ORIGINAL ARTICLE

The Clinical and Cognitive Spectrum of Artery of Percheron Infarction: 1-Year Follow-Up

Fatma Ece Çetin, Emre Kumral, Birgül Dere

ABSTRACT: ***Objective:*** Survivors of patients with artery of Percheron infarction (API) often have a prolonged and disabling form of cognitive impairment that remains insufficiently characterized. We aimed to examine the clinical and cognitive features of API in the short and long term after stroke. ***Methods:*** We reviewed 6400 patients with a first-ever stroke included in the Stroke Registry between 2011 and 2021. The diagnosis of API was based on clinical diagnosis and imaging confirmation. All patients underwent neuropsychological assessment at hospital stay and 1 year after stroke. A *z*-score of each patients' cognitive test point was calculated, and a *z*-score inferior to 2 was considered as pathological. ***Results:*** Of the 10 patients enrolled, all had cognitive impairment, consciousness, and behavioral disorders at stroke onset. Six patients had pure bilateral thalamic involvement while four had bilateral thalamic and rostral midbrain involvement. At 12 months, 50% of patients had global mental state scores 2 SD below the population mean (*z*-score mean ± SD, -2.17 ± 0.4). Most of the prefrontal cortex cognitive processes including executive functions such as planning and cognitive control (*z*-score mean ± SD, -3.92 ± 0.3), processing speed (-4.42 ± 0.5), working memory (-3.97 ± 0.3) were severely impaired at stroke onset. Especially in patients with thalamic and rostral midbrain involvement, deficiencies in executive function (*z*-score mean ± SD, -2.60 ± 0.4), processing speed (-2.22 ± 0.5), working (-3.76 ± 0.4), and episodic memory (-2.23 ± 0.3) continued 12 months after stroke. ***Conclusions:*** The occlusion of the artery of Percheron results in severe behavioral and cognitive disorders in the short and long term after stroke.

RÉSUMÉ : Spectre clinique et cognitif des infarctus de l'artère de Percheron : un suivi au bout d'un an. ***Objectif*** **:** Les survivants de patients atteints d'infarctus de l'artère de Percheron présentent souvent une forme prolongée et invalidante de déficience cognitive qui reste insuffisamment caractérisée. Notre objectif était d'examiner les caractéristiques cliniques et cognitives de l'API à court et à long terme après un AVC. ***Méthodes*** **:** Nous avons examiné 6400 patients ayant subi un premier AVC inclus dans le registre des accidents vasculaires cérébraux entre 2011 et 2021. Le diagnostic d'API était basé sur un diagnostic clinique et une confirmation par imagerie. Tous les patients ont subi une évaluation neuropsychologique à l'hospitalisation et un an après l'AVC. Un z-score du point de test cognitif de chaque patient a été calculé, et un *z*-score inférieur à 2 a été considéré comme pathologique. ***Résultats*** **:** Sur les 10 patients inclus, tous présentaient des troubles cognitifs, de la conscience et du comportement au début de l'AVC. Six patients avaient une atteinte thalamique bilatérale pure tandis que 4 avaient une atteinte bilatérale thalamique et rostrale mésencéphalique. À 12 mois, 50% des patients avaient des scores globaux d'état mental 2 SD inférieurs à la moyenne de la population (*z*-score moyen ± SD, -2.17 ± 0.4). La plupart des processus cognitifs du cortex préfrontal, y compris les fonctions exécutives telles que la planification et le contrôle cognitif (z-score moyen+SD, -3.92 ± 0.3), la vitesse de traitement (-4.42 ± 0.5), la mémoire de travail (-3.97 ± 0.3) étaient gravement altérées au début de l'AVC. En particulier chez les patients présentant une atteinte du thalamique et rostral mésencéphalique, des déficiences de la fonction exécutive (*z*-score moyen ± SD, -2.60 ± 0.4), de la vitesse de traitement (-2.22 ± 0.5), du travail (-3.76 ± 0.4) et de la mémoire épisodique (-2.23 ± 0.3) s'est poursuivie 12 mois après l'AVC. ***Conclusions*** **:** L'occlusion de l'artère de Percheron entraîne des troubles comportementaux et cognitifs sévères à court et à long terme après un AVC.

