South Asians have adverse cerebrovascular haemodynamics, despite equivalent blood pressure, compared with Europeans. This is due to their greater hyperglycaemia.

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Accepted 24 May 2011

Background South Asians have a 1.5-fold increased stroke mortality compared with Europeans, despite similar blood pressures (BP). We hypothesized that it is the greater hyperglycaemia in South Asians that increases stroke risk, by adversely affecting cerebrovascular haemodynamics.

Methods A population-based sample of 149 Europeans and 151 South Asians underwent metabolic profiling and concurrent measurement of finger BP using a Finapres and middle cerebral artery (MCA) blood flow velocity using transcranial Doppler ultrasound. Cerebrovascular autoregulation, cerebrovascular resistance [resistive index (RI) and pulsatility index (Pl)] were calculated. Means of cerebrovascular haemodynamic measures were compared by ethnicity, with the introduction of explanatory variables to a regression model to determine which variable could best account for ethnic differences.

Results Cerebrovascular resistance (RI) was $12.9 \times 10^3 (0.9–24.8, P = 0.04)$ greater in South Asians than Europeans. Systolic, diastolic and mean MCA velocities were also higher in South Asians (mean velocity $41.4 \pm 8.0 \text{cm/s}$ vs $38.0 \pm 8.0 \text{cm/s}$, respectively, $P = 0.001$). Low frequency gain, a measure of autoregulation, was worse in South Asians compared with Europeans ($0.50 \pm 0.01 \text{cm/s mm/Hg}$ vs $0.45 \pm 0.01 \text{cm/s mm/Hg}$, $P = 0.01$). RI positively correlated with HbA$_{1c}$ ($r = 0.184; P < 0.01$). Adjustment for BP could not explain the higher RI in South Asians, but adjustment for HbA$_{1c}$ abolished the ethnic difference in RI ($5.8 \times 10^3 (-6.5 \text{ to } 18.1, P = 0.4$).

Conclusions Cerebrovascular resistance and autoregulation are worse in South Asians than in Europeans, despite equivalent resting BP. The greater hyperglycaemia in South Asians accounts for their adverse
Introduction

Stroke is now the second leading cause of death worldwide. People of South Asian descent (i.e. people from India, Pakistan and Bangladesh) are particularly affected, with mortality rates approximately 1.5-fold higher than European origin populations.\(^1,2\) In comparison with the extensive information on ethnic differences in coronary risk, there are few plausible explanations for ethnic differences in stroke.

Elevated blood pressure (BP) is the strongest risk factor for stroke within any given population. But, between ethnic group comparisons are conflicting.\(^3\) overall, though South Asians appear to have lower BPs than Europeans.\(^6,7\) Strikingly, of the South Asian subgroups, Bangladeshi men have the highest relative stroke mortality compared with Europeans (standardized mortality ratio 2.49\(^1\)), yet the lowest resting BP, with systolic BP being just 121 mmHg compared with 131 mmHg (http://www.ic.nhs.uk, accessed August 24, 2010). The cardiovascular risk factor that best maps to stroke risk in South Asians is diabetes, the prevalence of which is elevated in all South Asian subgroups compared with Europeans, but with the greatest excess in Bangladeshis (standardized risk ratio 4.59). Diabetes and the broader spectrum of hyperglycaemia are known to alter cerebrovascular haemodynamics independently of hypertension,\(^8\) and proffer a potential mechanism to explain ethnic differences in stroke risk.

We therefore hypothesized that the greater hyperglycaemia in South Asians contributes to the elevated stroke risk in South Asians by adversely affecting cerebrovascular haemodynamics, namely, vascular resistance, flow velocity and cerebral autoregulation and we further excluded those with a past history of stroke, atrial fibrillation and carotid artery stenosis (>70%). Pre-menopausal women and those on hormone replacement therapy (HRT) were also excluded. An age, gender and ethnicity stratified sample was invited to participate, aiming for 150 individuals in each ethnic group (100 men and 50 women). The study was approved by the St Mary’s Hospital ethics committee and all participants gave written informed consent.

