Autonomic Consequences of Cerebral Hemisphere Infarction

Stephen A. Barron, MD; Ze’ev Rogovski, PhD; Jesaiah Hemli, MD

Background and Purpose  Recently, supraventricular tachycardia has been reported following right hemisphere stroke, suggesting a reduction in parasympathetic cardiac innervation after stroke of the right hemisphere. We performed power spectrum analysis of fluctuations in RR interval duration in the electrocardiogram in an attempt to determine how ischemic stroke influences autonomic cardiac innervation.

Methods  Power spectrum analysis of the variation in 256 consecutive electrocardiographic RR intervals was performed using the fast-Fourier transformation. The area under the spectral curve from 0 to 0.5 Hz and the area under that portion of the curve produced by parasympathetically mediated respiratory variations were determined in 20 patients with right-hemisphere and 20 patients with left-hemisphere ischemic stroke confirmed by computerized tomography. Data were compared with 40 age- and sex-matched healthy controls.

Results  Total cardiac autonomic innervation was reduced after a stroke of either hemisphere without regard to laterality. Cardiac parasympathetic innervation was reduced after stroke of either hemisphere with a significantly greater reduction after stroke on the right (P=2.9x10^-5).

Conclusions  Power spectral analysis of heart rate variability can detect autonomic consequences of stroke. The spectral data predict that, to the degree that cardiac arrhythmia is produced by unbalanced cardiac autonomic activity favoring the sympathetic system, such arrhythmias could be seen after stroke of either hemisphere and would be more common after cerebral infarction on the right. This is consistent with evidence from the recent literature. (Stroke. 1994;25:113-116.)

Key Words  • autonomic nervous system • cerebral infarction • electrocardiography • heart rate variability

The effect of disturbance of cerebral hemisphere function on the autonomic nervous system has been the focus of much investigation, particularly with reference to cardiovascular function.2,3 Evidence for cerebral hemisphere-autonomic interaction includes electrocardiographic (ECG) changes with a variety of neurological lesions, including subarachnoid hemorrhage, intracerebral hemorrhage, and ischemic stroke, as well as cardiac arrhythmia and even death associated with epileptic seizures.3 Lane et al4 have recently described a differential effect of cerebral infarction on cardiac rhythm. Supraventricular tachycardia was significantly associated with right hemisphere stroke, whereas patients with left hemisphere stroke tended to have more ventricular arrhythmias. The authors suggested that parasympathetic tone was reduced ipsilateral to the side of the cerebral infarction, thus producing a relative increase in sympathetic tone on that side.

Power spectrum analysis (PSA) of the beat-to-beat variation in RR interval duration in the ECG is a sensitive tool for assessing cardiac autonomic innervation and reflects the variability in heart rate resulting from both sympathetic and parasympathetic cardiovascular autonomic reflexes.2,5-8 The technique has identified reduced cardiac autonomic innervation in diabetes mellitus, chronic renal failure, and in familial dysautonomia.9-11

We have performed PSA of the heart rate variation from the ECGs of 40 patients with stroke in an effort to study how ischemic stroke influences cardiac autonomic innervation.

Subjects and Methods

Patients were hospitalized in the Neurology Service of the Rambam (Maimonides) Medical Center after a first stroke. All 40 patients suffered from ischemic cerebral infarction in the distribution of the carotid artery system, 20 having suffered from right hemisphere infarction, and 20 from left hemisphere infarction. Patients were studied from 4 to 11 days following the stroke, at which time they were either neurologically stable or improving.

Table 1 shows the age and sex distribution of the patients in each of the two groups.

Consecutive patients were admitted to the study if they fulfilled the following criteria: (1) the time of onset of the stroke was precisely known; (2) computerized tomography scan of the brain confirmed a single cerebral infarct consistent with the clinical localization of the stroke; (3) they did not have a coexisting condition known to affect the PSA of heart rate variability: diabetes mellitus,9 active cardiac ischemia12,13 congestive heart failure,14 or renal insufficiency15; (4) they were not receiving medications known to affect the autonomic nervous system; and (5) the stroke was in the distribution of the carotid artery. Although respiratory pattern was not a criterion for either entrance or exclusion from the study, all the patients herein reported had a clinically normal respiratory pattern with no evidence of respiratory distress.

PSA was performed at the bedside from an ECG acquired on-line through a personal computer from chest leads oriented to approximate frontal plane lead I. All patients were in sinus rhythm. Two hundred fifty-six consecutive RR intervals were identified and analyzed in each recording, which was made...
TABLE 1. Age and Sex of Patients With Right-Hemisphere and Left-Hemisphere Infarction

<table>
<thead>
<tr>
<th>Side</th>
<th>Mean</th>
<th>Range</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td>69.2</td>
<td>41-79</td>
<td>11</td>
<td>9</td>
</tr>
<tr>
<td>Left</td>
<td>68.4</td>
<td>44-83</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

with the patient lying supine. This time series of intervals was prepared for analysis by subtracting the mean interval of the array from each individual interval and passing the resulting series through a detrend filter and a Hanning window. Spectral analysis of the series was performed using the fast-Fourier transformation.