Keywords: Thalamus, Rostral midbrain, MRI, Artery of Percheron

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Introduction

Thalamic infarcts are classically classified into anterior, paramedian, inferolateral, and posterior territories, which are supplied, respectively, by the polar, paramedian, thalamogeniculate, and posterior choroidal arteries.[1,2] Occlusion of the artery of Percheron may lead to infarction of the bilateral paramedian thalami and that may extend to the rostral midbrain (API) with a multitude of neurologic signs and symptoms.[3–5] Previous case reports have been reported in the literature showing the presence of mental state disorder, behavioral amnesic disorder, aphasia/dysarthria, ocular movement disorders, motor deficits, cerebellar symptoms, and others.[6–14] Mental disorders and cognitive deficits following the API have not been systematically well studied and do not have a long follow-up after stroke. The aim of the present

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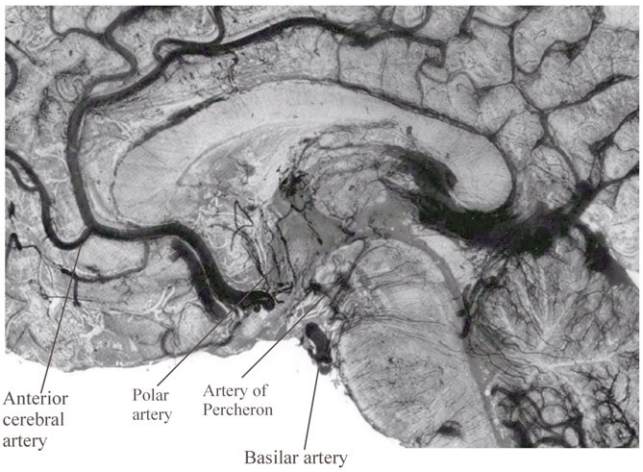

Figure 1: *Illustration of thalamic vascular complexity and artery of Percheron, as shown by injection of tracer substance into postmortem human blood vessels by Salamon.*[19]

study was to determine clinical, neuropsychological, and behavioral features of API by using MRI and neuropsychological assessment at hospital stay and at 12 months after stroke.

Subjects and Methods

Between 2011 and 2021, 6400 patients with ischemic stroke were admitted to the University Hospital Stroke Unit and were prospectively entered into the Stroke Registry.[15] A total of 152 patients with MRI-proven lesions restricted to the thalamus were identified. Among them, 132 patients had unilateral thalamic lesion and 39 had multiple lesions involving classical territories of the thalamus. Patients with old hemorrhagic lesions, old infarcts on imaging, or simultaneous acute unilateral or multiple lesions outside the thalamus were excluded from the study.

The initial MRI was performed in all cases within one week after stroke. Patient selection was based on the initial MRI performed during the first week. The infarction of artery of Percheron was characterized by bilateral lesions of the paramedian thalami with or without the rostral midbrain.[16,17] (Figure 1) All patients had a standardized evaluation for their symptoms, and there were no previously diagnosed conditions affecting their cognitive and behavioral functions. Prospectively recorded variables included age, gender, previous stroke, risk factors, blood pressure, clinical findings, etiological subtypes, pathogenesis, topography of lesions on DWI, and/or FLAIR MRI. Vascular and cardiac structures were examined by noninvasive modalities such as carotid-vertebral and transtracranial Doppler, magnetic resonance angiography, or CT angiography, 2D-echocardiography, and 24-h electrocardiography (Holter) monitoring. The cause of stroke was assessed according to the criteria described previously as large artery disease, small artery disease, cardioembolic, others, and unknown.[18] The study was approved by the ethics committee of the Ege University Medical Center review board, and a written informed consent was obtained from all participants or relatives.

