Regional Cerebral Blood Flow Decreases During Chronic and Acute Hyperglycemia

Robert B. Duckrow, Daniel C. Beard, and Robert W. Brennan

The presence of hyperglycemia prior to stroke or cardiac arrest can increase neuronal damage caused by brain ischemia. Acute hyperglycemia shows this effect in animal models of stroke. However, chronic hyperglycemia and chronic hyperglycemia with additional acute elevation of blood glucose are more common premorbid states for stroke patients. The effect of chronic hyperglycemia on regional cerebral blood flow (rCBF) is unclear but blood flow changes may play a role in this ischemic cell damage. We measured rCBF in awake restrained rats that had chronic hyperglycemia induced by treatment with streptozotocin. This was compared to that measured in rats made acutely hyperglycemic by injecting glucose into the peritoneal space. rCBF was measured in 17 brain regions using $^{[14]}$Ciodoantipyrine. During chronic hyperglycemia, when plasma glucose was 29 $\mu$m/ml, rCBF was decreased and a regional distribution of this effect was noted; 9 hindbrain regions showed a mean flow decrease of 14% while forebrain regions demonstrated less flow reduction. Acute elevation of plasma glucose during normoglycemia or superimposed on chronic hyperglycemia produced flow reductions of 7% for each 10 $\mu$m/ml increment in plasma glucose up to 60 $\mu$m/ml. Both chronic and acute hyperglycemia are associated with decreased rCBF and the mechanism for this effect does not appear to adapt to chronic hyperglycemia. (Stroke 1987;18:52-58)

Clinical studies suggest that hyperglycemia is a risk factor for stroke and that it increases brain injury during stroke or cardiac arrest. In animal models of stroke, acute hyperglycemia before ischemia increases mortality and the number of neurons that die. After transient ischemia, hyperglycemia increases and prolongs postischemic hypoperfusia and enhances the heterogeneity of reperfusion. However, in normal animals an acute elevation of plasma glucose is associated with decreased regional cerebral blood flow (rCBF). This effect could limit compensatory blood flow mechanisms during an ischemic event.

In clinical situations hyperglycemia, whether iatrogenic or the result of stroke itself, is seldom as acute or as severe as that induced in animal models of stroke. Also, diabetics are frequently exposed to acute increases in blood glucose superimposed on a background of chronic hyperglycemia. Little is known about the effect of chronic hyperglycemia on rCBF. For these reasons we measured rCBF in awake restrained rats that had a moderate chronic hyperglycemia produced by treatment with streptozotocin. We found that chronic hyperglycemia was associated with decreased rCBF. Also, a specific regional distribution of this effect was noted with hindbrain regions manifesting CBF decreases during chronic hyperglycemia.

**Materials and Methods**

The isotope 4-iodo[N-methyl-14C]antipyrine, 53 mCi/mmol, was obtained from Amersham, Arlington Heights, Ill. Streptozotocin, 2-deoxy-2-(methylamino-carbonyl)-aminoo-5,-d-glucopyranose, was obtained from Sigma Chemical, St. Louis, Mo. Alloxan, 5,6-deoxyuracil, was obtained from Eastman Kodak, Rochester, N.Y. d-Glucose was of the best available grade. Male Sprague-Dawley rats (Crl:SD) weighing 270-450 g were bought from Charles River Breeding Laboratories, Wilmington, Mass. They were allowed free access to food and water during the experiment.

**Animal Preparation**

Rats were anesthetized with 3% halothane mixed with 70% nitrous oxide and 30% oxygen in a closed chamber. After 5 minutes the rats were removed from the chamber and 0.6% halothane with nitrous oxide/oxygen was administered by face mask. Streptozotocin was used to induce a moderate hyperglycemic state lasting 3 weeks. Streptozotocin or an equivalent volume of drug vehicle, 1 ml/kg, was injected into an exposed femoral vein. Streptozotocin was dissolved in normal saline prior to injection and given at a dose of 60 mg/kg. Anesthesia was discontinued and the rats were returned to their cages for 3 weeks.

Alloxan was used to induce a severe hyperglycemic state within 48 hours. Alloxan was also mixed in normal saline prior to i.v. injection and given at a dose of 60 mg/kg. An equivalent volume of drug vehicle was used for sham controls. Rats given alloxan were housed for 48 hours before measuring rCBF.

