

CME

The thalamus and behavior

Effects of anatomically distinct strokes

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Abstract—Data on behavioral changes after thalamic lesion are sparse and largely based on isolated reports of patients with thalamic strokes. However, recent findings suggest that behavioral patterns can be delineated on the basis of the four main arterial thalamic territories. The anterior pattern consists mainly of perseverations and superimposition of unrelated information, apathy, and amnesia. After paramedian infarct, the most frequent features are disinhibition syndromes, with personality changes, loss of self-activation, amnesia, and, in the case of extensive lesions, thalamic “dementia”; this pattern may often be difficult to distinguish from primary psychiatric disorders, especially when neurologic dysfunction is lacking. After inferolateral lesion, executive dysfunction may develop but is often overlooked, although it may occasionally lead to severe long-term disability. After posterior lesion, whereas cognitive dysfunction with neglect and aphasia are well known, no specific behavioral syndrome has been reported. In the future, perfusion CT, functional MRI, and tractography using diffusion imaging in stroke patients may provide a better understanding of the role of the corticothalamic relationship in behavioral changes associated with thalamic stroke.

NEUROLOGY 2006;66:1817–1823

The first clinicopathologic study of thalamic stroke was published in 1906 by Dejerine and Roussy,¹ who emphasized sensorimotor disturbances. Twenty years later, cognitive deficits after isolated thalamic lesions were described by Hillemand² and Lhermitte,³ with “atypical” aphasia in patients with left lesions. Since then, although aphasia, agnosia, amnesia, and neglect have frequently been reported after thalamic strokes,^{4,6} behavioral changes have been rarely described. More recently, major advances in the understanding of the thalamus and behavior after stroke have been made due to the development of morphologic and functional imaging.

Methods. For the purpose of this review, we selected the patients reported in the literature with an adequate description of behavior secondary to radiologic-proven thalamic lesions. Although MRI is currently the best radiologic technique for stroke localization, patients with only a CT scan were also included because of the limited number of patients described with behavioral changes after thalamic lesion. We then grouped the patients according to the main vascular territories involved^{7–10} as defined by pathologic data (figure 1): 1) the anterior, tuberothalamic, or polar territory, supplied by the tuberothalamic or polar artery, which originates from the posterior communicating artery, or, in one-third of patients, by the paramedian or thalamoperforating arteries; 2) the paramedian territory, supplied by the thalamoperforating arteries, which originate from the first part of the posterior cerebral artery (P1); 3) the inferolateral or thalamogeniculate territory, supplied by the thalamogeniculate arteries, which originate from the second part of the posterior cerebral artery (P2); and 4) the

posterior territory, supplied by the medial and lateral branches of the posterior choroidal artery, which originates from P2.

Anterior territory infarction. Infarcts in the anterior thalamic territory account for about 12% of all thalamic infarcts (figure 2).⁶ Because these involve the anterior nuclei, which receive projections from the mamillothalamic tract (MTT) and are connected to the anterior limbic system (including the cingulate gyrus, hippocampus, parahippocampal formation, and orbitofrontal cortex) and to the medial and prefrontal cortex,^{11,12} most patients with anterior infarcts show a unique behavioral pattern, including superposition of unrelated information and perseverations (“anterior behavioral syndrome”), apathy, and amnesia.

According to the largest case series on anterior strokes,¹³ which included 12 patients and was based on CT and MRI, one of the more characteristic behavioral changes after anterior infarcts is the superposition of unrelated information, which has been named “palipsychism” from the Greek “palin” (again) and “psyche” (soul),¹³ with parallel expression of mental activities, irrespective of sequential order. The disorganization of output speech, with grammatically correct phrases, is usually characterized by intrusions of themes previously discussed with the medical staff or patient’s relatives unrelated to the

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Disclosure: The authors report no conflicts of interest.

Received August 24, 2005. Accepted in final form March 1, 2006.