Imaging Acquisition and Analysis

MRI was performed by 1.5 and 3 Tesla scanners (Siemens Sonata, Siemens Medical Solutions, Erlangen, Germany). MRI scanners consisted of axial T1-, T_2-weighted spin-echo, T_2 fluid-attenuated inversion recovery (FLAIR), and diffusion-weighted imaging (DWI). Two radiologists blinded to each other's decisions, visually identified and sequentially outlined lesion locations on DWI, FLAIR, and T_2-weighted images. Clinically relevant regions characterized by increased signal intensity in DWI and decreased intensity in apparent diffusion coefficient maps were considered as acute infarcts.

Neuropsychological Assessment

Neuropsychological assessment was performed 1 month (32 ± 7 days) and 12 months (350 ± 25 days) after stroke by two neuropsychologists with accreditation in neuropsychology, as part of the study protocol. Different aspects of cognitive functions have been assessed and classified into nine broad categories based on the similarity of the tasks; (1) global mental assessment was performed by Mini-Mental State Examination (MMSE; normal mean ± SD, 27 ± 3); (2) executive process was evaluated by the Trail Making Test-Part A (normal mean ± SD, 35.5 ± 10.5 s); (3) processing speed was assessed by the Stroop test (name color print of noncolor words (normal mean time ± SD, 16.10 ± 3.5 s); (4) working memory was assessed by digit span test which is a subtest of the Wechsler Memory Scales. Participants saw a sequence of numerical digits and are tasked to recall the sequence correctly (normal mean ± SD, 5.77 ± 1.1 (4–7); (5) eEpisodic memory was assessed by the Rey Auditory Verbal Learning Test (RAVLT), including measures of immediate free recall/new learning (List A Trials 1–3; normal mean ± SD, 6.3 ± 2.1); (6) semantic memory refers to the capacity for recollecting general knowledge and facts (ideas, meaning, and concepts) about the world. Controlled Oral Word Association test (normal mean ± SD of animals named, 18 ± 4.5) was used to measure the subject's capacity to generate words belonging to the category of animals; (7) delayed verbal memory was measured by delayed recall subtest of the RAVLT (normal mean ± SD, 10.2 ± 2.5); (8) visual memory and visuoconstructive abilities were assessed by Benton visual retention test. The examinee viewed form one set 10 designs for 10 s and immediately reproduced it from memory. Number correct score (i.e., the number of correctly reproduced designs) was taken into consideration (normal mean ± SD, $5.04.2 \pm 2.02$). Motor neglect, visuospatial neglect, and visual extinction were also assessed; (9) language skills such as verbal fluency (20 points), comprehension (20 points), naming (10 points) and word finding (10 points), repetition (10 points), reading (10 points), writing (10 points), and calculation (10 points) were tested with the Ege Aphasia Test. Total score is calculated as the sum of each subtest score (normal mean score ± SD, 85 ± 15 points).

We conducted an informative interview based on existing criteria for dementia and reviewed and verified the records of the primary care doctor or the National Health Data system. No API patient was diagnosed with dementia before.

The functional outcome and the degree of disability of patients were considered according to the modified Rankin Scale (mRS) score as the following: (1) favorable outcome (mRS score ≤ 2) and (2) unfavorable outcome (mRS score ≥ 3).

