Hyperhidrosis as a Reflection of Autonomic Failure in Patients With Acute Hemispheral Brain Infarction
An Evaporimetric Study
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Background and Purpose: Sweating dysfunction is one of the most frequently encountered symptoms of autonomic failure but has received scant attention in patients with cerebrovascular diseases. Our purpose was to evaluate the prevalence, pathogenesis, and clinical correlates of sweating dysfunction in stroke.

Methods: We studied sweating at baseline and after a heating stimulus in 53 patients with acute hemispheral brain infarction and in 40 healthy control subjects by using a quantitative evaporimetric method.

Results: Significant hyperhidrosis on the paretic side of the body was verified in 55% of the patients at baseline, in 74% after 5 minutes of heating, and in 77% after 10 minutes of heating. Hyperhidrosis was established throughout the body and correlated with the severity of paresis, the presence of reduced muscle tone, and the extensor plantar response.

Conclusions: The phenomenon of hyperhidrosis in hemiparetic patients reflecting autonomic dysfunction seems to be a common manifestation that should be listed among the expected consequences of brain infarction. This sweating disturbance might be attributed to a lesion of a putative sympathoinhibitory pathway controlling sweating. The failure of this pathway could also be related to other manifestations of sympathetic hyperfunction, e.g., cardiac complications. Therefore, assessment of sweating may provide a new, important aspect in the evaluation of stroke patients.

KEY WORDS • autonomic dysfunction • cerebral infarction • sweating

Although the occurrence of autonomic nervous system disturbances associated with cerebrovascular diseases has been well recognized, the full spectrum of autonomic dysfunction has not been carefully outlined. Emphasis has been paid particularly to abnormalities in cardiovascular regulation and to symptoms such as arrhythmias and ischemic heart damage and their prognostic value in stroke,1-3 but other aspects of autonomic failure have been given little attention.4-5 The lack of clinically applicable quantitative investigatory methods appropriate for studying the autonomic nervous system has evidently limited more detailed interest in the manifestations of autonomic failure in stroke.

Sweating dysfunction is one of the most obvious and frequently encountered symptoms of autonomic failure. As for hemiplegic stroke patients, it has been our clinical impression, and a frequent complaint of our patients, that the paretic side of the body sweats more profusely and feels colder than the unaffected side. However, this phenomenon of contralateral hyperhidrosis has been reported rarely in the available stroke literature,1,6-8 and its clinical significance has remained obscure because sweating has been assessed by non-quantitative methods only in basal conditions and controls have not been used. Now, as both the general knowledge of autonomic disturbances and the investigatory methods used for studying the autonomic nervous system have improved, more attention has been paid to the significance of autonomic failure for well-being, quality of life, consequences of diseases, and prognostic measures.

Because disturbed sweating is a common complaint in hemiparetic patients and because a quantitative evaporimetric method for investigating sweating has become available,9 we designed the present study to assess the significance of hidrosis in stroke. We aimed to evaluate the prevalence, severity, pathogenesis, and clinical significance of sweating dysfunction in acute hemispheric brain infarction.

Subjects and Methods
The study was carried out in the Department of Neurology, Oulu University Hospital. The protocol was approved by the Ethics Committee of the Medical Faculty, University of Oulu, and informed consent was obtained from each subject. Fifty-three consecutive patients (33 men and 20 women; mean±SD age, 54.6±10.4 years) with unilateral motor deficit caused by acute hemispheric brain infarction in the internal carotid artery territory were included in the study. Pa-
tients with symptoms or signs of any other central or peripheral nervous system lesion were excluded. Twenty-five patients had right and 28 had left hemispheral infarction.

To confirm the clinical diagnosis of acute brain infarction, all patients had undergone cerebral computed tomography (CT) on admission to the hospital. If the first CT examination was negative, then CT was repeated within 2 weeks. A hemispheral cortical infarct was verified in 24 cases and a subcortical infarct in 25. The CT was normal in four cases in spite of a clear clinical deficit attributable to hemispheral infarction.

Thirty-one patients had no preexisting disease and were taking no medication known to affect the autonomic nervous system. Twenty-two patients had non-insulin-dependent diabetes mellitus, 15 had arterial hypertension, and six had coronary heart disease. Sixteen patients were taking cardiovascular medication: β-adrenergic blocking agents in 10, calcium entry blockers in eight, diuretics in seven, digitals in eight, and nitroglycerin in three.