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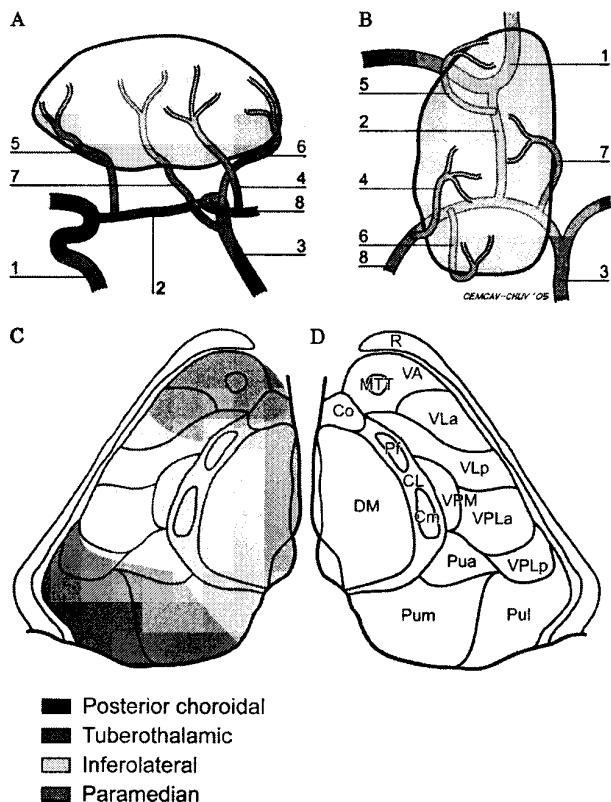


Figure 1. Schematic view of the arterial supply to the thalamus. (A) Lateral view; (B) view from above; (C, D) detailed relationship between the arterial territories and nuclear subgroups within the thalamus. 1 = carotid artery; 2 = posterior communicating artery; 3 = basilar artery; 4 = thalamogeniculate arteries; 5 = tuberothalamic artery; 6 = posterior choroidal artery; 7 = paramedian pedicle; 8 = posterior cerebral artery. Main thalamic nuclei and tracts: CL = central lateral; CM = centromedian; Co = commissural; Cp = commissural posterior; DM = dorsomedian; MTT = mamillothalamic tract; Pua = pulvinar anterior; Pum = pulvinar medial; Pul = pulvinar lateral; Pf = parafascicularis; R = reticular; VA = ventral anterior; VLa = ventral lateral anterior; VLp = ventral lateral posterior; VPLa = ventroposterolateral anterior; VPLp = ventroposterolateral posterior; VPM = ventroposteromedian.

current topic. This pattern was found in one of our patients with an MRI-proven right anterior infarct who correctly solved a calculation problem and simultaneously talked about his garden or explained the sequences of a journey while talking about family problems. In another patient with a left anterior infarct (figure 2), intrusions of previous topics and distorted memories were particularly noteworthy, in addition to short-term amnesia, ideomotor apraxia, and executive dysfunction. The pattern of "palipsychism" seems to be predominant in unconstrained speech, for example, in comments on news or historical facts and in the definition of words, contrasting with a relative preservation in performing automatic

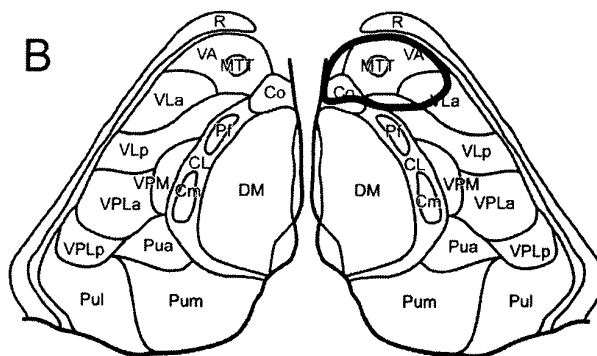


Figure 2. (A) Diffusion-weighted MRI of a left anterior thalamic infarct involving the anterior nuclei and mamillothalamic tract in a 58-year-old patient who presented with perseverations, incoherent speech with intrusion of previous topics, and distorted memories. (B) Schematic representation (see figure 1 for legend).

series. Frequently associated with perseverations in thought and output speech, "palipsychism" is reminiscent of "confusion of ideas" and should not be confused with aphasia or confusional state due to other causes.¹⁴

Anterograde amnesia, with better performance for recognition, is a constant finding and may persist several years after stroke. In some cases, visuospatial impairment is prominent after right lesions¹⁵ and verbal impairment after left lesions.¹⁶ After a left infarct, thalamofrontal disconnection was responsible for a distinctive mnemonic pattern, with disorganization of autobiographic recollection and newly

acquired information.¹⁶ Anatomic studies suggest that the amnesia results from interruption of the MTT and its projections to the cingulate gyrus, hippocampus, and orbitofrontal and prefrontal cortex.¹⁷ In patients with anterior infarcts,¹³ interruption of frontal projections may also explain the fantastic and bizarre confabulations, which are similar to those found after medial frontal lobe lesion.¹⁸ Aphasia is rare and usually consistent with transcortical motor aphasia. Spontaneous speech is reduced, with lack of speech initiation, hypophonia, and dysarthria.^{13,19} Poetic, fantastic, or extravagant paraphasias and neologisms may also be found. Visual neglect, topographic disorientation (after right¹⁹ or left or bilateral¹³ lesions), and constructional apraxia (after left lesion)¹⁹ are more rare.