Statistical Analysis

Descriptive statistics are reported as mean and range. The continuous variables were analyzed by using the Student *t*-test or

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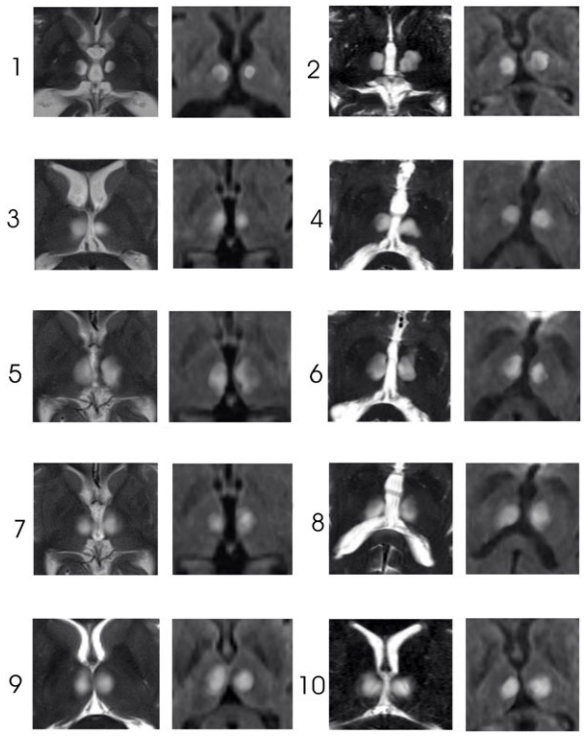

Figure 2: *T_2-weighted and DWI images (axial reconstructions) of the thalamus show the pattern of artery of Percheron territory infarct. Notice involving of the variant and classical lesions in each patient. Images are cropped to display the thalamus only.*

Kruskal–Wallis rank-sum test. We calculated *z*-scores for the neuropsychological tests at the baseline for all the patients, in order to combine the tasks. A *z*-score (standard score) of each patients' cognitive test point was calculated, and a *z*-score inferior to 2 indicating a 95% probability of the standard deviation (SD) from the mean was considered as pathological. All statistical analyses were conducted by using the SPSS 22.0 package for Windows (SPSS Inc., Chicago, IL).

Results

The patient population consisted of four females and six males, with a mean ± SDage of 63.6 ± 10.4 years (42 ± 75) and a mean educational level of 12 ± 2.35 years (6–16 years). All patients were right-handed, and all had bilateral lesions. Six patients (Nos. 1–6) had pure thalamic involvement, while 4 (Nos. 7–10) had thalamic and rostral midbrain involvement (Figure 2). Demographic and clinical features are given in Table 1.

Clinical Findings

On the first day of stroke, all patients had mental status changes, including hypersomnia with excessive and prolonged sleep (30%), stupor (30%), and decreased consciousness (40%). The main behavioral disorders in the early period of stroke were mutism (50%), apathy and abulia (40%), and confusion (10%). Subcortical type of aphasia characterized by dysarthria (70%), nonfluent speech (40%), phonemic paraphasia, anomia ve mild repetition deficit was present in three patients and transcortical motor aphasia in one patient (No. 7). Of ocular movement abnormalities, vertical gaze paresis was found in 6 patients. Patient 2 had ophtalmoplegia characterized with unilateral ptosis, loss of all extraocular movements, and primary position exotropia. There were neither voluntary eye movements nor eye movements in response to vestibular stimulation.

Three patients had retraction nystagmus (Nos. 5, 7, 9), and 2 (Nos. 8, 10) had Collier's sign. One month after stroke, eight patients had light touch impairment and a slight decrease in proprioception in both the upper and lower extremities. At this time, all Brunnstrom recovery stages of the upper extremities, hand, and lower extremities were checked, and it has revealed a mild decrease in muscle power of the extremities with a grade of 4 in seven patients. Four patients had ataxia and dysmetria, and 2 had asterixis 1 month after stroke.

