Evolution of Neurological, Neuropsychological and Sleep-Wake Disturbances After Paramedian Thalamic Stroke

Dirk M. Hermann, MD; Massimiliano Siccoli, MD; Peter Brugger, PhD; Karen Wachter, MD; Johannes Mathis, MD; Peter Achermann, PhD; Claudio L. Bassetti, MD

Background and Purpose—The clinical features and natural course of paramedian thalamic stroke is poorly known. The aim of this study was to characterize the evolution of neurological, neuropsychological, and sleep–wake deficits after paramedian thalamic stroke.

Methods—Forty-six consecutive patients, aged 48.4±16.6 years, were studied. Fourteen had bilateral, 16 left-sided, and 16 right-sided lesions. Assessment included neurological examinations, estimation of sleep needs, formal neuropsychological tests (n=27), and polysomnographies (n=31). Functional outcome was followed up over 1 year in 31 patients with the modified Rankin Scale and Barthel index.

Results—Oculomotor palsy (76% of patients), mild gait ataxia (67%), deficits of attention (63%), fluency and error control (59%), learning and memory (67%), and behavior (67%) were common in the acute stroke phase. Outcome was excellent with right-sided infarcts but mostly incomplete with bilateral and left-sided lesions. This was mainly related to persistent frontal lobe-related and cognitive deficits found in 100% bilateral and 90% left-sided, but only 33% right-sided strokes. Initially, hypersomnia was present in all patients associated with increased stage 1 sleep, reduced stage 2 sleep, and reduced sleep spindles. Sleep needs improved in patients with bilateral and almost disappeared with unilateral lesions after 1 year. Sleep architecture remained abnormal with the exception of sleep spindles that increased.

Conclusions—Whereas neurological deficits and hypersomnia recover to large extent in patients with paramedian thalamic stroke, the frontal lobe-related and cognitive deficits, which are mainly linked with bilateral and left-sided lesions, often persist. As such, stroke outcome is better in right-sided than bilateral or left-sided infarcts. (Stroke. 2008;39:62-68.)

Key Words: attention ■ cognition ■ hypersomnia ■ ischemic brain infarct ■ thalamus

Paramedian thalamic stroke presents with a stereotypical clinical picture often initiated by a short-lasting loss of consciousness followed by a hypersomnolent state in which sleep needs are markedly increased and the patient’s ability to maintain attention is reduced.1–4 Patients typically also exhibit neurological symptoms such as vertical gaze palsy and other oculomotor deficits, Horner’s syndrome, dysarthria, gait ataxia, and mild sensorimotor deficits.3–5,10

With the improvement of consciousness, neuropsychological problems such as executive, learning, and memory deficits become more evident.1,3,5,6,9,11–15 Sleep studies have shown an increased sleep duration with predominance of superficial sleep stages, increased sleep fragmentation, and decreased sleep spindles.2–4 Hypersomnia has been considered to result from the disruption of thalamic sleep-generating and arousal-maintaining mechanisms.1–3

Few reports suggested that neuropsychological abnormalities and sleep–wake disturbances may persist over several months poststroke.3,5,15 Overall, the prevalence of neurological, neuropsychological, and neurophysiological abnormalities as well as the long-term consequences of paramedian thalamic stroke is poorly known. The aim of this study was to analyze the development of clinical, neuropsychological, and sleep–wake abnormalities in the acute and postacute stroke phase and to identify factors influencing stroke recovery.

Materials and Methods

Neurological Examinations

Forty-six consecutive patients with ischemic paramedian thalamic stroke referred to the University Hospitals of Berne (1992 to 2000) and Zurich (2001 to 2004) were studied. All patients were seen by one of the authors (C.L.B.). A detailed medical history and neurological examination were always performed. Severity of neurological impairment was estimated by the Scandinavian Stroke Scale. In all but 2 patients, MRI was performed within 2 weeks after stroke. Diagnostic workup always included blood tests, electrocardiogram,
Neuropsychological Tests
Thirty-nine neuropsychological examinations were conducted in 27 patients. Eight patients had bilateral, 10 left-sided, and 9 right-sided lesions. In all patients, a first examination took place in the first month after stroke (between days 5 and 30; mean interval from stroke: 14.3±10.5 days). Follow-up studies were done in 12 patients (mean interval: 13.8±11.2 months). Four patients had bilateral, 5 left-sided, and 3 right-sided infarcts.