Paramedian territory infarction. Infarcts in the paramedian territory account for about 35% of all thalamic infarcts⁶ and involve mainly the dorsomedian and intralaminar nuclei (figures 3 and 4). The dorsomedian nucleus, divided into the anteromedial magnocellular nucleus, and posterolateral parvocellular nucleus, receives projections from the amygdala and has connections to the prefrontal cortex and ventral pallidum.²⁰ The intralaminar nuclei, including the centromedian, parafascicular nuclei, central medial, paracentral, and central lateral nuclei, project to the orbitofrontal and mediofrontal cortex, the motor and premotor cortex, and the internal globus pallidus.²¹ The classic features of acute paramedian infarcts include a decreased level of consciousness, vertical gaze paresis, and cognitive impairment.^{6,22,23} The behavioral changes become apparent when the decreased level of consciousness resolves. They consist mainly of personality changes with disinhibited behavior associated with apathy, loss of self-activation, and amnesia.

After paramedian strokes, several distinct personality changes with disinhibition syndromes, resulting from thalamofrontal disconnection, have been reported. These patterns may be difficult to distinguish from psychiatric pathologies. Cyclical psychosis and manic delirium, classically found in schizophrenic patients, have been reported in detail in two patients with paramedian strokes. The first patient showed episodes of delirium, joking, and improper comments with fantastic stories²⁴ interrupted by intervals of severe apathy. This fluctuation between periods of hyperactivity and periods of lack of spontaneity was also seen in another patient²⁵ described as a "zombie," sleeping and eating excessively, who, every 3 months, became, for a period of about 36 hours, frankly manic, cried, and had a labile affect, with "fuite des idées." In the first patient, the CT scan showed a right paramedian stroke, but MRI was not performed. In the second patient, MRI revealed bilateral paramedian stroke involving mainly the dorsomedian nucleus. Thus, it is not established whether a unilateral lesion is sufficient to induce cyclical psychosis and mania. In several psy-

