Ipsilateral Hypohidrosis in Brain Stem Infarction

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**Background and Purpose:** The brain stem is the most important autonomic processing center, but very little attention has been given to clinical manifestations of autonomic failure in brain stem stroke. Our purpose was to evaluate the prevalence, characteristics, and prognostic significance of sweating dysfunction in brain stem infarctions.

**Methods:** We carried out a prospective study using quantitative evaporation to investigate spontaneous and heat-stimulated sweating in 18 healthy control subjects and 18 patients with ischemic brain stem stroke in the acute phase and at 1 and 6 months after infarction.

**Results:** The sweating response induced by a heating stimulus was significantly lower on the ipsilateral side to the infarction than on the contralateral side. Constant ipsilateral hypohidrosis was established in 83% of the patients in the acute phase, in 100% at 1 month, and in 76% at 6 months after infarction. No differences of sweating response were found between medullary and pontine infarcts.

**Conclusions:** Hypohidrosis throughout the whole ipsilateral side of the body, a long-lasting phenomenon that has not previously been described, is an essential feature of autonomic failure in brain stem infarction. *(Stroke 1993;24:100–104)*

**Key Words** • autonomic dysfunction • brain stem infarction • sweating

The brain stem, where several neural pathways and nuclei form a network regulating vegetative functions, is the most important autonomic processing center. Although brain stem lesions typically cause serious autonomic disturbances, the significance of autonomic failure in brain stem infarctions has not been carefully elucidated. The occurrence of autonomic dysfunction involving cardiovascular and respiratory regulation has been presented previously only in a few case reports,1–6 and the frequency and prognostic value of these disorders has remained unsettled.

Disturbed sweating is a common manifestation of autonomic failure in acute hemispheric brain infarction,7 but it has been given little attention in brain stem infarctions. It has been stated that lesions in the hypothalamus, pontine tegmental area, and lateral medullary area may produce ipsilateral hemifacial hypohidrosis as a part of Horner’s syndrome as a result of disruption of descending sympathetic sudomotor fibers.8,9 However, only facial sweating has been assessed previously, the methods used being nonquantitative and the number of patients very small.10–12

Because the available knowledge of sweating dysfunction associated with brain stem stroke is scarce, we designed this present, prospective study. We assessed hypohidrosis quantitatively in patients with brain stem infarction to evaluate the prevalence, characteristics, and prognostic value of sweating dysfunction.

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**Subjects and Methods**

The study was carried out in the Department of Neurology, Oulu University Central Hospital. The protocol was approved by the Ethics Committee of the Medical Faculty, University of Oulu, and informed consent was obtained from each subject.

Eighteen consecutive patients (15 men and three women; mean±SD age, 52.8±11.2 years) with hemiparesis or unilateral sensory deficit caused by acute brain stem infarction were included in the study. Nine patients had the infarct in the pontine level of the brain stem and nine patients in the medullary level. Table 1 presents clinical features of the patients. Patients with manifestations of any other central or peripheral nervous system lesion and patients taking medication known to affect the autonomic nervous system were excluded.

All the patients had clinical deficits clearly attributable to brain stem infarction. Cerebral computed tomography verified a brain stem infarction in four cases, whereas the finding was normal in the remaining 14 patients.

The controls consisted of 18 healthy subjects (15 men and three women; mean±SD age, 50.2±11.6 years) who had no manifestations of any central or peripheral nervous disease and who were taking no medication known to affect the nervous system.

The sweating investigations were performed on all the patients from 1 to 7 (median, 5) days after the onset of clinical symptoms and were repeated at 1 and 6 months after infarction. One patient was not available at the 1-month follow-up visit and one patient at the 6-month follow-up visit. The sweating investigations were performed only once with the control subjects. Evaporation from the skin (as grams per square meter per hour) was measured by an evaporimeter (Evaporim-
TABLE 1. Clinical Features of Patients With Brain Stem Infarction