Neuropsychological Findings

(1) Global mental state assessed by MMSE was disturbed in all patients after stroke (*z*-score, mean ± SD: −4.07 ± 0.64; Table 2). In MMSE test conducted 1 year later, despite a significant decrease in negative *z*-scores, only four patients had a *z*-score of ≥−2 and could be considered within normal limits; (2) executive function assessed by the Trail Making Test-Part A was severely impaired at onset of stroke and 1 year after stroke improved significantly ($p < 0.001$); (3) processing speed which was assessed by Stroop test (name color print of noncolor words) was disturbed during hospitalization and improved 1 year after ictus ($p < 0.001$); (4) working memory was severely disturbed in all patients and did not recover well after 1 year of follow-up (mean ± SD, −3.97 ± 0.3 and −3.54 ± 0.4, respectively); (5) episodic memory was disturbed in parallel to working memory but improved significantly 1 year after stroke ($p < 0.001$); (6) semantic memory referring to facts (ideas, meanings, and concepts) was severely impaired in the first month of stroke, and a significant decrease in negative *z*-scores was observed in most patients 1 year after stroke (mean ± SD, −3.41 ± 0.5 and −1.88 ± 0.7, respectively); (7) delayed verbal memory recall and recognition was disturbed at stroke onset and improved mildly 1 year after ictus ($p < 0.001$); (8) visual memory was impaired in all patients at the onset of stroke, and most patients recovered during the 1 year follow-up period (mean ± SD, −3.88 ± 0.6 and 1.98 ± 0.5, respectively). Motor neglect was present in three patients (Nos. 1, 7, 10), visuospatial neglect in 4 (Nos. 1, 8, 9, 10) and visual extinction in 3 (Nos. 5, 9, 10); (9) total score of language was affected in all patients at the beginning of stroke, and most of the patients had decreased negative *z*-scores after 1 year ($p < 0.001$).

Hypersomnolence in patients lasted approximately 10–15 days in three patients (Nos. 4, 6, 8). When they were alone, they continued to nap for a while longer. But 3 months after stroke, sleep-wake cycles improved. After a mean of 13 months of follow-up (SD ± 3.6), only 1 (10%) patient (No. 5) had a good functional outcome (mRS score ≤ 2). Four patients had moderate disability, but able to walk without assistance (mRS score = 3) (Nos. 3, 4, 6, and 8). They could make plans for simple jobs and do simple household and maintenance chores. They had difficulty performing complex tasks and participating in life outside the home. Most of the patients (50%) were dependent and unable to walk without assistance (mRS score ≥ 4) (Nos. 1, 2, 7, 9, and 10). After 1 year of follow-up, five patients (Nos. 1, 7, 8, 9, 10) with

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Table 1: Risk factors, clinical findings, and etiology of patients with artery of percheron infarction

Patient	Sex	Age	Risk factors	Consciousness at stroke onset	Behavioural disorders	Ocular movement disorders	Motor deficit	Neuropsychological findings	Aphasia or dysarthria	Cerebellar signs/ dystonia	Cause of stroke
1	M	64	HT, Smk, Ob, CHD, AF	Decreased consciousness	Mutism, confusion, LOS	Upgaze palsy	Yes	Visuospatial neglect, motor neglect, ideational apraxia, memory deficits, frontal and executive dysfunction	Non-fluent aphasia, dysarthria	No	Cardioembolism
2	M	52	HT, DM, Hch, Ob, CHD, AF	Decreased consciousness	Apathy, abulia	Ophthalmoplegia	Yes	Ideomotor apraxia, memory deficits, frontal and executive dysfunction	Anomia	No	Small artery disease
3	M	68	Smk	Stupor	Apathy, abulia	Vertical gaze palsy	No	Ideational apraxia, memory deficits, frontal and executive dysfunction	Anomia, dysarthria	No	Unknown
4	F	69	HT, DM, Ob, CHD	Hypersomnia	Mutism, confusion, LOS	No	Yes	Visuospatial neglect, memory deficits, frontal and executive dysfunction	Aphasia, dysarthria	Ataxia/dysmetria	Small artery disease
5	F	70	HT, AF	Stupor	Confusion, agitation	Mydriasis, vertical gaze palsy	No	Visual extinction, memory deficits, frontal and executive dysfunction	Dysarthria	No	Cardioembolism
6	M	62	HT	Hypersomnia	Apathy, abulia	No	No	Ideomotor apraxia, memory deficits, memory deficits, frontal and executive dysfunction	Non-fluent aphasia, anomia	Ataxia/dysmetria, dystonia	Unknown
7	F	41	DM, Hch, Ob	Stupor	Mutism, confusion, LOS	Downgaze palsy	Yes	Motor neglect, ideational apraxia, FBL, memory deficits	Transcortical motor aphasia, dysarthria	No	Basilar artery stenosis (IA stent)
8	F	63	HT, Smk, CHD	Hypersomnia	Apathy, abulia, LOS	Mydriasis, third cranial nerve palsy	Yes	Visuospatial neglect, memory deficits, frontal and executive dysfunction	Aphasia, dysarthria	Ataxia/dysmetria	Small artery disease
9	M	78	HT, DM, Smk, Hch, Ob	Decreased consciousness	Mutism, confusion, LOS	Vertical gaze palsy	Yes	Visual extinction, ideational apraxia, FBL, memory deficits, frontal and executive dysfunction	Aphasia	Dystonia	Rostral basilar artery occlusion (embolectomy)
10	M	69	HT, Hch, Ob, AF	Decreased consciousness	Mutism, confusion, LOS	Mydriasis, vertical gaze palsy	Yes	Visuospatial neglect, motor neglect, visual extinction, ideational apraxia, memory deficits, frontal and executive dysfunction	Aphasia, dysarthria	Ataxia/dysmetria	Cardioembolism