Study methods

All participants attended the clinical investigation unit in the morning, having fasted from the night before. Only plain water was allowed during the fast. Ethnicity was again confirmed by birthplace of all four grandparents. In addition for Punjabi Sikhs, self-defined membership of this group according to the LOLIPOP survey was used. A questionnaire on demographics, health behaviours and medical history was completed. Height, weight, waist and hip circumference were measured according to a standard protocol.\(^2\) Sitting BP was measured three times according to British Hypertension Society guidelines using a validated automated device (OMRON 705CP) after a 5-min rest. The average of the final two readings was used in analysis. Fasting bloods were analysed as described previously.\(^9\) The homeostasis model assessment of insulin resistance (HOMA-IR) index was calculated (http://www.dtu.ox.ac.uk, accessed August 24, 2010). Metabolic syndrome was defined using published criteria.\(^10\)

Haemodynamic investigations were carried out with subjects lying supine in a temperature-controlled room. Measurements of flow were taken from the middle cerebral arteries bilaterally using transcranial Doppler ultrasound (TCD) with a Multi Dop T2 (DWL Compumedics, Singen, Germany) equipped with 2 MHz probes held in place by a headset. The probe was applied to the temporal window. It was not possible to obtain an adequate temporal window bilaterally in 18 participants (6%); in 15 participants the left temporal window could not be found and in 8 participants, the right temporal window could not be located. End tidal carbon dioxide was monitored concurrently using a Poet Transportable End-tidal monitor (Criticare systems, Waukesha, WI, USA). Carbon dioxide output signals were acquired simultaneously over four 5-min periods after a 20-min rest period. Data were A/D converted at a sampling rate of 200 Hz using...
a custom-built data acquisition module and saved on a PC for offline analysis.

Analysis was performed by an observer masked to all participant identifiers apart from ID number, using validated software.\textsuperscript{11} Traces were edited to exclude artefactual data spikes and resampled by spline interpolation at 0.2 s intervals. Values for mean, systolic and diastolic cerebral blood flow velocity (CBFV) and BP were calculated for each beat. As there is no clear standard measure of cerebrovascular resistance, we calculated the two most widely quoted in the literature resistance:\textsuperscript{12} Pourcelot’s resistive index (RI)\textsuperscript{13} and Gosling’s pulsatility index (PI)\textsuperscript{14} according to the following formulae:

\[
\text{RI} = \frac{\text{Systolic CBFV} - \text{diastolic CBFV}}{\text{Systolic CBFV}}
\]

\[
\text{PI} = \frac{\text{Systolic CBFV} - \text{diastolic CBFV}}{\text{Mean CBFV}}
\]

Cerebral autoregulation was determined from the CBFV responses to spontaneous fluctuations in mean arterial BP as described previously.\textsuperscript{11} In essence, transmission of changes in systemic blood pressure to the brain are damped by autoregulatory properties of the cerebral circulation, to avoid marked fluctuations in flow velocity. To determine this, the transfer function between mean arterial BP and CBFV fluctuations is computed with the fast Fourier transform leading to estimates of gain, phase and coherence. The low frequency range (0.07–0.15 Hz) is thought to reflect the autoregulatory component of the haemodynamic response. Gain is the ratio of velocity to BP amplitudes and therefore indicates the effectiveness with which BP fluctuations are damped in the cerebral circulation. Coherence estimates the strength of the linear relationship between mean velocity and pressure, ranging between 0 and 1. With reduced autoregulation coherence increases as pressure changes are directly transmitted to velocity. Finally, the phase shift is determined as the degree to which velocity changes lead those of pressure. This is attenuated in the presence of impaired autoregulation.

Central BP was derived from applanation tonometry of the radial artery (Sphygmocor, Version 6.2; PWV Medical Pty Ltd, Australia).\textsuperscript{15} Pulse transit time was measured between the carotid–femoral sites using an ECG-gated ultrasound ‘foot-to-foot’ method (Pulse Trace PT 2000, Micromedical Ltd, Kent, UK) and pulse wave velocity calculated.