Intraperitoneal injection of glucose produced an acute hyperglycemic state that peaked in 20 minutes. A 50% solution of d-glucose in water was given intraperitoneally at 6 and 8 ml/kg to produce 2 degrees of acute
hyperglycemia. It was also given to a subpopulation of streptozotocin-prepared rats at 6 ml/kg.

Prior to rCBF measurement anesthesia was induced and maintained as described above. Polyethylene catheters were placed in the 2 femoral arteries and the 2 femoral veins through wounds locally anesthetized with 1% procaine. If d-glucose was to be given, a peritoneal catheter was placed. Rats were immobilized by wrapping the hind legs and hips in a snug plaster cast and anesthesia was discontinued. The average halothane exposure time was 50 minutes. The head and shoulder girdle were placed in a guillotine. A shroud prevented visual distraction, and extraneous sound was minimized in the laboratory. Pulse rate and arterial blood pressure were monitored continuously using 1 arterial catheter. Sixty minutes after discontinuation of halothane the rats were awake, alert, and calm. If intraperitoneal glucose was to be given, it was done at that time. Twenty minutes later rCBF was measured. Arterial blood gases and pH were measured 10 minutes before measurement of rCBF. Arterial blood obtained during rCBF measurement was used to measure hematocrit and plasma osmolality as well as plasma glucose, sodium, and potassium concentration.

Measurement of rCBF

rCBF was measured by determining the activity of [14C]iodoantipyrine in brain regions isolated by gross dissection. After systemic anticoagulation with heparin (100 U), 70 ¼s of [14C]iodoantipyrine in normal saline was injected through a venous catheter at a rate of 17 ¼s/sec. The activity of this tracer in arterial blood was determined during injection by continuously collecting blood from the second arterial catheter, as described in a previous report. After 30 seconds of tracer exposure, the rat was decapitated, the brain was removed, and samples from 17 brain regions were obtained. These were weighed in tared scintillation vials, and tissue solubilizer was added as quickly as possible. At least 8 mg and usually 20 mg of brain tissue was obtained and weighed with 0.1 mg precision. rCBF was calculated using the equations presented by Eckman and associates. A blood–brain partition coefficient of 0.8 was used.

Analytical Methods

Arterial oxygen tension (Pao2), carbon dioxide tension (Paco2), and arterial pH were measured at 37° C (BMS 3 Mk 2; Radiometer Copenhagen, Westlake, Ohio). Plasma glucose was measured by the glucose oxidase method (Glucose Analyzer 2; Beckman Instruments, Fullerton, Calif.). Plasma osmolality was measured by freezing point depression (Osmette A; Precision Systems, Sudbury, Mass.). Plasma sodium and potassium were measured using flame photometry (Model 143; Instrumentation Laboratory, Lexington, Mass.). Hematocrit was measured using blood in 20- ¼s capillary tubes centrifuged at 11,000 rpm for 3 minutes.

Statistical Analysis

Rats that received streptozotocin or streptozotocin and intraperitoneal glucose were compared with sham-operated rats that were also housed for 3 weeks before measuring rCBF. Rats that received alloxan or only intraperitoneal glucose were compared with sham-operated rats that were housed for 48 hours. The significance of differences between treatment groups was
Table 1. Physiologic Variables for the Streptozotocin Treatment Group

<table>
<thead>
<tr>
<th>Treatment</th>
<th>n</th>
<th>Weight (g)</th>
<th>MABP (mm Hg)</th>
<th>Pulse (bpm)</th>
<th>pHa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline</td>
<td>6</td>
<td>392 ± 22</td>
<td>120 ± 6</td>
<td>482 ± 42</td>
<td>7.43 ± 0.02</td>
</tr>
<tr>
<td>Streptozotocin</td>
<td>7</td>
<td>302 ± 13*</td>
<td>119 ± 7</td>
<td>430 ± 38</td>
<td>7.43 ± 0.02</td>
</tr>
<tr>
<td>Streptozotocin + i.p. glucose</td>
<td>7</td>
<td>334 ± 32*</td>
<td>111 ± 8</td>
<td>365 ± 35*</td>
<td>7.36 ± 0.03*</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

i.p. = intraperitoneal; MABP = mean arterial blood pressure; pHa = arterial pH; bpm = beats per minute; Paco2 = arterial carbon dioxide tension; Pao2 = arterial oxygen tension; Hct = hematocrit; [Na+] = plasma sodium concentration; [K+] = plasma potassium concentration.

