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

Qing Hao, MD; Lawrence K.S. Wong, MD; Wen Hua Lin, MD; Thomas W.H. Leung, MRCP; Manfred Kaps, MD; Bernhard Rosengarten, MD

Background and Purpose—An ethnic extracranial 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;41:00-00.)

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

The extracranial 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. The neurovascular coupling denotes a brain-intrinsic regulative mechanism that adjusts local blood flow in accordance with the underlying cortical activity. 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 included in the study. All volunteers were nonsmokers, did not take drugs, and had no personal or family history of migraine, premature vascular disease, hypertension, diabetes mellitus, or hyperlipidemia. 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 included in the study. All volunteers were nonsmokers, did not take drugs, and had no personal or family history of migraine, premature vascular disease, hypertension, diabetes mellitus, or hyperlipidemia. The arterial blood pressure was measured noninvasively and included in the study. All volunteers were nonsmokers, did not take drugs, and had no personal or family history of migraine, premature vascular disease, hypertension, diabetes mellitus, or hyperlipidemia. The arterial blood pressure was measured noninvasively and included in the study. All volunteers were nonsmokers, did not take drugs, and had no personal or family history of migraine, premature vascular disease, hypertension, diabetes mellitus, or hyperlipidemia. The arterial blood pressure was measured noninvasively and included in the study. All volunteers were nonsmokers, did not take drugs, and had no personal or family history of migraine, premature vascular disease, hypertension, diabetes mellitus, or hyperlipidemia.
The initial hemodynamic response (horizontal arrow) resulting in a lag of approximately 2 seconds in Asians (gray curve) show a lag of approximately 2 seconds in the initial hemodynamic response to visual activation tasks compared to whites. The stabilized flow velocity levels under rest and activation as well as the dependence from the stimulus complexity were similar between groups.

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. 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. Further evidence comes from another study performing electric forepaw stimulation in rats. With the beginning of stimulation, a peak 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. 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


### Table. Group-Averaged Hemodynamic Responses for Each Task*

<table>
<thead>
<tr>
<th>Task</th>
<th>Statistics</th>
<th>White</th>
<th>Asian</th>
<th>Effect</th>
<th>Ethnic Effect</th>
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<tbody>
<tr>
<td>Resting flow velocity 3×4, cm/s</td>
<td>55±5</td>
<td>53±8</td>
<td>NS</td>
<td>NS</td>
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<tr>
<td>Resting flow velocity 6×8, cm/s</td>
<td>56±8</td>
<td>53±8</td>
<td>NS</td>
<td>NS</td>
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<tr>
<td>Resting flow velocity 12×16, cm/s</td>
<td>52±8</td>
<td>49±6</td>
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<td>NS</td>
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<tr>
<td>Gain 3×4, %</td>
<td>7±3</td>
<td>7±3</td>
<td>3×4–6×8: 0.03</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Gain 6×8, %</td>
<td>10±4</td>
<td>10±5</td>
<td>6×8–12×16: 0.01</td>
<td>NS</td>
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<td>12±5</td>
<td>13±6</td>
<td>3×4–12×16: &lt;0.001</td>
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<tr>
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<td>0.21±0.05</td>
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<tr>
<td>Natural frequency 6×8, rad/s</td>
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<td>0.21±0.05</td>
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<td></td>
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<tr>
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<td>0.24±0.06</td>
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<td>Rate time 3×4, s</td>
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<td>3×4–12×16: 0.002</td>
<td>NS</td>
<td></td>
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<tr>
<td>Rate time 6×8, s</td>
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<td>NS</td>
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<td></td>
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<tr>
<td>Rate time 12×16, s</td>
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<td>1.5±1.3</td>
<td>NS</td>
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</tbody>
</table>

*Data are given as mean±SD together with statistical results (Fisher post hoc test). NS indicates nonsignificant.

The initial hemodynamic response (horizontal arrow) resulting in a lag of approximately 2 seconds in the initial hemodynamic response to visual activation tasks (Figure) leading to a more delayed hemodynamic adaptation.

**Figure.** Modeled time course of group-averaged evoked flow velocity responses according to the 3×4 checkerboard pattern. Asians (gray curve) show a lag of approximately 2 seconds in the initial hemodynamic response (horizontal arrow) resulting in a flow velocity mismatch of approximately 28% (vertical arrow).
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