Neuropsychological examinations focused on 5 cognitive domains: (1) attention (Attention Test Battery16; d2 cancellation test17); (2) fluency and error control (verbal fluency: Thurstone and Thurstone20; naming/rule breaks; color–word interference: Stroop20); (3) memory with separate aspects of learning and active recall (both verbal and figural; Rey15; Osterrieth22); (4) speech and language (assessed clinically, noting presence/absence of dysarthria, word finding deficits, phonemic, semantic paraphasias, language comprehension difficulties, reading/writing problems). In cases with abnormalities, the Aachen Aphasia Test23 was used for quantitative and qualitative deficit grading; and (5) visuospatial functions were evaluated by a patient’s ability to recognize subjective contours, overlapping figure, line drawings, faces, and colors. Visuoconstructive abilities and presence/absence of hemispatial neglect were assessed by having patients copy simple geometric line drawings and a complex geometric figure.24 In addition to cognition, abnormalities in the following 6 behavioral-affective domains were recorded: somnolence, psychomotor slowing, euphoria/emotional lability, anosognosia, confabulations, and impulsivity. Deficits in the 5 cognitive domains were rated retrospectively by 2 senior neuropsychologists as absent, mild, or moderate–severe. Both raters were blinded to an individual patient’s stroke localization, and in cases of disagreement (<3% of scorings), a consensus rating was obtained.

Sleep History and Studies
A detailed history of sleep habits before stroke was always asked for, including estimated sleep needs (in hours/day). After the stroke, sleep needs were also repeatedly assessed at every consultation. In addition, a total of 56 overnight video polysomnographies were recorded in 31 patients using Neurofax (Nihon Kohden, Tokyo, Japan: 1992 to 2000) and Embla (Flaga, Reykjavik, Iceland: 2001 to 2004) sleep recording systems from 10 PM to 5 AM. Eleven patients had bilateral, 10 left-sided, and 10 right-sided lesions. Twenty patients received both polysomnographic and formal neuropsychological studies. Sleep scoring was done visually on 2 computer-based electroencephalographic (EEG) analysis systems (Nicolet-Ultrasom 2.1, Madison, Wis; Somnologica, Reykjavik, Iceland) according to Rechtschaffen and Kales.25 Sleep spindles per hour of sleep stage 2 were counted automatically both ipsilateral and contralateral to the infarct in patients assessed with Nicolet-Ultrasom 2.1.26 In all 31 patients, a first polysomnography took place in the first month after stroke (starting on day 3; mean interval from stroke: 9.7±9.4 days). In 6 patients, 2 additional follow-up polysomnographies were recorded 12 and 24 months thereafter. These patients were considered for a more detailed analysis of the evolution of sleep architecture changes.

In 4 patients (2 bilateral, 1 left-sided, one right-sided stroke), nocturnal EEG power spectra were computed during stage 2 sleep from sleep recordings obtained with a portable polygraphic amplifier (PS1).27 All patients were recorded once during the first 9 days after stroke. In 2 patients (one bilateral and the left-sided stroke), sleep recordings were repeated in the postacute phase (after 2 and 12 months). In the power spectra obtained, sleep spindle peaks were calculated.28 The spindle peak size was determined in the F3C3 derivation.

In 15 patients, actigraphies were performed (6 actigraphies in the first week, 3 after 1 month, 3 after 1 year, and 3 after 2 years). Actigraphies were registered over 7 days (Motion-Logger; Ambulatory Monitoring Inc, Ardsley, NY), and over this recording period, the average “time asleep”/24 hours was calculated.29 The average “time asleep” was then correlated with the subjectively estimated sleep needs.

Follow-Up Examinations
Thirty-one patients were followed up by clinical examination over at least 12 months (mean duration: 37.6±33.4 months; range, 12 to 131 months) and were included in a more detailed analysis of stroke recovery. Nine patients had bilateral, 10 left-sided, and 12 right-sided lesions (age 45.7±17.4, 42.0±14.2, and 42.6±16.7 years). All patients were examined at least once in the subacute phase (3 to 6 months after stroke) and after ≥1 year, in most cases more often. During all control examinations, neurological symptoms, neuropsychological deficits, and sleep–wake habits were carefully inquired and detailed neurological examinations performed. Outcome was evaluated using the modified Rankin Scale (mRS; ranging from 0=normal to 5=requiring constant and full supervision and care) and Barthel index (0 to 100 points).