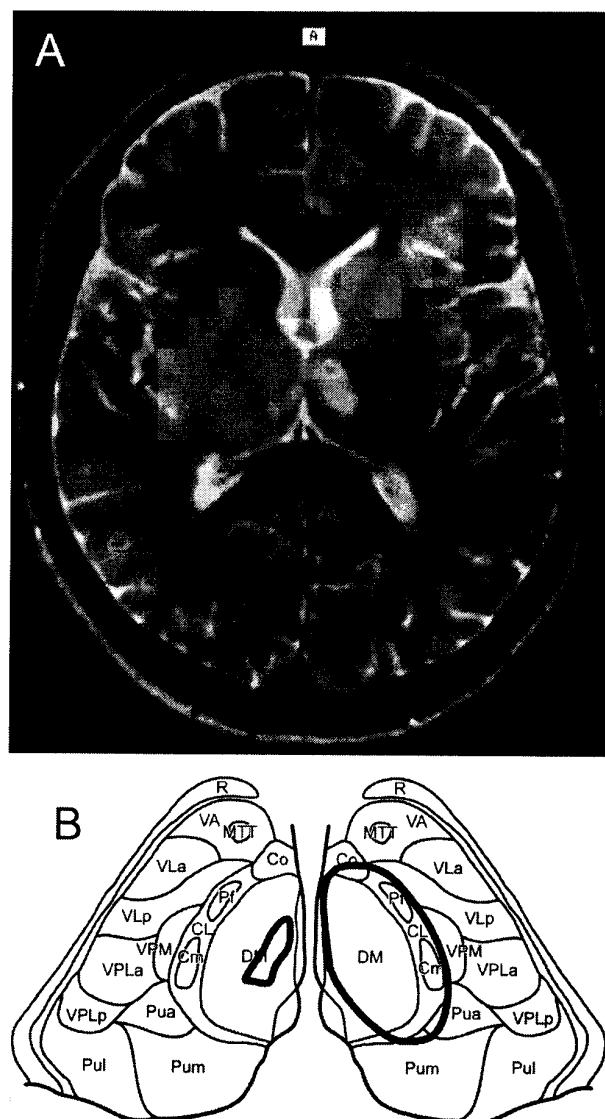


Figure 3. (A) T2-weighted MRI showing a bilateral paramedian stroke predominantly on the left side in a 39-year-old woman. This patient presented with improper behavior and inadequate and disinhibited comments to her husband. Three hours later, she complained she was "not able to control her eyes," then rapidly became comatose. Cognitive tests, performed 3 days later, showed persistent loss of self-activation and severe amnesia. (B) Schematic representation (see figure 1 for legend).

chiatric studies, the role of the dorsomedian nucleus in schizophrenia has been emphasized, with anatomic²⁶ and radiologic²⁷ data showing a reduction in dorsomedial volume and functional imaging²⁸ revealing thalamofrontotemporal cortex disconnection on PET studies in schizophrenic patients. Additionally, frontal-like syndromes secondary to thalamofrontal disconnection have been described in several patients with paramedian strokes. Utilization behavior, with excessive use of objects and inability to

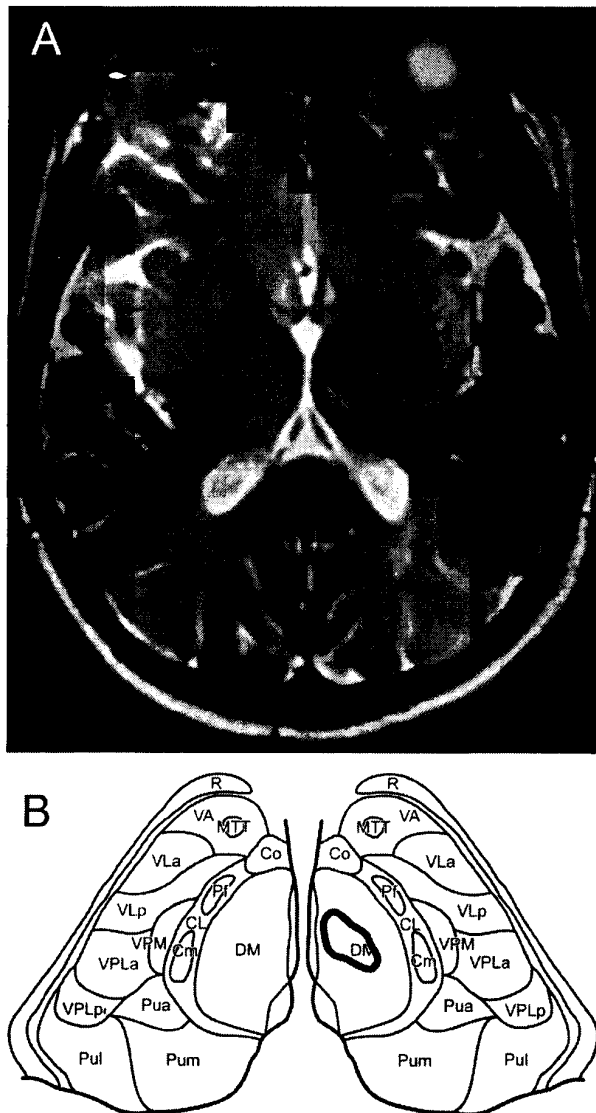


Figure 4. (A) T2-weighted MRI of a unilateral left paramedian infarct in a 54-year-old man who, during coronary angiography, presented sudden vertical diplopia and transient hypersomnolence. Cognitive tests, performed 2 days later, were entirely normal except for loss of self-activation. (B) Schematic representation (see figure 1 for legend).

regulate the interaction with the environment, was extensively described in two patients with right or bilateral thalamic intralaminar and dorsomedial nuclei infarcts.²⁹ The hypothesis of a thalamocortical disconnection was supported by SPECT studies revealing hypoperfusion of the right cerebral cortex, with some predominance of the frontal area. Another young patient with bilateral dorsomedial nuclei and intralaminar nuclei infarction on MRI showed characteristics of utilization behavior when she started to eat and smoke compulsively and only stopped when food or cigarettes were out of sight.³⁰ Disinhibition

behavior was also diagnosed, with inappropriate jokes and lack of shame. She was highly distractible and reacted to every auditory, visual, and tactile cue. Interestingly, disconnection of the temporal lobes, in addition to the frontal lobes, was revealed by PET studies, suggesting that frontal-like syndromes after paramedian infarcts may result from disconnection of a wider cortical area than the frontal lobe. This spectacular behavior may persist several months after stroke.³¹