*Value significantly different from control at p < 0.01 (Dunnett's test).
†Value significantly different from control at p < 0.05 (Dunnett's test).

Results

Rats treated with streptozotocin were hyperglycemic and had hyperosmotic plasma as indicated in Table 1. The mean plasma glucose was 29 μm/ml. After 3 weeks they weighed less than control rats, having gained no weight in the interval. Despite this they had equivalent blood pH, Paco2, Pao2, hematocrit, and plasma electrolyte concentrations. The mean flow reduction of all 17 brain regions was 11%, but a regional pattern of this flow reduction was evident (Table 2). Five of the 17 brain regions were significantly different from control values; all were nontelencephalic structures. The mean rCBF reduction in the 9 nontelencephalic regions was 14%. This regional distribution of flow reduction was accentuated when chronically hyperglycemic rats were given intraperitoneal glucose to produce an acute glycemic increment. The data are summarized in Figure 1. Figure 2 demonstrates that this pattern of flow suppression was independent of the rank order of the magnitude of basal rCBF.

Streptozotocin-treated rats that received an additional intraperitoneal glucose load showed a mean reduction in flow of 33% in nontelencephalic regions (Table 2). All of the rCBF values in nontelencephalic regions were significantly lower than control values. These rats were mildly acidotic, but mean Paco2 was normal (Table 1). Their Pao2 and hematocrit were higher and...
crease was significant in 5 and 9 of 17 brain regions for plasma sodium and potassium concentrations were lower than control values.

Intraperitoneal injection of 50% d-glucose at 6 and 8 ml/kg produced acute elevation of plasma glucose to 31 and 46 μmol/ml (Table 3) and mean flow decreases of 14 and 22% from control values (Table 4). The decrease was significant in 5 and 9 of 17 brain regions for the 2 doses of glucose respectively. The majority of the regions that showed a significant decrease were not telencephalic, as seen in Figure 3. The mean flow decreases of nontelencephalic regions were 19 and 25% of control values for the 2 degrees of acute hyperglycemia. There were expected increments of plasma glycemia. There were expected increments of plasma glucose and osmolality, accompanied by an elevation in hematocrit (Table 3). When the larger dose of glucose was given a mild fall in blood pressure and pH occurred. However, PacO₂ was not altered by either dose of glucose.

The flow reductions associated with equivalent hyperglycemia, whether acute (6 ml/kg) or chronic, were the same. A greater flow reduction was measured with the higher level of acute hyperglycemia (8 ml/kg) and when additional glucose was given to streptozotocin-treated rats. When the mean rCBF reduction for nontelencephalic regions was plotted as a function of plasma glucose, a negative linear dose–response effect was observed, as shown in Figure 4.

Alloxan produced hyperglycemia in 48 hours. However, the flow reductions observed did not reach statistical significance (see Table 4). The variation in rCBF values for alloxan-treated rats was larger than for other groups and may help explain the apparent lack of effect.

**Discussion**

Chronic hyperglycemia is associated with an rCBF reduction of the same magnitude as that seen with acute glucose elevation. In addition, when an acute increase in plasma glucose is superimposed on a chronic hyperglycemic state, a further decrease in rCBF is measured. The dose–response relation is linear, about −7% for each 10 μmol/ml of glucose elevation. This confirms and extends previous studies that reported reduced rCBF during acute hyperglycemia.

CBF reduction during streptozotocin-induced hyperglycemia has not been reported previously. In their study of brain glucose influx, Gjedde and Crone measured brain blood flow in streptozotocin-treated rats and did not report decreased CBF. However, their model differed from the one used in this report in that additional changes in blood glucose were induced using both insulin and glucose injections. This manipulation may have obscured the flow reduction associated with chronic hyperglycemia.

Three mechanisms should be considered to explain decreased rCBF during hyperglycemia: increased cerebrovascular resistance caused by plasma hyperosmolality, increased blood viscosity, and decreased cerebral metabolic rate.