CE=cardioembolic; DM=diabetes mellitus; F=female; FBL=facio-bucco-lingual-oral apraxia; HCh=hypercholeterolemia; HT=hypertension; IA stent=intra-arterial stent application; LOS=loss of self-activation; M=Male; Ob=Obesity; Smk: Current smoking.

A stent was applied to patient 7 due to 80%–90% basilar artery stenosis. In patient 9, embolectomy was performed for thrombus located in top of the basilar artery in 6 h after stroke.

Table 2: Neuropsychological examination and *z*-scores of tests of patients with artery of Percheron infarction

Neuropsychological examinations	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10
	1st/2nd	1st/2nd	1st/2nd	1st/2nd	1st/2nd	1st/2nd	1st/2nd	1st/2nd	1st/2nd	1st/2nd
Mini-mental state examination	−4.33/−2.33	−4.00/−1.67	−3.67/−2.00	−3.00/−2.00	−4.00/−1.67	−3.67/−200	−4.67/−2.33	−3.67/−2.33	−4.33/−2.67	−5.33/−2.67
Executive test (Trail Making A)	−3.85/−2.31	−3.77/−1.92	−3.69/−2.69	−3.62/−2.31	−3.92/−2.69	−3.62/−2.62	−4.15/−3.08	−4.00/−2.62	−4.15/−2.69	−4.46/−3.8
Processing speed (name color print of non-color words)	−4.40/−2.40	−3.80/−1.60	−3.60/−2.60	−4.60/−2.40	−3.80/−1.20	−4.40/−2.40	−4.80/−2.00	−4.60/−2.40	−5.00/−2.40	−5.20/−2.80
Working memory (Digit span forward-WMS)*	−4.00/−2.50	−3.70/−3.00	−3.85/−2.75	−3.90/−3.00	−3.50/−2.50	−3.75/−2.50	−4.25/−3.00	−4.00/−3.00	−4.25/−3.25	−4.50/−3.50
Episodic memory (Immediate free recall/new learning-RAVLT)**	−4.00/−1.50	−3.50/−2.00	−2.50/−2.00	−3.50/−3.00	−3.00/−1.50	−3.50/−2.50	−4.00/−2.00	−4.50/−2.25	−3.50/−2.50	−4.50/−3.00
Semantic memory (Verbal fluency)	−3.17/−1.67	−3.00/−1.00	−2.83/−2.00	−2.67/−1.33	−3.17/−1.00	−3.50/−1.33	−4.00/−2.50	−4.00/−2.67	−3.83/−2.50	−4.17/−2.83
Verbal memory	−4.00/−1.75	−3.75/−1.50	−3.75/−1.75	−3.50/−1.50	−3.50/−1.75	−3.50/−200	−3.75/−2.00	−4.00/−2.25	−4.00/−2.26	−4.25/−2.50
Delayed recall recognition	−3.00/−2.00	−2.50/−2.00	−3.00/−2.25	−2.75/−1.50	−3.00/−2.00	−3.25/−2.25	−4.00/−2.25	−4.00/−2.50	−3.75/−2.75	−4.25/−2.50
Visual memory (Benton visual retention test)	−3.60/−2.00	−3.40/−1.60	−3.20/−1.60	−3.00/−1.00	−4.00/−2.40	−3.80/−1.80	−4.20/−2.40	−4.60/−2.00	−4.20/−2.80	−4.80/−2.20
Language processing (Turkish Ege Aphasia test)	−2.50/−1.00	−3.13/−1.25	−3.38/−1.38	−2.50/−1.13	−2.25/−1.38	−2.88/−2.50	−3.38/−1.63	−3.75/−2.13	−3.63/−2.38	−3.88/−2.50