After unilateral, but especially after bilateral, infarcts, patients may become severely apathetic and asponaneous, as if they have lost motor and affective drive. Two patients with bilateral lesions of the dorsomedial and intralaminar nuclei, assessed by CT scan in one patient³² and by MRI in the other,³³ have been described in detail. Both showed no concern for their relatives and their illness and required constant external programming, appearing like robots. The term of "loss of psychic self-activation" has been proposed.³⁴ The intralaminar nuclei, especially the centromedian and parafascicular nuclei,²¹ seem to play an important role in arousal and motivation, with involvement of the striatal-ventral pallidal-frontomesial "motivational" and "limbic" loop and interruption of the posterior orbital and mesial frontal cortex projections, which project to the anterior cingulate gyrus and back to the striatum. A SPECT study highlighted the impact of paramedian structures on the frontomesial cortex.³³ In patients with extensive involvement of the centromedian and parafascicular nuclei who appear awake, fail to respond, and become active after relevant stimuli, akinetic mutism should be suspected and may represent a severe form of loss of psychic self-activation.

Amnesia is a frequent sign after paramedian infarcts. The role of the intralaminar and dorsomedial nuclei is debated. Patients with a lesion restricted to the intralaminar nuclei present with discrete amnesia, but severe distractibility,³⁵ which suggests that the intralaminar nuclei are probably not memory structures per se, but part of a functional system regulating attention for simultaneous activities. The role of the dorsomedial nucleus is more controversial.³⁶ Patients with lesions limited to the dorsomedial nucleus present with less severe amnesia than those with an anterior lesion.¹⁰ The dorsomedial nucleus is involved in executive processes and in processing the contents of the stimuli for storage and recall, whereas the anterior nuclei influence the selection of material to be stored and remembered.³⁷ More anecdotal is the description of transient global amnesia after left paramedian infarcts, with repetitive queries and temporary inability to form new memories.³⁸ Anatomic studies suggest that the anterior nuclei have numerous connections to the hippocampal formation, whereas the dorsomedial nucleus has more connections to the amygdala (amygdalofugal tract).^{39,40} Differential involvement of these two limbic circuits may explain the differences in amnesia after MTT or anterior nuclei lesions or after

dorsomedian lesions. Damage to both circuits may result in the most severe amnesia. Aphasia after paramedian infarcts, with reduced fluency sparing comprehension and repetition, is suggestive of transcortical motor aphasia. Exceptionally, with extensive left lesions, comprehension and repetition are impaired.⁴¹ Hypophonia associated with loss of initiative may be found, as well as semantic and phonologic paraphasias.⁴² Dysarthria is particularly severe after bilateral lesions.⁴³ Vascular dementia usually results from multiple lesions of the white matter.⁴⁴ Dementia due to a single lesion is rare but can occur after thalamic lesion, especially in the case of bilateral paramedian or anterior lesions. The diagnosis of dementia is made when impaired attention, apathy, and poor motivation have resolved. Subacute and progressive thalamic dementia⁴⁵ may also occur after venous thrombosis (figure 5). Total recovery after bilateral paramedian infarct is rare. The evolution is, in most cases, "neither severe nor good."²³

Inferolateral territory infarction. Infarcts in the inferolateral territory account for about 45% of all thalamic infarcts (figure 6).⁶ This territory includes the ventrolateral nucleus, ventroposterior nuclei (ventroposterolateral, ventroposteroinferior, and ventroposteromedian nuclei), and ventromedian nucleus. The ventrolateral nucleus has connections to the cerebellum and the motor and prefrontal cortex.⁴⁶ The ventroposterolateral nucleus receives inputs from the medial lemniscal and spinothalamic pathways, whereas the ventroposteromedial nucleus receives inputs from the trigeminothalamic pathway. The most common clinical pattern after inferolateral infarct is ataxia and hypesthesia.⁶ However, behavioral changes such as executive dysfunction and cognitive signs such as aphasia are often undiagnosed.