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age (years)</th>
<th>CT</th>
<th>Symptoms/signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medullary</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>M</td>
<td>43</td>
<td>–</td>
<td>Ipsilateral Horner’s syndrome, bulbar paresis, dizziness, contralateral sensory deficits</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>67</td>
<td>–</td>
<td>Lateral medullary syndrome</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>61</td>
<td>–</td>
<td>Lateral medullary syndrome</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>64</td>
<td>–</td>
<td>Lateral medullary syndrome</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>31</td>
<td>+</td>
<td>Lateral medullary syndrome</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>41</td>
<td>–</td>
<td>Ipsilateral Horner’s syndrome, dizziness, contralateral sensory deficits</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>58</td>
<td>–</td>
<td>Lateral medullary syndrome</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>57</td>
<td>–</td>
<td>Lateral medullary syndrome</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>64</td>
<td>–</td>
<td>Lateral medullary syndrome</td>
</tr>
<tr>
<td>Pontine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>53</td>
<td>+</td>
<td>Contralateral hemiparesis and sensory deficits, diplopia, dizziness</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>47</td>
<td>+</td>
<td>Contralateral hemiparesis and sensory deficits, ipsilateral trigeminal lesion</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>53</td>
<td>–</td>
<td>Contralateral sensory deficits, ipsilateral facial and trigeminal lesion, diplopia, dizziness</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>60</td>
<td>+</td>
<td>Contralateral hemiparesis, ipsilateral facial paresis, bulbar paresis</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>30</td>
<td>–</td>
<td>Ipsilateral trigeminal lesion, diplopia, bulbar paresis, ataxia, dizziness</td>
</tr>
<tr>
<td>15</td>
<td>M</td>
<td>50</td>
<td>–</td>
<td>Contralateral hemiparesis and sensory deficits, ipsilateral trigeminal lesion, bulbar paresis</td>
</tr>
<tr>
<td>16</td>
<td>F</td>
<td>67</td>
<td>–</td>
<td>Contralateral sensory deficits, bulbar paresis, ipsilateral facial, trigeminal, and oculomotor lesion</td>
</tr>
<tr>
<td>17</td>
<td>M</td>
<td>56</td>
<td>–</td>
<td>Contralateral hemiparesis, ipsilateral trigeminal lesion, diplopia, bulbar paresis, dizziness</td>
</tr>
<tr>
<td>18</td>
<td>M</td>
<td>48</td>
<td>–</td>
<td>Contralateral hemiparesis and sensory deficits, ipsilateral facial, trigeminal, and abducant lesion</td>
</tr>
</tbody>
</table>

CT, computed tomography; +, infarction visualized by cerebral CT; –, infarction not visualized by cerebral CT; M, male; F, female.

Sweating was always recorded in the same particular experiment room at a standard temperature of 24.0±0.5°C; the mean relative humidity of the room was kept at approximately 47%, and all drafts were eliminated. The heating stimulus was provided by four standard thermo packings (75°C/1,000 W) placed on the abdomen of the patient. In addition, the reclining subject was covered with a non-heat penetrating blanket from the level of the upper chest to the level of the knees to prevent heat escape. Evaporation rates were recorded at baseline and after 10 minutes of heating in six registration sites on both sides of the forehead and chest and on both forearms, hands, legs, and feet.

For quantifying the degree of individual sweating asymmetry, we defined a hidrosis index (HI), which is the ratio of the evaporation rates at the six registration sites on the contralateral side of the body to the evaporation rates at the corresponding six sites on the ipsilateral side of the body. When sweating is equal on both sides of the body, the index value is 1.00. In control subjects, the HI is the ratio of the evaporation rates on the right side of the body to the evaporation rates on the left side of the body. The HI is calculated as follows:

\[ HI = \frac{\Sigma E_c}{\Sigma E_i} \]

where \( \Sigma E \) is the sum evaporation rates at forehead, chest, forearm, hand, leg, and foot, respectively; c is the contralateral side; and i is the ipsilateral side.

Statistical analyses were performed by using the Wilcoxon matched pairs test to compare the evaporation rates of the ipsilateral and contralateral sides of the body. The Mann-Whitney two-sample test was used to test differences observed between the evaporation rates of the control subjects and those of the ipsilateral and contralateral sides of the infarction patients. The Mann-Whitney two-sample test was also used to compare the HI values of control subjects and of patients in the acute phase and at 1 and 6 months after infarction.

Results

At baseline, the mean evaporation rates on the side ipsilateral to the infarction tended to be lower compared with those of the contralateral side, but the differences were not significant. Figure 1 presents the mean evaporation rates after 10 minutes of heating stimulus on both sides of the body in the patient group. In the acute phase, significant ipsilateral hypo-
In the control group, the evaporation rates showed no asymmetry either at baseline or after the heating stimulus. Therefore, we used the mean value of the right and left evaporation rates as a reference value of each registration site.

Figure 2 presents the mean evaporation rates of the patients in the acute phase and those of the control subjects, after the heating stimulus. In the acute phase, significant ipsilateral hypohidrosis compared with the control subjects was found at all registration sites. The sweating response to the heating stimulus was also clearly lower on the contralateral side of the patients than in the control subjects. However, at 1 and 6 months after infarction, the ipsilateral hypohidrosis was still significant, but the sweating on the contralateral side of the patients was the same as that of the control subjects. Thus, although the ipsilateral hypohidrosis difference was maintained in the 6-month follow-up period, the contralateral side difference disappeared.

The HI values of the control subjects after the heating stimulus ranged between 0.96 and 1.05 (mean±SD, 1.01±0.02). In the patient group, the mean HI values were significantly higher than those of the control subjects: in the acute phase, 1.48±0.56 (p<0.0001); at 1 month after infarction, 1.48±0.41 (p<0.0001); and at 6 months after infarction, 1.57±0.82 (p<0.01) (Figure 3). Considering the mean HI of the control subjects ±2 SD as normal ranges of sweating, ipsilateral hypohidrosis was found in 15 of 18 patients (83%) in the acute phase, 17 of 17 patients (100%) at 1 month, and 13 of 17 patients (76%) at 6 months after the infarct.