Acute increases in plasma osmolality can change rCBF. Mannitol is commonly used to induce a transient hyperosmotic state, and the effect of glucose injection mimics that of mannitol even though glucose is rapidly transported into the brain and metabolized. Intravenous mannitol injection can decrease blood viscosity, lower intracranial pressure, and increase PacO₂. Direct application of hyperosmotic solutions to the surface of the brain causes pial artery dilatation. All of these factors would increase rCBF, and increases have been measured in humans with glioma, in normal baboons, and in dogs. However, in animals this flow increase has been transient, and a more persistent decrease in CBF has been noted after 20 minutes. Mechanisms for this decrease have not been postulated. However, when comparing changes induced by injection of glucose and mannitol, the

| Table 1. Physiologic Variables for i.p. Glucose and Alloxan Treatment Group |
|---|---|---|---|---|---|---|---|---|
| Treatment | n | Weight (g) | MABP (mm Hg) | Pulse (bpm) | pH | PacO₂ (mm Hg) | PaCO₂ (mm Hg) | Hct (%) | Plasma glucose (μmol/ml) | Osmolality (mOsm) |
| Saline | 6 | 358 ± 50 | 119 ± 8 | 476 ± 38 | 7.43 ± 0.01 | 38 ± 4 | 82 ± 7 | 43 ± 1 | 10.3 ± 1.0 | 285 ± 18 |
| 50% glucose 6 ml/kg i.p. | 5 | 414 ± 24 | 104 ± 11 | 494 ± 26 | 7.40 ± 0.02 | 40 ± 2 | 84 ± 8 | 48 ± 2* | 30.5 ± 8.3* | 312 ± 12* |
| 50% glucose 8 ml/kg i.p. | 4 | 332 ± 30 | 101 ± 7† | 504 ± 29 | 7.39 ± 0.01* | 39 ± 3 | 92 ± 2 | 46 ± 1* | 45.5 ± 4.3* | 314 ± 7* |
| Alloxan | 6 | 326 ± 27 | 111 ± 2 | 400 ± 60 | 7.28 ± 0.12† | 39 ± 4 | 100 ± 11 | 42 ± 2 | 51.2 ± 10.1* | 365 ± 31* |

Values are mean ± SD.

i.p. = intraperitoneal; MABP = mean arterial blood pressure; pH = arterial pH; bpm = beats per minute; PacO₂ = arterial carbon dioxide tension; PaCO₂ = arterial oxygen tension; Hct = hematocrit.

*Values significantly different from control (saline) at p < 0.01 (Dunnett).

†Values significantly different from control (saline) at p < 0.05 (Dunnett).
Table 4. Regional Cerebral Blood Flow for i.p. Glucose and Alloxan Treatment Groups