Statistics
Clinical scores, sleep, and sleep architecture changes were analyzed by one-way analysis of variance followed by least significant differences tests or by 2-way analysis of variance. Follow-up examinations were evaluated by repeated measurement analysis of variance. Neuropsychological results were examined by Fisher exact tests. Relationships between subjectively estimated sleep needs and actigraphically determined “time asleep” were evaluated by Pearson’s correlations. All data are expressed as means±SD. Probability values <0.05 were considered significant.

Results
Patients’ Characteristics
Thirty-four male and 12 female patients with a mean age of 48.4±16.6 years (range, 16 to 83 years) were prospectively included. There were 14 bilateral, 16 left-sided, and 16 right-sided strokes. Three of 46 patients had a personal history of strokes (2 striatal infarcts, one centrum semiovale infarct) and 4 patients a history of transient ischemic attacks. Six patients revealed silent lesions in MRI scans (2 cortical, one striatal, one anterior thalamic, 2 cerebellar lesions).

Vascular Risk Factors
Nine patients had arterial hypertension and 12 hypercholesteremia. Twenty-one patients were smokers (24.5±16.5 pack-years) and 16 habitual snorers. Nine patients had a positive family history for vascular diseases and one patient diabetes mellitus.

Stroke Etiology
The presumed stroke etiology was arterioarterial embolism in 4 patients (macroangiopathy in 3, vertebral dissection in one patient) and cardioembolism in 3 patients (atrial fibrillation in 2, mechanical valve replacement in one patient). In 20 patients, a patent foramen ovale was found, 9 of which were associated either with atrial septum aneurysm or a spontane-
ous interatrial shunt. In all other patients, stroke etiology remained unknown.

**Neurological Observations**

In 9 patients, stroke onset was accompanied by a short-lasting loss of consciousness (7 of 14 bilateral, one of 16 left-sided, one of 16 right-sided strokes), which usually lasted less than 1 hour.

The most common focal neurological findings were oculomotor deficits (most commonly vertical gaze palsy; n=35 of 46=76% of patients), anisocoria (14 of 46=30%), facial sensory deficits (4 of 46=9%), facial nerve palsy (19 of 46=41%), glossopharyngeal palsy/swallowing difficulties (2 of 46=4%), lingual palsy (4 of 46=9%), dysarthria (24 of 46=52%), mild gait ataxia (31 of 46=67%), sensory deficits of arms/legs (6 of 46=13%), mild motor deficits of arms/legs (24 of 46=52%), hypogeusia/hyposmia (4 of 46=9%), and visual deficits (2 of 46=4%). The prevalence of focal symptoms/signs did not depend on the stroke side.

**Evolution of Neurological Deficits/Stroke Outcome**

Focal neurological deficits mostly recovered within a few weeks to months from stroke. Only 12 of 31 patients had focal neurological abnormalities after 1 year (oculomotor deficits in 6, gait ataxia in one, arm motor deficits in one, dysarthria/swallowing difficulties in 4 patients). In 4 of these patients, neurological abnormalities were very mild and not recognized any more by the patients. The Scandinavian Stroke Scale, which was 47.6±5.2 for bilateral, 49.1±3.8 for left-sided, and 50.3±5.2 for right-sided infarcts immediately after stroke, largely normalized within 1 year (Scandinavian Stroke Scale: 56.9±1.2 for bilateral, 57.4±1.3 for left-sided, and 58.0±0.0 for right-sided injuries; n=31).

Stroke recovery was excellent in patients with right-sided stroke (mRS at 12 months: 0.3±0.6; Figure 1). Eight of 11 patients with right-sided lesions exhibited no residual deficits after 1 year. On the other hand, recovery was incomplete after bilateral (mRS: 2.8±1.1) and left-sided (1.7±1.2) infarcts (Figure 1). The poor recovery was accompanied by persisting everyday life deficits in the latter groups (Barthel index after 1 year: 75.6±21.1 in bilateral, 91.0±16.1 in left-sided, 98.3±5.8 in right-sided infarcts; Figure 1).