Baroreflex sensitivity was calculated by beat-to-beat sequence analysis as previously described.\textsuperscript{9}

Statistical analysis and study power

With 150 individuals in each ethnic group, at 5% significance, we could detect a standardized difference (SD) between ethnic groups in any given cerebrovascular haemodynamic variable of at least 0.35 SD with 80% power, allowing for data incompleteness. There are no previous studies of ethnic differences in TCD parameters, but an SD of 1 has been noted when comparing people with relatively severe diabetes with controls.\textsuperscript{8} We have previously reported an ethnic difference in fasting glucose of 0.4–0.6 of an SD,\textsuperscript{5} thus the ethnic difference in cerebral haemodynamics, if our hypothesis is correct, should be of a similar magnitude and easily detectable with our sample size.

Statistical analysis was carried out using STATA version 11.0. Data are presented as means ± SD, or medians (interquartile range) for skewed data. Haemodynamic outcomes are presented as means ± standard error (SE). Skewed data were log transformed prior to analysis. The mean of right and left TCD measures was used, except for individuals in whom only one side could be imaged; in those cases the single side measures were used. Middle cerebral artery stenosis may alter cerebral haemodynamics. A threshold of 80 cm/s mean flow velocity on TCD can reliably be used to exclude such individuals.\textsuperscript{16} No individuals were excluded when this threshold was applied. Ethnic differences in continuous variables were compared using analysis of covariance (ANCOVA) after adjustment for age and sex. Bivariate associations were assessed using Pearson’s correlation coefficient. Interactions were sought. Additional adjustment for potential confounders was performed using multivariate regression. Categorical variables were compared using the chi-square test. A P-value was taken as statistically significant.

Results

A total of 149 Europeans and 151 South Asians participated; they did not differ significantly from the source LOLIPOP population. Europeans and South Asians had similar ages and resting BP, although treatment rates for hypertension were higher in South Asians (Table 1). Diabetes was more common in South Asians, as were other indicators of hyperglycaemia, insulin resistance and the metabolic syndrome. Smoking rates were higher in Europeans than South Asians.

Cerebrovascular resistance, measured either as RI or PI, was elevated in South Asians (Table 2). South Asians also had higher mean, systolic and diastolic cerebral blood flow velocity (CBFV). These ethnic differences persisted when analysis excluded those receiving any cardiovascular medications (statins or antihypertensive therapy, n = 175, mean CBFV South Asians 59.9 ± 0.6 cm/s vs Europeans 58.6 ± 0.5 cm/s, P = 0.05) and when analysis was restricted to never smokers (n = 161, South Asians 60.4 ± 0.05 cm/s vs Europeans 58.5 ± 0.7 cm/s, P = 0.03). Further exclusion of people with established doctor-diagnosed heart disease did not alter ethnic differences in flow or resistance.

Low frequency gain in CBFV was greater in South Asians, indicating that velocity changes in BP...
fluctuations were poorly damped, implying loss of cerebrovascular autoregulation. These ethnic differences persisted when those receiving cardiovascular medication were excluded (Europeans 0.46 [95% confidence interval (CI) 0.43–0.49] cm/s mm/Hg, South Asians 0.51 [95% CI 0.47–0.55] cm/s mm/Hg, \( P = 0.05 \)). Coherence and phase did not differ.

To avoid concerns associated with multiple testing, further statistical analysis was restricted to key indicator measures of cerebrovascular haemodynamics,
specifically, RI, mean cerebral blood flow velocity and low frequency gain. RI was positively correlated with age, central BP, glucose, insulin resistance and HbA1c, well into the normal range (Table 3, Figure 1). People with hypertension, diabetes and known coronary heart disease had higher resistance (RI) than those without (Figure 2a). In contrast, mean cerebral blood flow velocity was negatively correlated with age and mean arterial BP and was lower in those without coronary heart disease, but exhibited no association with diabetes or hyperglycaemia (Table 3 and Figure 2b).