<table>
<thead>
<tr>
<th>Region</th>
<th>Saline (6)</th>
<th>50% glucose 6 ml/kg (5)</th>
<th>50% glucose 8 ml/kg (4)</th>
<th>Alloxan (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor cortex</td>
<td>1.69 ± 0.10</td>
<td>1.52 ± 0.09</td>
<td>1.41 ± 0.15</td>
<td>1.43 ± 0.19</td>
</tr>
<tr>
<td>Sensory cortex</td>
<td>1.91 ± 0.12</td>
<td>1.77 ± 0.11</td>
<td>1.70 ± 0.09</td>
<td>1.79 ± 0.19</td>
</tr>
<tr>
<td>Auditory cortex</td>
<td>2.19 ± 0.20</td>
<td>1.89 ± 0.14</td>
<td>1.98 ± 0.17</td>
<td>1.99 ± 0.33</td>
</tr>
<tr>
<td>Visual cortex</td>
<td>1.80 ± 0.09</td>
<td>1.68 ± 0.08</td>
<td>1.58 ± 0.14</td>
<td>1.66 ± 0.22</td>
</tr>
<tr>
<td>Olfactory lobe</td>
<td>2.13 ± 0.21</td>
<td>1.80 ± 0.10</td>
<td>1.47 ± 0.19</td>
<td>1.77 ± 0.27</td>
</tr>
<tr>
<td>Caudate-putamen</td>
<td>1.37 ± 0.06</td>
<td>1.29 ± 0.07</td>
<td>1.16 ± 0.05</td>
<td>1.29 ± 0.16</td>
</tr>
<tr>
<td>Thalamus</td>
<td>1.70 ± 0.04</td>
<td>1.46 ± 0.10</td>
<td>1.25 ± 0.10*</td>
<td>1.38 ± 0.19</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>1.17 ± 0.05</td>
<td>1.07 ± 0.07</td>
<td>0.87 ± 0.05*</td>
<td>0.90 ± 0.12</td>
</tr>
<tr>
<td>Hypothalamus</td>
<td>1.61 ± 0.04</td>
<td>1.26 ± 0.06*</td>
<td>1.21 ± 0.13†</td>
<td>1.34 ± 0.24</td>
</tr>
<tr>
<td>Superior colliculus</td>
<td>1.92 ± 0.04</td>
<td>1.62 ± 0.13</td>
<td>1.58 ± 0.12†</td>
<td>1.79 ± 0.36</td>
</tr>
<tr>
<td>Inferior colliculus</td>
<td>2.71 ± 0.15</td>
<td>1.98 ± 0.18†</td>
<td>1.75 ± 0.16†</td>
<td>2.03 ± 0.34</td>
</tr>
<tr>
<td>Mesencephalon</td>
<td>1.58 ± 0.06</td>
<td>1.29 ± 0.09†</td>
<td>1.10 ± 0.05*</td>
<td>1.31 ± 0.17</td>
</tr>
<tr>
<td>Pons</td>
<td>1.57 ± 0.10</td>
<td>1.23 ± 0.06†</td>
<td>1.15 ± 0.10†</td>
<td>1.36 ± 0.24</td>
</tr>
<tr>
<td>Pyramidal tract</td>
<td>1.37 ± 0.08</td>
<td>1.16 ± 0.06</td>
<td>1.26 ± 0.17</td>
<td>1.17 ± 0.20</td>
</tr>
<tr>
<td>Medulla</td>
<td>1.53 ± 0.10</td>
<td>1.30 ± 0.06</td>
<td>1.21 ± 0.15</td>
<td>1.35 ± 0.27</td>
</tr>
<tr>
<td>Subcortical white</td>
<td>0.80 ± 0.10</td>
<td>0.72 ± 0.06</td>
<td>0.61 ± 0.02†</td>
<td>0.72 ± 0.10</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>1.59 ± 0.06</td>
<td>1.27 ± 0.08†</td>
<td>1.01 ± 0.07*</td>
<td>1.29 ± 0.18</td>
</tr>
</tbody>
</table>

Values are mean of n ± SEM.
rcBF = regional cerebral blood flow; i.p. = intraperitoneal.
* Values significantly different from control (saline) at \( p < 0.05 \) (Dunnett).
† Values significantly different from control (saline) at \( p < 0.01 \) (Dunnett).

FIGURE 3. Regional cerebral blood flows (rCBF) for rats made acutely hyperglycemic by intraperitoneal glucose injection are expressed as a percent of control flow values. (Open bars = flow values for the group that received 6 ml/kg of D-glucose; closed bars = flow values for the group that received 8 ml/kg of D-glucose; error bars = 1 SEM; * = \( p < 0.05 \); ** = \( p < 0.01 \) [Dunnett's test].)
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reduction in rCBF that accompanies hyperglycemia." Parallel increase in plasma sodium did not occur in the erythrocytes, or vessel walls found in diabetes that reproduce the chronic changes in plasma proteins, be ascribed in part to increased plasma fibrinogen, reduced erythrocyte deformability, or increased adhesion of erythrocytes to endothelial cells. However, models of acute or chronic hyperglycemia may not reproduce the chronic changes in plasma proteins, erythrocytes, or vessel walls found in diabetes that influence blood viscosity.

Hematocrit, a major determinant of blood viscosity, increased in all groups of rats that received intraperitoneal glucose injections. This could be due to a fluid shift from blood to the peritoneal space. However, a parallel increase in plasma sodium did not occur in the one group in which it was measured. The assumption that rCBF will be affected by altered blood viscosity in the face of normal vascular autoregulation has been questioned. The arterial oxygen content, which is determined in part by hematocrit, is perhaps a more important determinant of rCBF. These factors, while important to understanding the rCBF changes measured, do not indicate why regional variation in rCBF occurs.