**Neuropsychological Findings**

**Cognitive Deficits**

Results are summarized in Table 1. Deficits in attention (17 of 27=63% of patients), fluency and error control (16 of 27=59%), and learning and memory (18 of 27=67%) were most prevalent. All patients with bilateral and most patients with left-sided infarcts revealed attention deficits. On the other hand, only a few patients with right-sided lesions had attention abnormalities.

Fluency and error control as well as learning and memory recall were affected in most patients with bilateral and left-sided infarcts but were rarely compromised after right-sided stroke. Speech and language were abnormal in half of the patients with bilateral and left-sided lesions, but was never affected with right-sided infarcts.

Serious difficulties in visuospatial processing were almost absent. A tactile or visual hemineglect was seen in 2 patients with bilateral and one patient with right-sided stroke. One patient with left-sided stroke revealed constructional apraxia attributed to visuospatial deficits.

**Behavioral Changes**

Findings are summarized in Table 2. Eighteen of 27 patients (67%) revealed behavioral deficits, patients with bilateral stroke always revealing abnormalities in at least one entity. Some changes (anosognosia, confabulation) were found only in patients with bilateral infarcts, and others (decreased
impulsivity) only after left-sided lesions. Other changes (psychomotor slowing, euphoria/emotional lability) were similarly present in all three stroke localizations.

**Neuropsychological Findings in the Recovery Phase**

Although 3 of 3 patients with right-sided stroke subjected to neuropsychological follow-up tests exhibited normal results in their second test, zero of 4 patients with bilateral and only 2 of 5 patients with left-sided infarcts exhibited full recovery. Attention, fluency, and error control as well as learning and memory remained abnormal. Partial improvements were seen in 2 of 4 patients with bilateral and one of 5 patients with left-sided stroke.

**Sleep–Wake Disturbances (sleep needs/hypersomnia)**

All patients exhibited increased sleep needs within the first 24 hours poststroke (Figure 1). Hypersomnia was more pronounced in patients with bilateral than left- or right-sided infarcts (Figure 1). Hypersomnia often markedly improved within 12 months poststroke. Self-estimated sleep needs similarly decreased in patients with bilateral, with left-sided, and right-sided infarcts (Figure 1). After 1 year, sleep needs remained elevated above prestroke values by 3.1 ± 2.1 hours/day in patients with bilateral (n = 9 patients), but only by 1.2 ± 0.9 hours/day in left-sided (n = 10) and 0.8 ± 1.5 hours/day in right-sided (n = 12) stroke.

In patients investigated over more than 12 months (n = 16 patients with follow-ups ≥2 years), sleep needs further decreased. Sleep needs finally normalized in 9 of 12 patients with unilateral stroke, but remained elevated in 4 of 4 patients with bilateral infarcts (abnormal sleep needs: ≥1 hour/24 hour above prestroke values).

Validation studies in 15 patients confirmed that the subjectively estimated sleep needs correlated well with the actigraphically determined "time asleep" (y = −0.505 + 1.003x; r = 0.975, P < 0.001; y = actigraphical "time asleep," x = subjectively reported sleep duration).

**Sleep–Wake Studies**

**Polysomnographies**

Compared with control subjects examined in our hospital because of peripheral neurological diseases (n = 12), patients with thalamic stroke revealed a nonsignificantly lower sleep efficiency, a significantly higher proportion of stage 1, and a significantly lower proportion of stage 2 sleep (Table 3). Stages 3/4 and rapid eye movement sleep were not significantly altered. Sleep spindles were decreased in patients with paramedian thalamic stroke when compared with control subjects (Table 3). Patients with unilateral stroke had higher sleep spindles counts than patients with bilateral infarcts (P < 0.05). In 6 patients recorded at least 3 times after stroke, the proportion of sleep stages did not significantly change from the acute to chronic phase. Sleep spindles, however, increased over 2 years from stroke (Table 4).

**Electroencephalographic Power Spectra**

Spectral EEG analysis performed in the first week after stroke revealed either a small (0.31 [lg power/μV^2/0.25 Hz]; patient 1) or absent (0.00; patient 2) frontocentral sleep spindle peak in 2 patients with bilateral paramedian thalamic infarcts.