Executive functions relate to the planning, initiation, and regulation of goal-directed behavior,⁴⁷ and their dysfunction can lead to long-term disability. In contrast to amnesia, they are not restricted to a specific thalamic structure, as tests used to assess executive functions draw on several functions such as working memory and attentive processes.⁴⁸ Executive dysfunction and affective changes were described in six of nine patients with inferolateral lesions (all confirmed by MRI) with impairment of verbal and figural fluencies and performances in Stroop-like tasks.⁴⁹ These behavioral changes showed similarities with those found after cerebellar lesions,⁵⁰ emphasizing the impact of the lateral thalamus on cerebellofrontal connections. Aphasia is rarely reported after vascular lesion of the lateral nuclei,⁵¹ which is surprising given their numerous projections to the temporal and parietal lobes.⁵² However, in a recent study,¹⁰ mild transcortical motor aphasia with reduced fluency was found in almost one-third of patients. Ideomotor apraxia was demonstrated in a patient with a right lesion when he was asked to do common tasks such as brushing his teeth or using a screwdriver.⁵³ Another patient

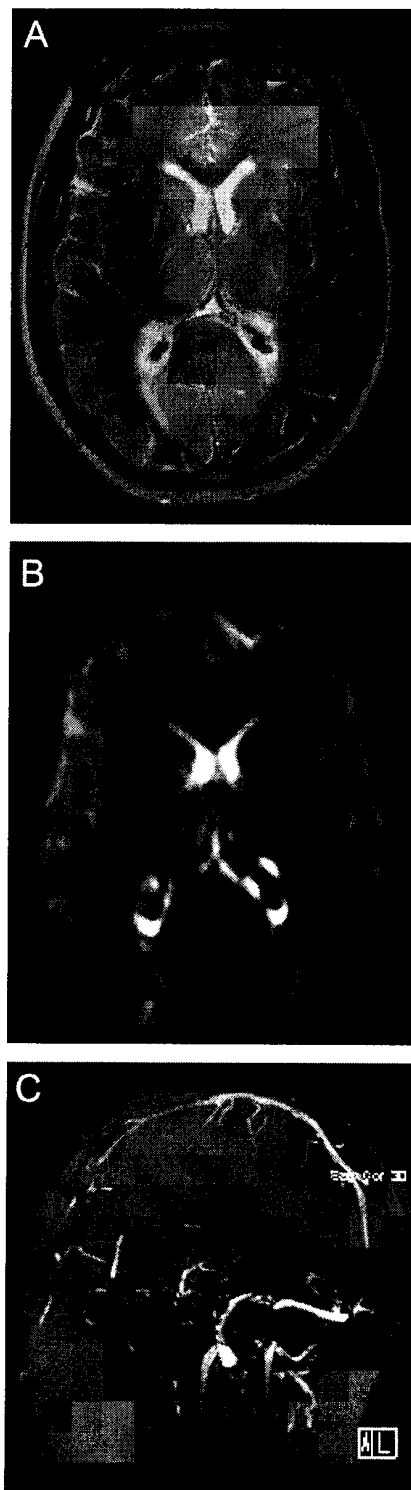


Figure 5. (A) T2-weighted and (B) diffusion-weighted MRI, showing bilateral venous infarct predominantly on the right side in a 18-year-old woman who, 3 days after unusual headaches, presented a decreased level of consciousness. Cognitive tests showed a lack of self-activation, severe attentional deficits, anosognosia, severe verbal and visuospatial amnesia, and a diminished capacity for abstraction and problem solving. (C) Venous angio-MRI showed absence of the sinus rectus and deep cerebral veins.

