimulation. This mathematically differing pattern of nitric oxide liberation resembles that of the time course of the rate time parameter.

Alternatively, environmental effects on neurovascular coupling could have resulted in the difference because a change in diet can also modify cerebrovascular risk.8

This pilot study indicates an ethnic effect on the neurovascular coupling. Although we excluded the typical vascular risk factors, environmental and lifestyle factors have not been strictly controlled and need to be considered in future studies. Larger sample size is also necessary to further explore the neurovascular coupling, underlying cause of the ethnic difference in development intracranial atherosclerosis.

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Disclosures
None.

References
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