### Table 1. Neuropsychological Deficits in the First Month After Stroke in 27 Patients With Paramedian Thalamic Infarcts

<table>
<thead>
<tr>
<th>Deficit</th>
<th>Stroke Laterality</th>
<th>Bilateral</th>
<th>Left</th>
<th>Right</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None</td>
<td>Mild</td>
<td>Moderate to Severe</td>
<td>None</td>
</tr>
<tr>
<td>Attention</td>
<td>0/8</td>
<td>5/8</td>
<td>3/8</td>
<td>4/10</td>
</tr>
<tr>
<td>Fluency and error control</td>
<td>2/8</td>
<td>3/8</td>
<td>3/8</td>
<td>1/10</td>
</tr>
<tr>
<td>Memory</td>
<td>2/8</td>
<td>4/8</td>
<td>2/8</td>
<td>3/10</td>
</tr>
<tr>
<td>Learning</td>
<td>1/8</td>
<td>4/8</td>
<td>3/8</td>
<td>1/10</td>
</tr>
<tr>
<td>Recall</td>
<td>4/8</td>
<td>3/8</td>
<td>1/8</td>
<td>5/10</td>
</tr>
<tr>
<td>Speech/language</td>
<td>6/8</td>
<td>2/8</td>
<td>0/8</td>
<td>9/10</td>
</tr>
</tbody>
</table>

Data are prevalence numbers for each stroke topography. Numbers shown in bold significantly differ from the other stroke localizations (P < 0.05 on Fisher exact tests).

### Table 2. Behavior Changes in the First Month After Stroke in 27 Patients With Paramedian Thalamic Infarcts

<table>
<thead>
<tr>
<th></th>
<th>Somnolence</th>
<th>Psychomotor Slowing</th>
<th>Euphoria/Emotional Lability</th>
<th>Anosognosia</th>
<th>Confabulations</th>
<th>Decreased Impulsivity</th>
<th>Increased Impulsivity</th>
<th>No Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral</td>
<td>2/8</td>
<td>1/8</td>
<td>2/8</td>
<td>1/8</td>
<td>2/8</td>
<td>0/8</td>
<td>1/8</td>
<td>0/8</td>
</tr>
<tr>
<td>Left</td>
<td>0/10</td>
<td>3/10</td>
<td>1/10</td>
<td>0/10</td>
<td>0/10</td>
<td>3/10</td>
<td>0/10</td>
<td>3/10</td>
</tr>
<tr>
<td>Right</td>
<td>0/9</td>
<td>1/9</td>
<td>1/9</td>
<td>0/9</td>
<td>0/9</td>
<td>0/9</td>
<td>1/9</td>
<td>6/9</td>
</tr>
</tbody>
</table>

Data are prevalence numbers for each stroke topography. Numbers shown in bold significantly differ from the other stroke localizations (P < 0.05 in Fisher exact tests).
Table 3. Effects of Stroke Topography on Sleep Architecture in the Acute Phase (first month) After Stroke in 31 Patients With Paramedian Thalamic Infarcts and 12 Control Subjects

<table>
<thead>
<tr>
<th>Stroke Laterality</th>
<th>Control Subjects§ (n=12)</th>
<th>Stroke Laterality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bilateral (n=11)</td>
<td>Left (n=10)</td>
</tr>
<tr>
<td>Age</td>
<td>47.0±4.0</td>
<td>49.2±15.9</td>
</tr>
<tr>
<td>Recording time, min</td>
<td>453±42</td>
<td>402±40</td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>88±9</td>
<td>86±9</td>
</tr>
<tr>
<td>Stage 1, %</td>
<td>15±7</td>
<td>31±24*</td>
</tr>
<tr>
<td>Stage 2, %</td>
<td>57±9</td>
<td>34±16†</td>
</tr>
<tr>
<td>Stage 3/4, %</td>
<td>9±8</td>
<td>9±11</td>
</tr>
<tr>
<td>Rapid eye movement sleep, %</td>
<td>19±5</td>
<td>19±14</td>
</tr>
<tr>
<td>Spindle density, hours⁻¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lesion side</td>
<td>308±13</td>
<td>80±56†</td>
</tr>
<tr>
<td>Contralateral</td>
<td>168±98†</td>
<td>122±81</td>
</tr>
</tbody>
</table>

Data are means±SD.

*P<0.05/†P<0.01 compared with control subjects.
‡P=0.05 compared with bilateral stroke patients (one-way analysis of variance followed by least significant difference tests).
§Control group of hospitalized patients with peripheral neurological diseases.

