

Chronic Cognitive Impairment Following Laterothalamic Infarcts

A Study of 9 Cases

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Background: The occlusion of the lateral thalamic arteries leads to infarcts of ventrolateral thalamic nuclei, the ventroposterior nucleus, and the rostrolateral part of pulvinar, and produces hemisensory loss with or without hemiataxia. Cognitive impairment after such strokes has not been systematically studied.

Objective: To determine the nature and the extent of long-lasting cognitive deficits following lateral thalamic strokes.

Design: Case series.

Setting: Neurology department, Lausanne University Hospital, Lausanne, Switzerland.

Patients: Nine patients with hemisensory loss due to an isolated laterothalamic infarct.

Main Outcome Measures: Three to 6 months after stroke onset, standard neuropsychologic evaluation, including testing of language, ideomotor and constructive praxis, visual gnosis, spatial attention, learning abilities, and executive functions.

Results: Six of 9 patients showed some degree of cognitive impairment. Executive functions tasks, particularly verbal fluency, were impaired in 5 patients (4 with right and 1 with left lesion). Learning and delayed recall in visuospatial and verbal tasks, but not in recognition, were impaired in 3 patients (2 with right and 1 with left lesion). Difficulties in visual gnosis were observed in 1 patient with right lesion while word-finding difficulties were observed in 1 patient with left lesion.

Conclusions: Our observations show that while learning, naming, and gnostic difficulties fit with the classical verbal/nonverbal dichotomy (left and right hemisphere, respectively), executive dysfunctions, including verbal fluency tasks, were more dominant after right thalamic infarcts. Although the observed deficits appeared to be less severe than those generally found with dorsomedial and polar thalamic strokes, the dominance of executive dysfunction suggests that ventrolateral thalamic lesions may disrupt frontothalamic subcortical loops.

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ISOLATED THALAMIC infarctions include (1) inferolateral or thalamogeniculate infarction, with pure hemisensory loss or hemiataxia-hyposesthesia; (2) anterior, polar, or tuberothalamic infarcts, with executive neuropsychologic dysfunction; (3) posterior choroidal infarcts, mainly with visual hemifield disorders; and (4) paramedian (dorsomedial) infarcts, with decreased consciousness and neuropsychologic and behavioral consequences.¹ Thalamic damage, depending on the territory involved, induces various cognitive dysfunctions, including aphasia,² apraxia,³ neglect,^{4,5} memory disturbances,⁶ and executive dysfunction,⁵ but also manic episodes⁷ and palipsychism.⁵

An isolated occlusion of the lateral thalamic arteries, leading to an infarct of ventrolateral thalamic nuclei, the ventral pos-

terior nucleus, and the rostrolateral part of pulvinar, is thought to produce little cognitive disturbance.⁸ Rarely, "parietal" cognitive signs (tactile extinction, anosognosia, aphasia, and apraxia) have been reported, but these were restrained to the acute phase.⁹ Lateral thalamotomies may also induce transient aphasic or attentional deficits.¹⁰ However, long-lasting cognitive modifications related to lateral thalamic infarcts have not been systematically investigated in prior studies. In this article, we sought to characterize the nature and the extent of cognitive dysfunctions occurring after lateral thalamic stroke.

METHODS

In this study, hemisensory deficit (Dejerine-Roussy syndrome) was chosen as the cardinal clinical sign for study inclusion. Of the 801 pa-