The control subjects consisted of 40 healthy individuals (23 men and 17 women; mean±SD age, 50.8±9.7 years) who had no symptoms or signs of any central or peripheral nervous system disease and who were taking no medication known to affect the nervous system.

The sweating investigations were performed on the patients 1–7 (median, 5) days after the onset of clinical symptoms of brain infarction. We measured evaporation using the method introduced by Nilsson; fluid loss from the skin (sweating) is measured as grams per square meter per hour by an evaporimeter (Evaporimeter EP1; Servo Med, Stockholm, Sweden). This device determines the skin water loss by calculating the vapor pressure gradient in the water vapor boundary layer surrounding the skin with special sensors in a single probe. This gradient is proportional to the amount of water vapor passing through the boundary layer per unit time and area. Previously this method has been found useful in studying sweating disturbances in patients with e.g., parkinsonism and cluster headache.

Sweating was always recorded in the same experiment room at a standard temperature of 24.0±0.5°C, the mean relative humidity of the room being kept at approximately 47% and all draft being eliminated. The heating stimulus was provided by four standard thermo packings (75°C/1,000 W) placed on the abdomen. 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 in six registration sites on both sides of the forehead and chest and in both forearms, hands, legs, and feet were recorded at baseline and after 5 and 10 minutes of heating.

Because the absolute evaporation rates varied, we designed a hidrosis index to describe the sweating asymmetry between the paretic and nonparetic sides of the body. The hidrosis index is the ratio of the evaporation rates at the six registration sites on the paretic side of the body to the evaporation rates at the corresponding six sites on the nonparetic side of the body. When sweating is equal on the two sides of the body, the value of the hidrosis index is 1.00.

For quantifying the degree of muscle weakness, the following rating scale was used: 0, complete paralysis; 1, minimal contraction; 2, active movement with gravity eliminated; 3, weak contraction against gravity; 4, active movement against gravity and resistance; and 5, normal strength.

Evaporation of the paretic and nonparetic sides was analyzed by using the paired t test. Student's t test was used for comparing hidrosis indexes between the patient and control groups and for correlating hyperhidrosis and clinical symptoms in the patients. Linear regression was used in analyzing the relation between the degrees of paresis and hyperhidrosis.

**Results**

Evaporation rates in the six registration sites on both sides of the body in the patients are presented in Figure 1. Evaporation on the paretic side was already more pronounced than that on the nonparetic side at baseline (Figure 1, top left). After 5 and 10 minutes of heating, sweating was even more pronounced throughout the paretic side, the difference being significant for all registration sites (Figures 1, top right and 1, bottom).

Evaporation rates of the control subjects showed no asymmetry either at baseline or after the heating stimulus.

The hidrosis indexes of the patient and control groups are presented in Table 1. The hidrosis index of the patient group was significantly higher than that of the control group at baseline and after 5 and 10 minutes of heating (p<0.001 for all), indicating considerable hyperhidrosis on the whole paretic side of the body. Table 2 shows the percentage of patients with excessive asymmetrical sweating at baseline and after 5 and 10 minutes of heating. At baseline 55% of the patients, and after heating stimulus up to 77% of the patients, showed hyperhidrosis on the paretic side.

Table 3 presents the relations between hyperhidrosis at baseline and after 5 and 10 minutes of heating and clinical signs. There were no significant differences in sweating response between the male and female patients, between patients with right and left hemispheral infarction, or between patients with cortical and subcortical infarction. Hyperhidrosis on the paretic side of the body was significantly more pronounced in patients with flaccid paresis than in hemiparetic patients with normal muscle tone and in patients with an extensor plantar response than in those with a flexor plantar response. Hyperhidrosis also seemed to be more obvious in patients with accelerated tendon reflexes and in patients with sensory hemisymptoms than in those without these phenomena, but significant differences could not be established.

There was a linear correlation between muscle weakness and the magnitude of hyperhidrosis on the paretic side of the body. A significant correlation was found in the arm and leg after 5 (p=0.003, r=0.372 and p=0.004, r=0.366, respectively) and 10 (p=0.04, r=0.252 and p=0.005, r=0.357, respectively) minutes of heating.