*The Wechsler Memory Scale (WMS).
**Rey-Auditory Verbal Learning Test (RAVLT).

impaired daily living activities and global mental *z*-scores below 2 were considered as thalamic dementia. They could respond to uncomplicated words and engage in simple dialog. They were mentally apathetic with late response and depressed. None of these patients fully functioned as a parent or sibling. The most common causes of API were cardioembolism and small artery disease in the vertebrobasilar system (three patients each). Two patients had large artery disease.

Discussion

Our study showed that patients with API may have oculomotor disorders, aphasia, motor deficits, as well as severe cognitive impairment in the first month of stroke. Although the patients survived, most of the cognitive disorders did not improve well after a long follow-up period. Despite the impairment of executive processing, memory, and linguistic abilities in nearly all patients, it was observed that negative z-scores were higher and remained longer in those with rostral midbrain involvement. These patients can be noted as "top of the basilar artery" (TOB) syndrome, as they involve a range of visual, oculomotor, and behavioral abnormalities, often without significant motor dysfunction.[19] Occlusive vascular diseases of the rostral basilar artery can cause infarction of the midbrain, thalamus, which can lead to specific clinical manifestations of TOB syndrome.

In our study, there were prominent mutism, confusion, and loss of initiation in the early period of stroke. Therefore, the first tests of the patients were carried out toward the end of the first month when the general condition of the patients improved. Even in this period, *z*-scores were found to be significantly lower in neuropsychological tests. In previous studies, cognitive problems such as attention difficulties, linguistic deficits, and memory problems in patients with bilateral paramedian thalamic infarction were reported.[13,14,20] However, there are some limitations in these studies. It was not clear which neuropsychological deficits were impaired in detail, how long they were followed up, and how much they recovered. Some of them included other bilateral thalamic territories and examined heterogeneous infarct types.[21,22] The detailed findings of different cognitive problems in patients with API has not been assessed separately. The mechanism of attention, executive function, processing speed, and working memory impairments after bilateral thalamomesencephalic lesions may be due to many different subnucleus involvement. The lack of attention caused by the mesencephalic reticular formation and the interruption of the ascending noradrenergic pathways in the intralaminar nuclei do not allow good consolidation and retrieving processes leading to the formation and activation of memory traces. Moreover, the mediodorsal nucleus of the thalamus (MD) has been implicated in executive functions because of its significant efferent and afferent interconnectivity with the prefrontal cortex, cingulate cortex, insular cortex, supplementary motor cortex, reticular thalamus, basal ganglia, and output structures of the pallidum.[23]