Discussion

Our series is the first prospective and quantitative study aiming to assess the incidence and magnitude of sweating abnormalities associated with ischemic brain stem stroke. In the present study, we demonstrated ipsilateral hypohidrosis in all patients during the 6-month follow-up. Contrary to previous reports stating that unilateral hypohidrosis typically involves the ipsilateral side of the face and sometimes the upper chest,8-12 the present results reveal clear-cut ipsilateral hypohidrosis after a heating stimulus throughout the whole body. This seems to differ from earlier observations of unilateral sweating dysfunction associated with acute hemispherical brain infarction, which results in hyperhidrosis on the contralateral side of the face and upper body14 or on the whole paretic side of the body.7 Moreover, in the present study, no differences of sweating response were found between the medullary and pontine infarcts. The HI proved to be a sensitive and useful method for quantifying the degree of individual sweating asymmetry.

Although the phenomenon of ipsilateral facial hypohidrosis as a part of Horner’s syndrome is well known, little is known previously about sweating dysfunction in general in brain stem infarcts. List and Peet10 investigated sweating response to a heating stimulus in eight patients with a vascular brain stem lesion and found ipsilateral hypohidrosis in six cases and a symmetric sweating response in one case. Morris et al11 reported ipsilateral facial hypohidrosis in two patients with pontine infarction and a symmetric sweating response in two patients with lateral medullary infarction, all the cases having the clinical signs of Horner’s syndrome.
Furthermore, Salvesen et al. assessed hidrosis by evaporationmetry in three patients with lateral medullary infarction and found ipsilateral facial hypohidrosis after a heating stimulus in all of them. Because of rather crude investigation methods and lack of controls, the prevalence and characteristics of sweating dysfunction have not been elucidated previously.

The prognostic value of sweating dysfunction related to brain stem infarctions has not been discussed previously, but it has been asserted that unilateral hypohidrosis associated with brain stem infarction is a transient phenomenon that usually disappears together with other clinical disorders. The present results, however, do not support such claims, because the degree of hypohidrosis remained unchanged during the 6-month follow-up in spite of improvement of other signs. On the other hand, the outcome of our patients was favorable: None of them died, and by the 6-month follow-up most of them had only minor neurological deficits. Because as many as 83% of the patients showed ipsilateral hypohidrosis in the acute phase, sweating dysfunction may be considered an essential nontransient part of the phenomenology of brain stem infarction rather than a sign of poor prognosis.

It has been suggested that unilateral hypohidrosis associated with brain stem lesions in the same locations as those of the present series is a result of the interruption of the mostly uncrossed excitatory sweating pathway that descends from the hypothalamus via the brain stem to the intermediolateral column of the spinal cord. Experimental studies support this hypothesis, but the exact origin, course, and terminations of these hypothalamo-autonomic connections are still obscure. The available few reports of cases with autopsy suggest that the pathway supplying sympathetic sudomotor neurons runs through the tegmental area of the mesencephalon and pons and more caudally the posterolateral area of the medulla. The first area is typically disturbed by the occlusion of the superior cerebellar artery and the latter by the occlusion of the posterior inferior cerebellar artery, causing Wallen-berg's syndrome. Moreover, surgical lesions placed in the thalamus for treatment of Parkinson's disease or dystonia may sometimes cause loss of sweating on the ipsilateral side of the body.

In addition to ipsilateral hypohidrosis, the sweating response to the heating stimulus was also clearly lower on the contralateral side of the patients than that in the control subjects in the acute phase after infarction, but the difference disappeared during the follow-up. This contralateral hypohidrosis may be related to generalized hypohidrosis in the acute phase of brain stem infarction due to, for example, altered hormone or neurotransmitter levels, or it may be related to lesions of the corticospinal, spinothalamic, or other brain stem neural pathways. Furthermore, the descending sudomotor pathway from hypothalamus may be partly crossed, causing hypohidrosis on both sides of the body as suggested by Appenzeller. Further studies are needed to solve the pathogenesis of this phenomenon.

In conclusion, ipsilateral hypohidrosis seems to be a more frequent and long-lasting phenomenon than has been proposed so far in brain stem stroke. Evaporationmetry provides a novel and sensitive quantitative method for estimating this reflection of sympathetic hypofunction. Reliable recognition of sweating dysfunction may be important, because this damage of the autonomic nervous system possibly also manifests itself as other disturbances, such as cardiovascular and respiratory complications.

![Figure 2. Bar graph shows mean evaporation rates (g/m²/h) ± SEM after heating stimulus at six registration sites on ipsilateral (filled bar) and contralateral (shaded bar) side of the body in patients with acute brain stem infarction and the reference evaporation rate of control subjects (open bar). *p<0.05, **p<0.01, ***p<0.001, ipsilateral and contralateral sides compared with those of control subjects.](http://stroke.ahajournals.org/)

![Figure 3. Graph shows hidrosis indexes of control subjects and of patients with brain stem infarction after heating stimulus in the acute phase, at 1 month, and at 6 months after infarction. The mean of each group is marked with a line. *p<0.01, **p<0.0001, patients compared with control subjects.](http://stroke.ahajournals.org/)
References

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