**Discussion**

The present study, carried out on 53 consecutive patients with acute hemispheral brain infarction, is the first aiming to quantify sweating dysfunction associated with ischemic stroke. Significant hyperhidrosis was found on the paretic side of the body in 55% of the patients at baseline and in >70% after the heating
FIGURE 1. Bar graphs of mean±SEM evaporation rates at six registration sites on paretic (filled bars) and nonparetic (shaded bars) sides of body in 53 patients with acute hemispheric brain infarction at baseline (top left), after 5 minutes of heating (top right), and after 10 minutes of heating (bottom left). *p<0.05, **p<0.01, ***p<0.001 different from nonparetic side by paired t test.

stimulus. Evaporation rates on the paretic side were already high at baseline and became even more pronounced after heating. Significant hyperhidrosis was established at all recording sites. Hyperhidrosis was found to bear a clear correlation with the degree of muscle weakness, the presence of reduced muscle tone, and the presence of an extensor plantar response.

Previously, excessive sweating on the paretic side of the body after hemispheric brain infarction had been considered unusual. Labar et al observed profuse unilateral hyperhidrosis in six of 633 consecutive patients with ischemic hemispheric stroke, but the method they used to assess hyperhidrosis was inspection and not quantitative. Profuse unilateral sweating was apparent by visual inspection after the heating stimulus in only four of our 53 patients, but hyperhidrosis could be demonstrated in the great majority of patients by using the evaporimetric method. However, during the test the patients themselves only occasionally reported differences in sweating sensation between the paretic and nonparetic sides of the body. On the other hand, patients often complained that the paretic limb felt cold.

In previous studies it has been reported that unilateral hyperhidrosis typically involves the paretic arm and face, but our study revealed excessive sweating at all six registration sites throughout the paretic side of the body, most obviously the forehead and hand. In those areas where the absolute evaporation rates were already high at baseline (forehead and hand), the responses and differences between the affected and nonaffected sides seemed to be clearer than in other parts of the body.

Increased sweating on the paretic side of the body has been reported in patients with large brain infarcts involving the insular cortex or both superficial cortical and deep subcortical structures and is said to be associated with severe neurological deficit and poor prognosis. As to the severity of sweating dysfunction in our patients, no differences were found between patients with cortical infarcts and those with subcortical infarcts. Moreover, the responses seemed to be equal in patients

TABLE 1. Hidrosis Indexes of Patients With Hemispheric Brain Infarction and Control Subjects at Baseline and After 5 and 10 Minutes of Heating Stimulus

<table>
<thead>
<tr>
<th>Time</th>
<th>Patients (n=53)</th>
<th>Controls (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>1.16±0.25*</td>
<td>0.99±0.04</td>
</tr>
<tr>
<td>5 minutes</td>
<td>1.40±0.42*</td>
<td>1.01±0.04</td>
</tr>
<tr>
<td>10 minutes</td>
<td>1.42±0.48*</td>
<td>1.01±0.05</td>
</tr>
</tbody>
</table>

Values are mean±2 SD.

* p<0.001 different from controls by Student's t test.
TABLE 3. Relations Between Clinical Findings and Magnitude of Hyperhidrosis in 53 Patients With Hemispheral Brain Infarction at Baseline and After 5 and 10 Minutes of Heating Stimulus