We sought to determine explanations for ethnic differences in cerebrovascular resistance (RI) (Table 4). This now presents the ethnic difference (South Asian–European) in RI, multiplied by $10^3$ for ease of presentation. Age and gender were forced into a basic model and additional cardiovascular risk factors, known to be correlated with RI, were added separately to see which of these best explained (i.e. attenuated) the ethnic difference in RI. The basic ethnic difference in RI was $12.9\times 10^3$ (0.9, 24.8, $P=0.04$). Ethnic differences in RI were not abolished when adjusted for any measure of BP, but were markedly attenuated and lost statistical significance when any measure of hyperglycaemia was used. Addition of mean arterial pressure made no significant additional contribution to accounting for the ethnic difference in RI and there was no evidence for an interaction between BP and HbA1c ($P=0.9$). The second greatest attenuation in the ethnic difference in RI was observed when WHR was added to the model, but only modest additional attenuation in the ethnic difference in RI was observed when WHR was added to a model containing HbA1c ($4.6$ vs $5.8\times 10^3$).

Low frequency gain was negatively correlated with cardiovascular risk factors (Table 3). However, ethnic differences in gain could not be accounted for by multivariate adjustment. In a model that included age, sex, insulin, central systolic pressure, pulse wave velocity and baroreflex sensitivity, the ethnic difference in gain was increased [Europeans 0.43 (95% CI 0.40–0.46) cm/s mm/Hg, South Asians 0.51 (95% CI 0.48–0.54 cm/s mm/Hg), $P<0.0001$].

**Table 3** Correlation coefficients between RI, mean cerebral blood flow velocity (mean CBFV), LF gain and CVD risk factors

<table>
<thead>
<tr>
<th>Variable</th>
<th>RI</th>
<th>$P$-value</th>
<th>Mean CBFV</th>
<th>$P$-value</th>
<th>LF gain</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.504</td>
<td>$&lt;0.01$</td>
<td>−0.229</td>
<td>$&lt;0.01$</td>
<td>−0.207</td>
<td>0.001</td>
</tr>
<tr>
<td>MAP</td>
<td>0.021</td>
<td>0.7</td>
<td>−0.138</td>
<td>0.03</td>
<td>−0.307</td>
<td>$&lt;0.0001$</td>
</tr>
<tr>
<td>Baroreflex sensitivity</td>
<td>−0.171</td>
<td>0.01</td>
<td>−0.066</td>
<td>0.3</td>
<td>−0.295</td>
<td>$&lt;0.0001$</td>
</tr>
<tr>
<td>PWV</td>
<td>0.338</td>
<td>$&lt;0.0001$</td>
<td>−0.157</td>
<td>0.01</td>
<td>−0.158</td>
<td>0.01</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>0.195</td>
<td>$&lt;0.01$</td>
<td>−0.065</td>
<td>0.3</td>
<td>−0.039</td>
<td>0.6</td>
</tr>
<tr>
<td>HbA1c</td>
<td>0.259</td>
<td>$&lt;0.01$</td>
<td>−0.043</td>
<td>0.5</td>
<td>0.027</td>
<td>0.7</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>0.121</td>
<td>0.05</td>
<td>−0.040</td>
<td>0.5</td>
<td>−0.215</td>
<td>0.002</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>−0.024</td>
<td>0.7</td>
<td>0.006</td>
<td>0.9</td>
<td>−0.164</td>
<td>0.01</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>−0.069</td>
<td>0.3</td>
<td>−0.047</td>
<td>0.5</td>
<td>0.124</td>
<td>0.05</td>
</tr>
<tr>
<td>BMI</td>
<td>0.011</td>
<td>0.9</td>
<td>−0.121</td>
<td>0.05</td>
<td>−0.043</td>
<td>0.5</td>
</tr>
<tr>
<td>WHR</td>
<td>0.085</td>
<td>0.2</td>
<td>−0.260</td>
<td>$&lt;0.001$</td>
<td>−0.071</td>
<td>0.3</td>
</tr>
</tbody>
</table>

MAP, mean arterial pressure; SBP, systolic blood pressure; PWV, pulse wave velocity; HOMA-IR, homeostasis model assessment of insulin resistance; BMI, body mass index; WHR, waist hip ratio.