tients admitted between January 1998 and September 2000 for a first stroke, 9 (1.1%) had hemisensory loss with a single lateral thalamic infarct on magnetic resonance imaging (MRI). Patients with larger lesions involving other thalamic territories, previous stroke, or preexisting neuropsychologic impairments were excluded. Magnetic resonance imaging evidence of white matter disease, cerebral atrophy, and ventricular enlargement, as well as the absence of MRI testing, were also exclusion factors. In the 9 patients included in this study, infarcts concerned either the thalamogeniculate or the anterior-most part of the lateroposterior choroidal arteries (patients 2, 4, 8, and 9) (**Figure**). Intracranial and extracranial echotomography or MR angiography showed no significant additional vertebral or posterior cerebral stenosis. All patients had at least a 5-mm thick sagittal T1-weighted MRI (repetition time [TR], 510 milliseconds; echo time [TE], 12 milliseconds; number of excitations [NEX], 1; field of view [FOV], 230 × 230; matrix, 192 × 256; 30% gap) and a transverse 5-mm thick fast spin-echo T2-weighted MRI (TR, 3800 milliseconds; TE, 90 milliseconds; NEX, 2; FOV, 173 × 230; matrix, 190 × 256; 30% gap). Six patients had a T1-weighted MRI after gadolinium injection (TR, 510 milliseconds; TE, 12 milliseconds; NEX, 1; FOV, 173 × 230; matrix, 190 × 256; 5-mm thick; 30% gap). The neuroradiologic evaluation was undertaken 12 ± 8 days (mean ± SD) after the stroke (**Table**).

After a neurologic control (3-6 months after discharge) to exclude any new neurologic event, the patients underwent a 90-minute neuropsychologic examination (NPE). This NPE sought to verify the presence of possible instrumental symptoms (language, praxis, or gnosis impairments) as seen after larger thalamic infarcts and to evaluate learning abilities and executive functions, which are affected by anterior thalamic lesions.⁵ To assess language difficulties, a French version of the Boston Naming test¹¹ and a written text comprehension task of the MT86¹² were used. Ideomotor (5 gestures) and constructive praxis (2- or 3-dimensional drawing) were evaluated clinically. Visual and spatial gnosis were evaluated using the Poppelreuter overlapping figures,¹¹ the Hooper visual organization test,¹¹ the line bisection test,¹¹ and the clinical search of visual extinction. Cortical tactile functions were not studied, owing to sensory deficits. Verbal and visual short-term memory have been assessed by the Hebb digit span and the Corsi blocks test, respectively.¹¹ Learning abilities and long-term memory have been assessed using a standard list of verbal or spatial stimuli (Rey auditory-verbal and figural learning tasks using 15 or 10 items depending on age¹³). Two aspects of executive functions were also investigated: planning and research strategies were assessed through verbal (category and letter fluency) and figural fluency tasks,¹¹ and selective attention and inhibition abilities through a Stroop-like naming task.

For both clinically evaluated (necessitating a clinical judgment, ie, ideomotor and constructive praxis, visual extinction, line bisection, and overlapping figures) and standardized tests, only those indicating impairment in patients are presented in the Table. In patients with a major poststroke depression (as assessed by the Hospital Anxiety and Depression scale¹⁴), NPE was undertaken after antidepressive therapy.

Patients' performances were transformed into z scores (number of SDs characterizing a patient's performance in comparison with the mean performance of a matched control group). To improve the evaluation specificity, only z scores corresponding at least to 2 SDs below the mean were considered pathological.

RESULTS

All patients (9 right-handed; age, mean ± SD, 56 ± 15 years) had a pure hemisensory loss due to an isolated lateral thalamic infarct (5 right and 4 left lesions) (Table and Figure).

Among these patients, 5 also had transient hemiataxia.⁸ The NPE was performed 6.7 ± 3 (mean ± SD) months after the stroke. Six patients (66%) showed cognitive impairment affecting at least 1 cognitive domain (Table), without side (2/4 left and 4/5 right lesions) predominance.

No relationship was observed between the presence of neuropsychologic impairment and age (age, mean ± SD, 58 ± 7 years for abnormal and 53 ± 27 years for normal NPE; *P* = .72) or the delay to NPE (7.8 ± 3.6 months for abnormal and 4.3 ± 1.5 months for normal NPE; *P* = .16). Neither affective changes nor the presence of transient hemiataxia were associated with cognitive dysfunction.

In the cognitively impaired patients, there were signs of both subcortical and temporoparietal dysfunction. Almost every impaired patient had some executive or memory dysfunction. Concerning memory, either learning only or learning and delayed recall (but not recognition) was affected in 3 (1 left and 2 right lesions). Visuospatial memory was deficient in 2 patients with right stroke while verbal learning impairment was found after 1 left lesion. These deficits were moderate or severe in the specific tests. None of the patients had a clinically significant amnesic syndrome.