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No.</th>
<th>Baseline</th>
<th>5 min</th>
<th>10 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>33</td>
<td>1.19±0.31</td>
<td>1.37±0.45</td>
<td>1.38±0.47</td>
</tr>
<tr>
<td>Female</td>
<td>20</td>
<td>1.18±0.32</td>
<td>1.42±0.38</td>
<td>1.48±0.49</td>
</tr>
<tr>
<td>Hemiparesis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>28</td>
<td>1.21±0.32</td>
<td>1.33±0.41</td>
<td>1.37±0.50</td>
</tr>
<tr>
<td>Right</td>
<td>25</td>
<td>1.15±0.29</td>
<td>1.42±0.48</td>
<td>1.47±0.45</td>
</tr>
<tr>
<td>Infarct*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortical</td>
<td>24</td>
<td>1.21±0.39</td>
<td>1.38±0.42</td>
<td>1.38±0.50</td>
</tr>
<tr>
<td>Subcortical</td>
<td>25</td>
<td>1.16±0.25</td>
<td>1.43±0.45</td>
<td>1.48±0.48</td>
</tr>
<tr>
<td>Muscle tone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>28</td>
<td>1.16±0.24</td>
<td>1.27±0.32</td>
<td>1.26±0.29</td>
</tr>
<tr>
<td>Flaccid paresis</td>
<td>20</td>
<td>1.25±0.41</td>
<td>1.52±0.51</td>
<td>1.63±0.60†</td>
</tr>
<tr>
<td>Spastic paresis</td>
<td>5</td>
<td>1.07±0.10</td>
<td>1.53±0.37</td>
<td>1.46±0.45</td>
</tr>
<tr>
<td>Tendon reflexes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonaccelerated</td>
<td>22</td>
<td>1.17±0.32</td>
<td>1.35±0.38</td>
<td>1.30±0.28</td>
</tr>
<tr>
<td>Accelerated</td>
<td>31</td>
<td>1.19±0.31</td>
<td>1.42±0.45</td>
<td>1.47±0.53</td>
</tr>
<tr>
<td>Plantar response</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flexor</td>
<td>21</td>
<td>1.13±0.20</td>
<td>1.21±0.21</td>
<td>1.23±0.24</td>
</tr>
<tr>
<td>Extensor</td>
<td>32</td>
<td>1.22±0.36</td>
<td>1.50±0.49†</td>
<td>1.54±0.55§</td>
</tr>
<tr>
<td>Sensation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>27</td>
<td>1.13±0.23</td>
<td>1.31±0.35</td>
<td>1.34±0.46</td>
</tr>
<tr>
<td>Hemi hypesthesia</td>
<td>24</td>
<td>1.25±0.38</td>
<td>1.45±0.49</td>
<td>1.50±0.50</td>
</tr>
</tbody>
</table>

Hidrosis index as mean±SD.
*Four patients with normal computed tomogram not included.
†p<0.05, ‡p<0.01 different from patients with normal muscle tone by Student's t test.
§p<0.05 different from patients with flexor plantar response by Student's t test.
|| Two patients not eligible because of ataxia.

Lower evaporation rates on the paretic side than on the nonparetic side (hypohidrosis) were observed in two patients at baseline and in four after 10 minutes of heating. All these patients had a CT-verified hemispheral brain infarct compatible with the clinical signs. Two of these six patients were taking medication for coronary artery disease. Neither their medication nor any clinical feature in them or in the remaining four patients explained the observed hypohidrosis.

The pathogenesis of unilateral hyperhidrosis associated with a hemispheral cerebral lesion is still uncertain. The observed hyperhidrosis could be explained by disruption of a putative inhibitory neural pathway that controls sweating of the contralateral face and body, as has been suggested previously on the grounds of human and animal studies. This pathway might originate in a variety of cortical areas, project to the brain stem, cross in the medulla, and make terminal connections with the contralateral spinal cord. It has been suggested that the pathway follows the pyramidal tract, a hypothesis that is supported by the present study in that a clear-cut association was established between hyperhidrosis and various signs of pyramidal tract lesion (extensor plantar response, abnormal muscle tone, and degree of motor deficit). Further evidence for an association of the pathway with the pyramidal tract is derived from the report of Awada et al, who described a patient with excessive bilateral sweating after basilar artery occlusion. Magnetic resonance imaging showed a paramedian infarct at the upper pontine level damaging the corticospinal tracts. Similarly, severe constant symmetrical hyperhidrosis below the ninth thoracic dermatome has been reported in a patient with spinal cord lesion, caused by a bilateral pyramidal tract lesion. The cause of the phenomenon was thought to be bilateral disruption of the putative inhibitory neural pathway controlling sweating.

In addition to explaining disturbances in the control of sweating, failure of the suggested sympathoinhibitory pathway might also explain some other manifestations of sympathetic hyperfunction in patients with stroke, such as cold extremities on the paretic side. Failure in the putative pathway could also be reflected as cardiac arrhythmias and ischemic heart lesions, which are common complications of stroke.

It can be concluded that ischemic brain infarction almost inevitably also damages the autonomic nervous system. In the present study, we demonstrated pro-
nounced hyperhidrosis as a reflection of failure of the sympathoinhibitory regulation. Establishment of the clinical significance of this new finding calls for further studies.

References

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