Table 4. Evolution of Sleep Architecture During Stroke Recovery in 6 Patients With Paramedian Thalamic Infarcts

<table>
<thead>
<tr>
<th>Recording time, min</th>
<th>1st Month</th>
<th>12 Months</th>
<th>24 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep, %</td>
<td>88±10</td>
<td>92±8</td>
<td>87±9</td>
</tr>
<tr>
<td>Stage 1, %</td>
<td>44±22</td>
<td>44±19</td>
<td>40±24</td>
</tr>
<tr>
<td>Stage 2, %</td>
<td>32±8</td>
<td>36±14</td>
<td>31±17</td>
</tr>
<tr>
<td>Stage 3/4, %</td>
<td>15±15</td>
<td>8±9</td>
<td>10±13</td>
</tr>
<tr>
<td>Rapid eye movement sleep, %</td>
<td>9±4</td>
<td>10±4</td>
<td>10±9</td>
</tr>
<tr>
<td>Spindle density, hours⁻¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lesion side</td>
<td>129±113</td>
<td>164±105</td>
<td>206±101*</td>
</tr>
<tr>
<td>Contralateral</td>
<td>117±94</td>
<td>157±76</td>
<td>200±100</td>
</tr>
</tbody>
</table>

Data are means±SD.

*Repeated-measurement analysis of variance with significant time effect (F₁,₁₀=6.319; P<0.05).

Predictors of Stroke Recovery

To identify factors predicting stroke recovery, we next compared patients exhibiting complete or almost-complete (mRS =1) and incomplete (mRS =2) recovery 1 year after stroke. Compared with patients exhibiting complete or almost-complete recovery, patients with poor outcome were older (P<0.05) and more frequently exhibited stroke involvement of the left thalamus (P<0.01). Besides, stroke presented more often with an initial loss of consciousness (P<0.05). Patients with incomplete recovery also revealed higher sleep needs immediately after their stroke (P<0.01) and after 1 year (P<0.01). The severity of neurological symptoms, measured by the Scandinavian Stroke Scale, sleep efficiency, and sleep architecture, did not correlate with stroke outcome.

Discussion

Our article offers a detailed and comprehensive analysis of focal neurological, neuropsychological, and sleep–wake disturbances after paramedian thalamic stroke. Our main findings are (1) long-term recovery after paramedian thalamic stroke is significantly better in right-sided than in bilateral and left-sided infarcts; (2) bilateral and left-sided but not right-sided strokes regularly present with deficits in executive functions and memory, which may persist in the subacute phase and explain the unfavorable outcome; and (3) post-stroke hypersomnia improves considerably within months, whereas sleep EEG changes, besides a moderate improvement in sleep spindle activity, may remain unchanged for years.

In this study, patients were consecutively included. As a typical university department of neurology diagnoses between 2 and 5 paramedian thalamic strokes each year, patients in this study were collected over more than a decade. During this time, we systematically investigated neurological, neuropsychological, and sleep–wake deficits wherever possible in a routine clinical setting. We are therefore confident that our data set is representative for this stroke syndrome. In our study, not all patients received all 3 kinds of data analysis (clinical recovery, neuropsychological, and sleep assessments), which was impossible for logistical reasons related to patient care. We compensated this lack of a uniform patient collective by sampling sufficiently high patient numbers in all 3 data subsets providing the statistical power to draw reliable conclusions regarding the previously mentioned hemispheric influences on stroke outcome, neuropsychological deficits, and sleep.

Stroke Recovery Is Better in Right-Sided Than in Bilateral and Left-Sided Infarcts

Our finding that stroke recovery, assessed by the mRS, depends on the lesion side is new. In fact, detrimental outcomes have previously been reported mainly after bilateral paramedian thalamic lesions.9,13,15,27 The unfavorable outcome in bilateral and left-sided strokes in our study was clearly not attributed to persistent focal neurological abnormalities. In fact, only 12 of 31 patients exhibited focal neurological signs after 1 year, and abnormalities in these patients were often mild and no more recognized by the patients. These observations challenge previous reports, in
which persistent neurological deficits have been emphasized.28,29