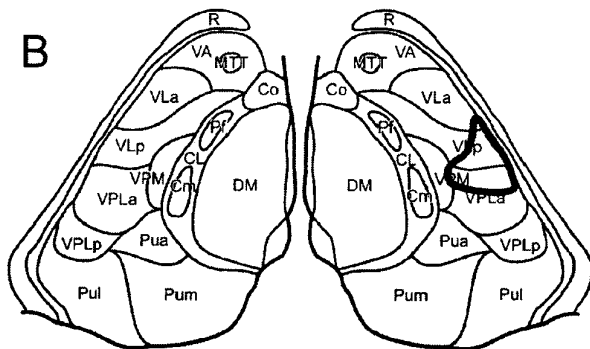
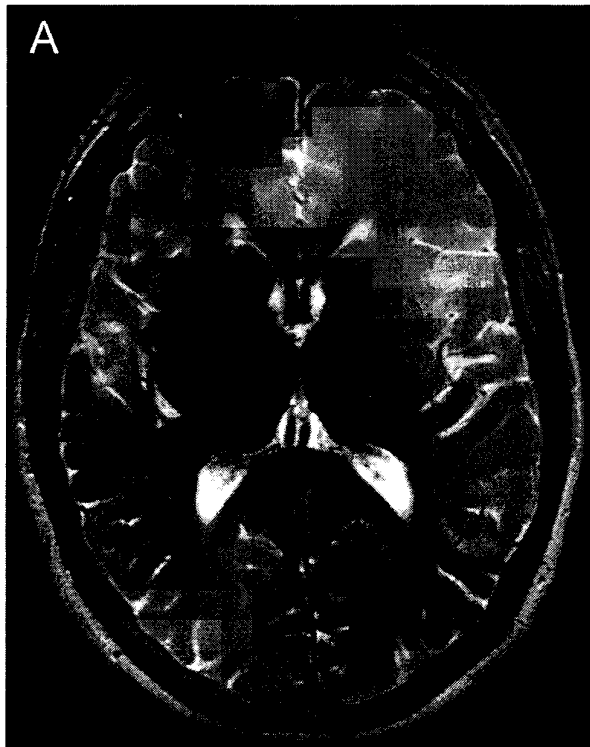


Figure 6. (A) T2-weighted MRI of a left inferolateral thalamic infarct in the territory of the thalamogeniculate arteries in a 58-year-old man showing executive dysfunction with verbal fluency difficulties, pathologic response inhibition, and pathologic conceptual ability, in addition to a right sensory and ataxic hemisindrome. (B) Schematic representation (see figure 1 for legend).

was unable to use a toothbrush either in pantomime or when given the object itself.⁵⁴

Posterior territory infarction. Infarcts in the posterior territory account for 8% of all thalamic strokes.⁶ The pulvinar is the main component of the posterior nuclei and can be divided into three main parts,⁵ the medial pulvinar, with projections to the parieto-occipital cortex,⁵⁵ prefrontal cortex, cingulum, and parahippocampal cortex,⁵⁶ and the inferior and the lateral pulvinar, with connections to the occipital, parietal, and temporal lobes.⁵⁷ The most fre-

quent signs are hypoesthesia and homonymous horizontal sectoranopsia (involvement of the lateral geniculate body).

No specific behavioral syndrome seems to result from a posterior lesion. However, neuropsychological signs have been described in some cases. Spatial neglect is mainly found after a medial pulvinar lesion resulting from thalamotemporal interruption rather than thalamoparietal interruption.⁵⁸ Aphasia is rarely reported, probably because of compensatory mechanisms.

Limitations. There are several limitations that prevent a definitive conclusion from being drawn about the specificity of the different behavioral patterns according to the four main territories. This review is based on a limited number of case reports or small series using different neuroradiologic techniques. Postmortem anatomic descriptions are, unfortunately, rare, as thalamic infarcts are rarely life threatening. Additionally, infarcts in variant territories, resulting from borderzone ischemia or arterial variation, may occur, and several different subcortical-cortical loops may therefore be involved simultaneously. In terms of the clinical description of the different case reports, the patient's prestroke emotional status is rarely reported, although it may change the behavioral pattern after stroke.

Conclusions. After thalamic strokes, behavioral manifestations are multiple, and virtually all "cortical" syndromes may be mimicked by thalamic strokes, which reflect the role of the "little brain" of the thalamus in behavior and cognition. Behavioral syndromes with personality changes, associated with anterior and paramedian lesions, may often be difficult to distinguish from primary psychiatric disorders, especially when neurologic dysfunction is lacking. Further description of abnormal behavior after thalamic infarcts, for example, may provide a better understanding of the mechanisms of schizophrenia. New imaging techniques, such as perfusion CT and high-resolution MRI, will help in understanding the impact of thalamic lesion on the cortex. In addition, tractography, together with the more frequent use of functional imaging such as SPECT or PET, may provide important information on connections between the thalamus and cortex^{59,60} and help determine the role of the different thalamic nuclei in behavior. However, these new techniques will be useless without the close attention of the clinician to the often tenuous changes in behavior in patients with suspected stroke.

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