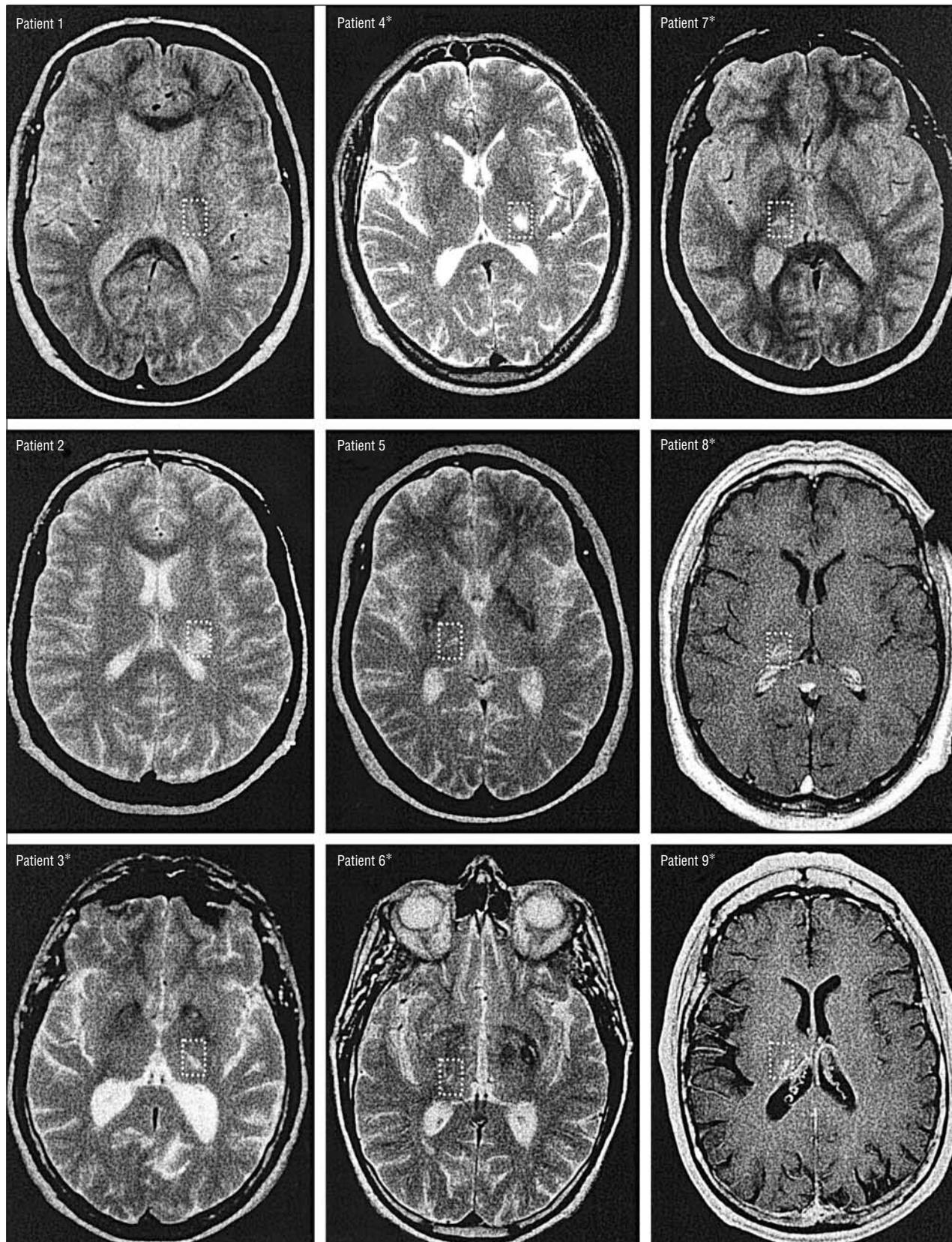
Considering executive dysfunctions, difficulties affecting verbal fluency (category or letter) (Table), figural fluency, or Stroop-like tasks were found in 5 patients. Results analysis suggested that executive dysfunction may depend on the lesion side since 4 of 5 patients had right infarcts. Among these 4 patients, 2 had coexisting visuospatial learning and memory impairment. Difficulties in digit span were present with other impairments in only 1 patient (9).