Cognitive Deficits Are More Prominent After Bilateral and Left-Sided Infarcts

The poor outcome in patients with left-sided paramedian thalamic lesions was well explained by impairments of frontal lobe-related functions such as fluency and error control as well as of learning, memory, and language, which were more severe in patients with bilateral and left-sided lesions in whom they also recovered incompletely. Previous studies, mostly in small series, have emphasized severe memory deficits after bilateral infarcts.9,13,15,27 A few case reports have also described persistent verbal and visual amnesia after left-sided lesions.30–32 Cognitive changes in patients involving the left-sided thalamus may anatomically be explained by lesions of the hippocampal memory loop (also known as Papez circuit), which connects the hippocampus with the mammillary bodies and anterior thalamus.33 Brain lesions involving the hippocampal loop induce a failure of information storage, ie, amnesia.34,35 The observation that fluency and error control, learning, and memory were most severely affected after infarcts involving the left thalamus is in line with a laterality of the hippocampal loop for these functions.

Attention and Behavioral Deficits Are Most Prominent After Bilateral Infarcts

Attention and behavioral changes have been reported after bilateral and, less commonly, unilateral paramedian thalamic stroke. Patients may exhibit “pseudopsychiatric” syndromes with emotional lability, disinhibition, frontal-like behavior, personality changes, or delirium.9,13,15 In our series, attention and behavioral deficits were in fact present in all patients with bilateral and unilateral paramedian thalamic lesions. In patients with bilateral infarcts, behavioral changes were sometimes profound and attention deficits mostly did not recover completely in the postacute phase. Unfortunately, neuropsychological follow-up studies were performed only in a relatively small number of patients. This precludes more detailed conclusions about the recovery of the cognitive and behavioral deficits.

Although attention deficits in patients with bilateral stroke are most likely related to the interruption of ascending reticular arousal systems (see also subsequently), the behavior changes may reflect a dysfunction of the lateral limbic loop, which links the dorsomedial thalamus with the orbitofrontal cortex and amygdala.33 In contrast to hippocampal loop lesions causing pure amnesia,34,35 lesions of the lateral limbic loop typically evoke amnesia associated with behavior changes and confabulation tendency.36 Our observation that behavioral changes were particularly prominent after bilateral infarcts does not exclude the possibility reported in the literature that in single patients, unilateral lesions of the lateral limbic loop may exhibit behavioral abnormalities at least in the peracute phase (up to 4 days from stroke), which was not assessed by our clinical neuropsychologists.

Sleep Architecture Does Not Recover Despite Improvement of Sleep Needs/Sleep Spindles

Sleep architecture did not show any improvement over time in this study despite a decrease in sleep needs and some increase in sleep spindle activity. In fact, stage 1 sleep, which was increased in the acute stroke phase independent of the stroke hemisphere affected, as well as stage 2 sleep and sleep spindles, which were reduced, remained abnormal representing a sort of “sleep EEG signature” of paramedian thalamic infarcts. Our data are in line with previous observations in a small patient series in which persistent disturbances in sleep patterns were seen.3 The absent recovery of sleep architecture may in parts reflect an insufficient improvement of mechanisms underlying sleep spindles production and more generally sleep consolidation.

Relationship Between Sleep–Wake Disturbances and Neuropsychological Deficits

The increased sleep needs in patients with bilateral paramedian thalamic infarcts persisting over months or years2–4
together with the long-lasting daytime apathy\textsuperscript{1,3,5–7,15} previously suggested that sleep disturbances and neuropsychological changes in this syndrome are linked. The dissociation in our study between sleep architecture and neuropsychological disturbances challenges the hypothesis of a simple relationship between sleep EEG and cognitive impairments.

However, elevated sleep needs were predictive for a moderate to poor stroke outcome, which in turn was associated with persistent attention disturbances, besides impairments of executive functions, learning, and memory. This observation could give support to the hypothesis that hypersomnia is linked with attention rather than cognitive changes, pointing toward a common dysfunction in arousal systems. As such, the integrity of ascending reticular arousal networks rather than that of sleep-generating systems may be relevant for the recovery from paramedian thalamic stroke.

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\textbf{Disclosures}

None.

\textbf{References}

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Dirk M. Hermann, Massimiliano Siccoli, Peter Brugger, Karen Wachter, Johannes Mathis, Peter Achermann and Claudio L. Bassetti

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