In patients with API, orientation to time and place, perception, executive processing, attention span and concentration, memory, language skills, purposeful behavior were all disturbed in the early period of stroke but this was more prominent in patients with rostral midbrain involvement. In this study, it has been determined that different memory systems are affected in API lesions. Memory is not a unitary process, with different types of

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memory (e.g., working, episodic, semantic, short, and delayed memory) associated with dissociable neural systems, traditionally involving medial temporal, lateral prefrontal, mammillary body, amygdala, and even cerebellar hemisphere structures. Animal and human lesion studies also provided strong evidence for the role of specific thalamic nuclei in selective component processes of memory.[24] Thalamic nuclei and broader regions have been shown to be selectively associated with encoding, retrieval, recollection, and familiarity. In particular, the anterior thalamic nucleus, which is directly connected to the hippocampus via the fornix and indirectly connected to the mammillary bodies via the mammillothalamic tract, is associated with encoding content and contextual information, that is, semantic memory processes; the medial dorsal thalamic nucleus with its connections to the prefrontal cortex and the limbic system (amygdala via the ventroamygdalofugal pathway) is related to executive aspects of memory, including memory retrieval of information necessary for working and episodic memory; and intralaminar/midline thalamic nuclei connected to the parietal lobe play a role in the attention, arousal, and awareness and activation of the cortical regions required for the processing of information that needs to be remembered in a short and long time.[25]

It was observed that cognitive functions improved in parallel with the improvement in activities of daily living in patients with API within 1 year after stroke. However, this improvement was never at the rate of population mean, as seen in *z*-scores. One of the major reasons for the improvement in cognitive abilities may be greater improvement of perception and attention, increased motor skills, and better cooperation with the environment, requiring multiple thalamic subnucleus, and tract function.[13,14,26] However, 1 year after stroke, execution and processing speed, concentration and memory especially working and semantic memory were still worse in the patients with rostral midbrain involvement. In patients with thalamic and rostral midbrain involvement, these cognitive functions are more impaired because they contain complex anatomical connections, including thalamic-frontal-striatal connections and require more than one center to work.

Most of the causes of stroke in patients with API were cardioembolism and atherosclerotic small artery and large artery disease. Such pathologies can affect artery of Percheron with embolism from the heart or large arteries, resulting in severe cognitive impairment. We did not analyze acute stroke treatment efficacy on clinical and cognitive functions due to the low number of patients. In a previous study, the outcome has been reported to be better in sudden-onset API patients who undergo thrombolysis within 6 h of onset.[27,28] In selected patients, the window for thrombectomy is believed to be longer, possibly up to 24 h.

There are limitations of the study. Our results need to be interpreted carefully because our study has a limited sample size. Assessing neuropsychological disturbances in patients with cognitive disabilities remains a complex challenge, partly due to insufficient studies for scientific evidence on this topic. However, the strengths of the current series are that the study site is a tertiary referral institution with the prospective enrollment of patients and that the site uses a standard neuropsychological assessment protocol for patients with ischemic stroke. Another confounding factor that may affect the perception and performance of patients may be depression. It has previously been shown that depression can be associated with attention and memory disorders.[29]

As conclusion, this study was conducted to remind that patients diagnosed with API may have severe cognitive impairments as well as motor and speech impairments in the long term. With the widespread use of thrombolysis and embolectomy in stroke treatment, the rapid diagnosis of the involvement of this territory can greatly prevent the development of severe clinic and cognitive disorders.

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Author Contributions

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Study concept or design. Emre Kumral
Acquisition of data. Birgül Dere, Fatma Ece Çetin
Analysis or interpretation of data. Emre Kumral
Study supervision or coordination. Emre Kumral

Conflicts of Interest

We have no actual or potential conflicts of interest for all authors involved in this paper.

Ethical Committee Approval

Ege University Medical Ethical Committee was approved this study following the principles outlined in the Helsinki Declaration before starting the study (1998).

Ege University Medical Ethical Committee

(EUMEC 2010/57).

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