Finally, 2 patients (4 and 8) had temporoparietal signs in relationship with their lesion side, since naming impairment and difficulties in the Poppelreuter figure (testing visual agnosia) were found in 1 left (patient 4) and 1 right stroke (patient 8), respectively. No patient showed impaired spatial span, language comprehension difficulties, constructional apraxia, or spatial neglect.

The MRIs (Figure) suggest the implication of different nuclei within the lateral thalamic nuclei, particularly the lateroposterior and the ventroposterolateral nuclei, but also, to some extent, the ventrolateral nucleus. Although no formal lesion volume could be calculated from the 5-mm slices used in our clinical practice, this factor did not appear to predict the importance of the deficits. Patients 2 and 4 (Figure), who showed the largest lesions, were not more severely affected than the other patients, as evidenced by the NPE.

COMMENT

We systematically evaluated long-term cognitive dysfunction after lateral thalamic stroke, and observed a high prevalence of cognitive impairment (66% of patients) affecting at least 1 cognitive domain. This relatively high incidence of cognitive impairment cannot be attributed to a statistical bias induced by the number of tests used, since marginal deficits (see "Methods" section) were not considered. It also cannot be attributed to possible pre-



Magnetic resonance images of lateral thalamic infarcts in the 9 patients (4 with left and 5 with right lesions). T2-weighted axial slices are shown for 7 patients and T1-weighted images (for best demonstration of the lesions) for 2 patients. The asterisks indicate cognitively impaired patients.

Neuropsychologic Data on 9 Patients With Thalamic Infarcts

| Patient/Age, y/Sex | Side | DNRE, d | Ataxia | HAD | NPE | DNPE, mo | BN | POP | DS | VL | VSL | VF | FF | STR |
|--------------------|------|---------|--------|------------|----------|----------|-----|------------|-----|-----|-----|-----|-----|-----|
| 1/73/M | L | 23 | - | ... | Normal | 3 | ... | ... | ... | ... | ... | ... | ... | ... |
| 2/22/M | L | 6 | - | ... | Normal | 6 | ... | ... | ... | ... | ... | ... | ... | ... |
| 3/53/M | L | 2 | + | Anxiety | Abnormal | 4 | ... | ... | ... | -2 | ... | ... | ... | ... |
| 4/50/M | L | 18 | + | Depression | Abnormal | 6 | -2 | ... | ... | ... | ... | ... | -2 | ... |
| 5/65/W | R | 23 | + | Depression | Normal | 4 | ... | ... | ... | ... | ... | ... | ... | ... |
| 6/59/M | R | 9 | - | ... | Abnormal | 4 | ... | ... | ... | ... | ... | ... | -3 | -2 |
| 7/52/M | R | 7 | + | ... | Abnormal | 14 | ... | ... | ... | ... | ... | -2 | ... | ... |
| 8/63/M | R | 15 | + | ... | Abnormal | 10 | ... | Pathologic | ... | ... | -2 | -2 | -3 | ... |
| 9/68/W | R | 9 | - | ... | Abnormal | 6 | ... | ... | -2 | ... | -3 | -3 | ... | -3 |

Abbreviations: BN, Boston Naming; DNPE, delay between stroke and neuropsychologic evaluation; DNRE, delay between stroke and neuroradiologic evaluation; DS, Digit Span; ellipses, not applicable; FF, figural fluency; POP, Poppelreuter; STR, Stroop-like task; VF, verbal fluency; VL, verbal learning; VSL, visuospatial learning.

stroke mild cognitive impairments¹⁵ or poststroke affective changes. First, all patients with previously documented (clinically or radiologically) stroke or neuropsychologic impairment were not included. Second, MRI showed no radiologic signs of vascular disease. Third, the prevalence (~3%) of mild cognitive impairment in the general population¹⁵ is low. Finally, the depressive symptoms revealed in 2 patients did not correlate with cognitive dysfunction.