Cerebral blood flow will fall if cerebral metabolic rate decreases. The blood flow to any single brain region is linked to the metabolic rate of that region. The constant of proportionality for this relation may change under global pathologic conditions, but it will remain the same throughout the brain. If the relation between flow and metabolic rate is preserved during hyperglycemia, any decrease in metabolic rate may be accompanied by decreased CBF. There are data that suggest an association of hyperglycemia with decreased metabolic rate. Hyperglycemia can inhibit oxygen consumption in rat brain and tumor tissue.

Also, Kety and associates observed that, when compared with laboratory controls, oxygen consumption decreased 18% and CBF decreased 17% in hyperglycemic patients who were acidic but alert. It is known that metabolic acidosis can change the relation between flow and metabolism. However, in the current study streptozotocin did not produce metabolic acidosis. If the flow–metabolism coupling is preserved during hyperglycemia, a decrease in cerebral metabolic rate could contribute to the measured flow reduction.

Regional variation in the degree of flow reduction during hyperglycemia was not expected. Nontelencephalic regions demonstrated flow reduction while telencephalic regions did not. Although the choice of an anatomic boundary for classification is somewhat arbitrary, it is helpful because it emphasizes that rCBF reduction was not confined to brain regions with low basal blood flow. For example, nontelencephalic brain regions with high resting blood flow, such as the inferior colliculus, had decreased blood flow during hyperglycemia.

Anatomic variation in rCBF and metabolic rate of glucose utilization suggest anatomic explanations for differences in regional function. A rostral–caudal gradient of brain blood flow reduction has been measured previously in neonatal dogs during asphyxia. In that study, in contrast to the findings presented here, forebrain blood flow decreased while hindbrain blood flow increased. It was suggested that this effect might be related to the known density gradient of adrenergic innervation of cerebral blood vessels. A similar logic was used to explain the rostral–caudal gradient of suppression of glucose utilization measured during althesin-induced anesthesia, specifically, that steroid receptors may be present in the brain with their greatest density being in the forebrain.

The presence of regional variation in CBF reduction during hyperglycemia suggests that systemic changes induced by glucose, such as hyperosmolality or hyperviscosity, may not mediate the flow reduction. These factors should affect all brain regions equally. The presence of a rostral–caudal gradient raises the possibility that the reduction may be mediated by region-specific flow regulation mechanisms — specifically, those involving neural modulation of vascular resistance.

Alloxan treatment produced an unstable model for the study of rCBF during hyperglycemia. Alloxan-induced hyperglycemia failed to produce significant rCBF reduction. The variance in both rCBF and plasma glucose data was larger than in other groups. In an attempt to define the source of this variance, multiple blood samples were obtained from the tail vein of alloxan-treated rats over a 48-hour period. Repeated measurements during the first 48 hours after alloxan injection indicated that plasma glucose first rose to 45 μm/ml at 20 hours, fell to 4 μm/ml at 28 hours, and returned to 50 μm/ml at the time of rCBF measure-
ment. This indicates that rCBF was determined during a period of relatively rapid change in blood glucose levels. This probably explains the greater variance in glucose measurement at the time of rCBF determination, as seen in Table 3. It is assumed that this variance renders the allometric model unsuitable.

Decreased rCBF is measured during chronic and acute hyperglycemia. The degree of flow reduction is similar at equal and clinically relevant plasma glucose concentrations (blood glucose = 380 mg/dl), whether the hyperglycemia is chronic or acute. This indicates that the mechanism for this effect does not adapt with time. The relation between degree of hyperglycemia and of rCBF depression is linear and a regional distribution of the flow decrease is present. These factors may contribute to the pathophysiology of stroke and cardiac arrest and suggest possible mechanisms for the deleterious effects of hyperglycemia in those conditions.

References

17. Shenkin HA, Spitz EB, Grant FC, Kety SS: The acute effects on the cerebral circulation of the reduction of increased intracranial pressure by means of intravenous glucose or ventricular drainage. J Neurol Sci 1948;5:466–470
22. Forbes HS, Nason GI: The cerebral circulation. XII. Vascular responses to (A) hypertonic solutions and (B) withdrawal of cerebrospinal fluid. Arch Neurol Psychiatry 1935;34:533–547

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http://stroke.ahajournals.org/content/18/1/52