**Discussion**

We show that middle cerebral artery flow velocity and cerebrovascular resistance are elevated in South Asians compared with Europeans. Whereas brachial and central BPs are equivalent in the two ethnic groups, South Asians are, as anticipated, markedly hyperglycaemic and this abnormality appears to account for their greater cerebrovascular resistance. In addition, the low frequency gain in cerebral blood flow velocity, i.e. the ability to damp transmission of BP fluctuations to cerebral blood flow, is impaired in South
Asians compared with Europeans. These adverse cerebrovascular haemodynamic patterns in South Asians, in part at least as a consequence of their known greater burden of hyperglycaemia, may contribute to the 1.5-fold greater risk of stroke, even though BP is not particularly elevated. These findings persisted when analyses took account of previous cardiovascular disease history, smoking status and cardiovascular medications.

Cerebrovascular resistance is known to increase with age and BP\textsuperscript{17,18} and is an important determinant of stroke risk. A single standard deviation increase in cerebrovascular resistance confers an approximately 2-fold increased risk of stroke.\textsuperscript{19} In our study, cerebrovascular resistance was approximately a quarter of a standard deviation higher in South Asians than Europeans, which would predict around a 25% elevated stroke risk. This is similar to the actual excess stroke risk observed.

Measures of resistance (RI and PI) are calculated from and therefore strongly related to flow velocity. Flow velocity decreases with ageing and hypertension,\textsuperscript{20} and is lower in men than women. In contrast, resistance increases with age and hypertension and is higher in men than women, i.e. the inverse of associations observed with flow. However, the effect of diabetes on RI and flow does not follow this inverse pattern. Resistance is elevated in the presence of diabetes,\textsuperscript{18} whereas, paradoxically, flow velocity is not reduced and may even be elevated, when compared with people without diabetes, as we confirm here.\textsuperscript{18,20} Our finding of both elevated resistance and flow velocity in South Asians compared with Europeans provides further support that hyperglycaemia is responsible for ethnic differences in cerebral haemodynamics. Reports of a 'dose–response' relationship between diabetes duration and elevated PI (independent of age, hypertension and other CVD risk factors) are consistent with our suggestion that diabetes markedly impairs selective elements of cerebrovascular haemodynamics.\textsuperscript{18,20} We go further than this by showing, in a representative sample of the general population (unselected for disease), that the relationship between glycaemia and RI extends across the range of glycaemia and is not simply restricted to people with diabetes.

People with both diabetes and microvascular complications have more adverse cerebrovascular
Table 4 Multivariate analysis to determine explanations for ethnic differences in RI

<table>
<thead>
<tr>
<th>Variables in model</th>
<th>Difference in RI (\times 10^3) between South Asians and Europeans</th>
<th>95% CI</th>
<th>(P)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, gender</td>
<td>12.9 0.9–24.8</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Age, gender, MAP</td>
<td>13.0 1.0–25.0</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Age, gender, diagnosed hypertension</td>
<td>12.5 0.4–24.7</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Age, gender, central systolic pressure</td>
<td>11.3 -0.6 to 23.1</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>Age, gender, glucose</td>
<td>9.0 6.5–20.9</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Age, gender, HbA1c</td>
<td>5.8 2.6–18.1</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Age, gender, HOMA</td>
<td>9.6 2.1–21.5</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Age, gender, diabetes</td>
<td>8.0 2.4–20.3</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Age, gender, metabolic syndrome</td>
<td>12.5 -0.6 to 24.4</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Age, gender, BMI</td>
<td>13.3 1.3 to 25.2</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Age, gender, WHR</td>
<td>10.5 -1.8 to 22.8</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>Age, gender, HbA1c MAP</td>
<td>5.9 -6.4 to 18.3</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Age, gender, HbA1c, MAP</td>
<td>4.6 -6.4 to 18.3</td>
<td>0.3</td>
<td></td>
</tr>
</tbody>
</table>

RI multiplied by \(10^3\).
SBP, systolic blood pressure; DBP, diastolic blood pressure; HOMA-IR, homeostasis model assessment of insulin resistance; WHR, waist hip ratio.

Factors with adverse cerebrovascular haemodynamics. Teasing out the exact relationship would require longitudinal measures with magnetic resonance (MR) imaging. Yet, our observation of a graded relationship between cerebrovascular resistance and glycated haemoglobin, rather than a threshold or stepped effect that may be anticipated with the presence or absence of infarcts, would lend support to our proposed direct association between hyperglycaemia and cerebrovascular resistance.