The pattern of deficits was variable among patients. This variability could be due either to interindividual differences in lesion localization, cortical diaschisis induced by thalamic lesions,⁹ or to different degrees of functional reorganization. That the thalamic syndrome was rather homogenous and that there was some variability in the delay between stroke and NPE would favor, at least partly, the last explanation. The most dominant neuropsychologic deficits concerned executive functions. To a lesser extent, cognitive impairments concerned effortful learning abilities and long-term memory. Finally, although minor and not reported spontaneously, some instrumental (aphasic and agnosic) signs were observed in 2 patients in relationship with the lesion side. Perceptual agnosic signs, as seen after right-sided brain damage,¹⁶ were found in 1 right thalamic lesion (patient 8). Naming impairment, involving left thalamotemporoparietal circuits,¹⁷ were found in 1 patient (4) with a left-sided lesion. Difficulties in tasks testing visuospatial and verbal long-term memory were found in 3 patients and were also related to the lesion side. This impairment was not due to improper encoding, as recognition was flawless, but rather to learning and recall strategies, as found in frontosubcortical loop dysfunction or in left and right temporal lobe epilepsy.¹⁸

Concerning executive dysfunction, particularly impairment in verbal and figural fluency, the results do not fit with the verbal/nonverbal dichotomy initially proposed for left/right frontal lesions¹⁹ or with the accepted role of left frontal structures in verbal fluency performances.²⁰ Unexpectedly, we found that 4 of 5 patients who showed executive impairments that included verbal fluency had a right thalamic infarct. The coexistence of impaired verbal fluency with other dysexecutive signs, but independently of other aphasic deficits, supports the nonlinguistic nature of these troubles. Other nonlinguis-

tic processes, particularly, attention, planning, and searching strategies, are thought to be involved in verbal fluency.¹¹ Impaired verbal fluency has been described in anterior right thalamic lesions.²¹ Lateral thalamic lesions alter attentional processing, such as orienting responses in animals.²² Whether such processes rely on the projections from the right thalamus to the right frontal cortex necessitates further investigation with a larger number of patients. Alternatively, one can propose that these deficits result from the interruption, although minor, of the crossed right thalamic-left frontal projections.²³

Our findings support the hypothesis of a relationship between the lateral thalamus, particularly the right side, and frontosubcortical loops. The preferential alteration of executive function by strokes on the right side must be considered cautiously because of the small number of patients, but is noteworthy given the role of the right hemisphere in some aspects of executive function, such as selective attention. Clinical and stimulation studies suggest that the lateral thalamus is not only involved in sensory processing (ventroposterolateral nucleus) but also in cerebellum-induced motor adaptation (ventrolateral nucleus),²⁴ cognitive and motor aspects of language production,²⁵ arousal, and attention.²⁶ Studies in monkeys indicate that the dorsal globus pallidus and cerebellar ventral dentatus nucleus project to frontocortical areas via the caudolateral thalamus.²⁷ It is also known that cerebellar lesions may impair executive functions.²⁸ In light of all of this evidence, it can be hypothesized that at least some of the observed cognitive impairments are attributable to the damage of the cerebellothalamic pathways. The involvement of subthalamic pathways, as a part of the midbrain reticular ascending system, also cannot be excluded.²⁹

The limitations of our anatomical analysis do not allow us to establish unequivocally whether the lesion of one or another lateral thalamic nucleus is more involved in these deficits. That transient ataxia indicates that the lesions were small and confined to lateral thalamic areas. The deficits in the instrumental domain, shown in some patients, also indicate that the lateral thalamus subdivisions may differently contribute to cognitive functions. Further studies, including a larger sample of patients and using accurate MRI analysis of lesion volume and extension within the lateral thalamus subdivi-

sions and metabolic imaging or diffuse tensor tractography, might also help to elucidate the role that lateral thalamic nuclei play in human cognition.

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