The power spectrum displays three areas of concentration of spectral power between 0 to 0.5 Hz, each attributed to a different autonomic cardiovascular control mechanism.5,7 Fig 1 shows a spectral curve from a normal subject. The area under the spectral curve from 0 to 0.5 Hz is the total spectral power (TSP). Of the three indicated areas of power density, the best characterized is that appearing at the highest frequency, generally above 0.2 Hz, labeled "1" in Fig 1. This spectral region reflects heart rate changes associated with respiration and we term this area of spectral density, indicated by the arrows in Fig 1, the respiratory related activity (RRA). The RRA is the expression in the frequency domain of the respiratory sinus arrhythmia, a purely parasympathetic phenomenon.15 It is totally blocked by atropine.7 The area of the RRA is thus a quantified expression of the parasympathetic vagal innervation of the heart.

A midfrequency zone of spectral density, labeled "2" in Fig 1, reflects heart rate variability resulting from baroreceptor regulation of blood pressure and is a mixed sympathetic-parasympathetic control system. It is significantly but incompletely blocked by atropine.7 The low-frequency peak, labeled "3" in Fig 1, has been the least well studied. It reflects heart rate changes involved in thermoregulation but is also influenced by the renin-angiotensin system.5,7 The unlabeled peak in Fig 1 represents slow trends in heart rate variation and is not considered further.

Normal values for TSP and RRA were determined from the PSA of 40 healthy age- and sex-matched volunteers.

Results

The significance of differences in means was determined by Student's $t$ test for unmatched pairs, $\alpha=0.05$. Fig 2 shows a representative PSA from a patient after stroke. The patient, a 64-year-old man, had a stroke of the right hemisphere. Note the absence of an obvious high-frequency peak, labeled "1" in Fig 1.

Table 2 shows the mean TSP in normal subjects and in the patients with stroke. There was a marked reduction in TSP after infarction in either hemisphere in comparison to normal subjects. There was no significant difference in TSP between the two patient groups, $P=.092$.

Table 2 also shows the RRA in normal subjects and the patients with stroke. There was a significant reduction in RRA after infarction in either hemisphere in comparison to normal subjects, with the reduction after right hemisphere stroke significantly greater than after left hemisphere stroke, $P=2.9\times10^{-5}$.

There was no difference in mean respiratory rate after right- and left-hemisphere strokes (19 breaths per minute in both groups).

Discussion

The results indicate that autonomic cardiac innervation is reduced after ischemic infarction of either cerebral hemisphere. Factors known to affect the PSA were specifically excluded in our patients and it is reasonable to assert that the reduction in autonomic activity was the result of the stroke. The greater reduction in RRA after right hemisphere infarction is in accord with the speculations of Lane et al,4 who anticipated a reduction in ipsilateral parasympathetic innervation after right hemisphere stroke. Our data show a similar but less significant reduction of parasympathetic innervation after left hemisphere stroke as well. To the degree that a cardiac arrhythmia is produced under conditions of unbalanced cardiac autonomic innervation favoring the sympathetic nervous system, our data would predict an increased incidence of such arrhythmias after stroke in either hemisphere, with a greater incidence of these arrhythmias after right hemisphere stroke than after left hemisphere stroke. The number of patients in each group is too small to allow meaningful stratification according to the localization of the infarction within the hemisphere; however, because patients with verte-

![Fig 1. Graph of results of spectral analysis of heart rate variability in a normal subject. The spectrum of the respiratory-related activity (1), baroregulation (2), and thermoregulation (3) are indicated.](http://stroke.ahajournals.org/Downloaded from http://stroke.ahajournals.org)
brosbasilar strokes were excluded from this report, no patient had an infarction exclusively of the occipital lobe.

The data are compatible with the reported observation that heart rate variability associated with cognitive tasks requiring the mobilization of attention is absent in patients after right hemisphere stroke.16

Cardiac autonomic innervation originates in brain stem (parasympathetic) and spinal (sympathetic) nuclei. An anatomic basis for cerebral hemispheric influences on autonomic function is provided by projections onto autonomic nuclei from cortical, amygdaloid, hypothalamic, and limbic structures.1,3 Cerebral infarction presumably reduces cardiac autonomic innervation by removal of ipsilateral suprasegmental stimulation of the primary autonomic nuclei. Additional evidence for some lateralization of function of the autonomic nuclei themselves is the recent demonstration of a correlation between systemic hypertension and neurovascular compression of the ninth and tenth cranial nerves only at the left side of the medulla.17

Lateralization of peripheral autonomic innervation of the heart is well established. In the experimental animal, ablation of the left stellate ganglion increases the threshold of ventricular fibrillation whereas right stellate ganglion ablation produces the opposite effect.18 In humans, before treatment with β-blockers, the recurrent ventricular fibrillation associated with the long QT interval syndrome was successfully treated with left stellate ganglion ablation.19 It is also known that the sinoatrial node is preferentially innervated by the right vagus, whereas the atrioventricular node receives more of its parasympathetic innervation from the left vagus.20-22 This latter observation might predict that parasympathetic effects of left hemisphere lesions would be expressed less strongly at the sinoatrial node than those of right hemisphere lesions.

We conclude that PSA of heart rate variation can identify reduced autonomic cardiac activity after unilateral ischemic infarction. Right hemisphere infarction is associated with a greater decrease in cardiac parasympathetic activity than is left hemisphere infarction, a possible explanation for the reported greater incidence of some types of cardiac arrhythmias after right hemisphere stroke. We recommend further use of the technique of PSA of heart rate variation in the investigation of the autonomic consequences of cerebral hemisphere infarction.

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**References**


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