We show that cerebrovascular autoregulation is also impaired in South Asians. Low frequency gain in cerebral blood flow velocity was significantly elevated, indicating a poorer ability to damp transmission of BP fluctuations to cerebral blood flow. There are no previous studies of ethnic comparisons of cerebrovascular autoregulation. However, an elevation in gain (a clinically important elevation, although not reaching statistical significance owing to lack of study power) and a reduction in phase in association with uncomplicated diabetes have previously been reported. \(^{27}\) Given our hypothesis, i.e. that diabetes and the wider spectrum of hyperglycaemia would be responsible for adverse cerebral haemodynamics, we were surprised to find, first that there was no ethnic difference in phase and second that unlike resistance, no cardiovascular risk factor, including hyperglycaemia, could account for the ethnic difference observed in autoregulation.

This study has several strengths. A population-based study is less prone to bias than one which excludes people with cardiovascular risk factors (specifically hypertension and diabetes, which in any case are highly correlated), \(^{17,18}\) and will have few, if any individuals with sufficient large or small vessel disease to affect cerebrovascular haemodynamics. Further, the sample was large enough to allow detailed multivariate statistical analysis. We could also explore associations between cerebrovascular haemodynamics and measures of BP and glycaemia continuously across a wide range, rather than between a sometimes arbitrary dichotomy of people with and without a specific condition. Our findings can therefore be generalized to the whole population, where the stroke mortality differentials are observed. A single observer (R.H.) analysed all assessments of autoregulation, eliminating inter-observer variability. The failure rate for TCD data capture was low (15%). An inter-ethnic comparison, where usually tight correlations between key risk factors differ markedly, may help to prioritize or rank their relative importance in the development of disease. Thus, as South Asians are hyperglycaemic, but do not have markedly elevated mean arterial pressures compared with Europeans, we can suggest that the ‘excess’ stroke risk in South Asians may be related to hyperglycaemia. The South Asian sample was limited to Punjabi Sikhs, the majority South Asian population in this part of London. However, although South Asian subgroups differ in terms of lifestyle.
and health behaviour patterns, they are all hyperglycaemic and all have elevated rates of diabetes compared with people of European origin and all share an excess stroke risk; thus, these findings in Punjabi Sikhs are likely to be generalizable to all South Asian subgroups.

In conclusion, we show that cerebrovascular autoregulation is impaired in South Asians and cerebrovascular resistance elevated. The latter is attributable to hyperglycaemia in the South Asian population. These cerebrovascular haemodynamic abnormalities may account for the greater stroke risk of South Asians at any level of BP. The adverse effect of hyperglycaemia is not restricted to people with diabetes, as it is observed across the normal range of glucose and HbA1c, thereby highlighting the importance of early prevention of abnormal glucose tolerance and the need to tightly control blood glucose once diabetes occurs, regardless of BP. In a population where one in five adults has diabetes, this presents an urgent public health problem.

**Funding**

Project grant PG/05/096 from the British Heart Foundation.

**Acknowledgements**

We would like to thank Chloe Page and Emma Coady for their help in data collection and also Laura Villis for data entry. N.C., A.D.H. and S.A.McG.T. acknowledge the support of the NIHR Biomedical Research Centre Scheme.

**Conflict of interest:** None declared.

## KEY MESSAGES

- People of South Asian descent worldwide have stroke risks that are 1.5–2 times greater than European origin populations, yet, mean blood pressure is generally found to be lower.
- Ethnic subgroup differences in diabetes prevalence map closely to stroke mortality differences.
- Blood velocity and resistance to flow in the middle cerebral artery is greater in South Asians compared with Europeans, whereas autoregulation of flow is poorer.
- The greater cerebrovascular resistance in South Asians compared with Europeans is not accounted for by ethnic differences in blood pressure, but is accounted for by measures of hyperglycaemia such as blood glucose and glycated haemoglobin.
- Our findings indicate that hyperglycaemia, rather than blood pressure, may underlie the excess stroke risk in South Asians. This hypothesis needs to be tested in longitudinal studies.

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