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Isolated hippocampal infarcts: Vascular and neuropsychological findings

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ABSTRACT

Background and Purpose: The hippocampus plays a role in the verbal and spatial memory processing, learning, and emotions. The purpose of this study was to determine clinical, etiological, and radiological features of isolated hippocampal infarcts.
Methods: We reviewed, 6800 patients with first-ever ischaemic stroke included in our Stroke Registry between 2004 and 2014. Among them we studied 19 patients with an acute isolated hippocampal infarct confirmed by MRI.
Results: Among 6800 patients, 19 patients (0.03%) showed ischaemic lesions in the hippocampal artery territory, allowing us to delineate 5 variant distributions; (1) anterior hippocampal infarcts (4 patients [21%]) were present with altered consciousness, transient visual vivid hallucinations, and transient global amnesia with episodic and verbal memory deficits. (2) Posterior hippocampal infarcts (3 patients [16%]) developed dizziness and dullness at stroke onset, confusion, episodic and procedural memory deficit and verbal learning deficit. (3) Unilateral complete hippocampal infarcts were present (4 patients [21%]) with confusion, object specific hallucinations, intense mood states changes as well as impulsivity or depressive behaviour. Memory dysfunctions were found in all patients. (4) Bilateral hippocampal infarcts (3 patients [16%]) had cognitive deficits and memory deficits in all patients. All patients had difficulties retrieving specific autobiographical events and retrieving recent memory, and disturbances of learning in verbal and visual task. Hippocampal dementia was observed in 2 patients with severe immediate, delayed verbal and visual memory deficits, dysexecutive syndrome, deficits in responding to feedback and error correction with dull and aimless appearance lasting several months. (5) Small circumscribed (punctiform) hippocampal infarcts (5 patients [26%]) showed dizziness or dullness sensation and difficulties finding words or objects that they use everyday. Cardioembolism (10; 53%) and large-artery disease of the vertebrobasilar system (6; 32%) were the main stroke mechanisms.
Conclusions: We described topographic patterns of hippocampal infarction with distinct manifestations and etiologies. We thought that different patterns of hippocampal infarcts are the result of variation in hippocampal arterial supply or reflect a source of embolism.

1. Introduction

The hippocampus is mostly involved in memory processing, learning, and emotions [1]. The hippocampus has an arc shape and a dilated anterior segment and a narrow posterior segment. It comprises three parts, the head, body and tail which each has a ventricular part and a extraventricular part on the medial surface of the temporal lobe [2]. Russian neuropsychiatrist Wladimir von Bechterew described the first patient with isolated hippocampal infarct in 1900, presenting amnesia, false memories and apathy having bilateral softening of the uncus and Ammon's horn revealed on postmortem examination [3]. The hippocampus is supplied by the collateral branches of the posterior cerebral artery (PCA) and the anterior choroidal artery, which form the network of superficial hippocampal arteries that in turn lead to deep intrahippocampal arteries located intraparenchymally [4–6].

Previous reports evaluated the clinical consequences of hippocampal infarcts in patients with concomitant lesions involving the territory of PCA, anterior choroidal artery, and thalamus [7–12]. MRI studies of the latest studies mostly described patients with unilateral or bilateral PCA stroke presenting clinical syndromes outside the hippocampus. There are no specific studies devoted to the clinical patterns of isolated hippocampal infarcts. The aim of the present study was to determine clinical, anatomical, etiological, and radiological features of isolated hippocampal infarcts by using MRI and neuropsychological evaluation.

2. Subjects and Methods

Between 2004 and 2014, 6800 patients with first-ever ischaemic stroke were admitted to the Neurology Department of the Ege University Hospital and prospectively entered in the Ege Stroke Registry [13]. A total of 224 (0.3%) patients with MRI-proven ischaemic lesions

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restricted to the PCA and hippocampus were identified. In our Registry only 16 patients had unilateral isolated hippocampal lesion, 3 had bilateral lesions involving the hippocampus (0.03%). Patients with old hemorrhagic lesions, old infarcts on imaging, or simultaneous acute unilateral or multiple lesions outside the hippocampus were excluded.

All patients were examined clinically by at least 1 of us and had undergone a comprehensive neuropsychological examination by a battery of tests. MRI was performed within 48 h of admission by 1.5 T or 3 T scanners (Siemens Sonata, Siemens Medical Solutions, Erlangen, Germany). MRI scanners consisted of axial T_1-, T_2-weighted spin-echo, T_2 fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI) used to exclude concomitant infarct outside the hippocampus. Axial T_2-weighted FLAIR or DWI images were used to define lesion size and site. Intracranial and extracranial Doppler ultrasonography with frequency spectral analysis, 12-lead electrocardiography, a minimum of 7 days of cardiovascular monitoring, and standard laboratory tests were performed in all patients. Magnetic resonance- or CT-angiography, 2D echocardiography, and 24-hour electrocardiography (Holter) monitoring were performed on selected patients, depending on the suspected aetiology.

The following risk factors were recorded: age, sex, hypertension, glucose, HbA1c levels, obesity, physical activity, current cigarette smoking, uric acid, hyperhomocysteinemia, serum total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, apolipoprotein A (ApoA), apolipoprotein B (ApoB), and lipoprotein (a) (Lp [a]). The aetiology of stroke was determined according to criteria described previously [14] as large-artery-disease, small-artery disease, cardioembolic, other, and unknown. The lesion territories were grouped according to their anatomic location within the hippocampus such as; anterior hippocampal territory, posterior hippocampal territory, unilateral complete hippocampal territory, bilateral hippocampal territory, and small circumscribed (punctiform) hippocampal territory, as reported previously [12,15].

(Fig. 1) The study was approved by the ethics committee of the Ege University Medical Center, and written informed consent was obtained from all participants.

2.1. Neuropsychological Examination

All patients underwent standardized neuropsychological testing within the first week of stroke to assess cognitive functions including: orientation, working memory (short term memory), episodic and semantic memory, procedural memory, verbal and visual memory, behavioural memory, object location memory, motor sequence learning, and spatial skills. The identification and quantification of deficits in cognitive functions derived from neuropsychological tests. From those tests especially pertaining to the hippocampus, memory tests are used to assess functions related to processes of declarative memory, involving episodic memory, semantic memory and procedural memory. Such neuropsychological tests reveal learning, recognition and recall of different materials. We studied verbal, visual and behavioural memory functions. The Rey Auditory Verbal Learning Test-Turkish version (RAVLT) was used to assess auditory–verbal learning and episodic and procedural memory by giving participants 15 unrelated words repeated over five different trials and asking them to reproduce all the words [16]. Another list of 15 unrelated words was given to the patient to reproduce the list immediately and after a 30 min delay. RAVLT variables were used for short delay recall, long delay recall, long delay cued recall, and total recognition discriminability. The Benton Visual Retention Test (BVRT) consisted of tests measuring visuoperception and visuoconstructive abilities with three sets of cards containing ten different geometric figures [17]. The Rivermead Behavioural Test-II (RBMT-II) was performed to measure duties that patients encounter to independently manage their lives (belongings, appointments-delayed recall, story-immediate recall, route-immediate and delayed recall, messages-immediate and delayed recall) [18]. Object location memory (or positional memory) was assessed by

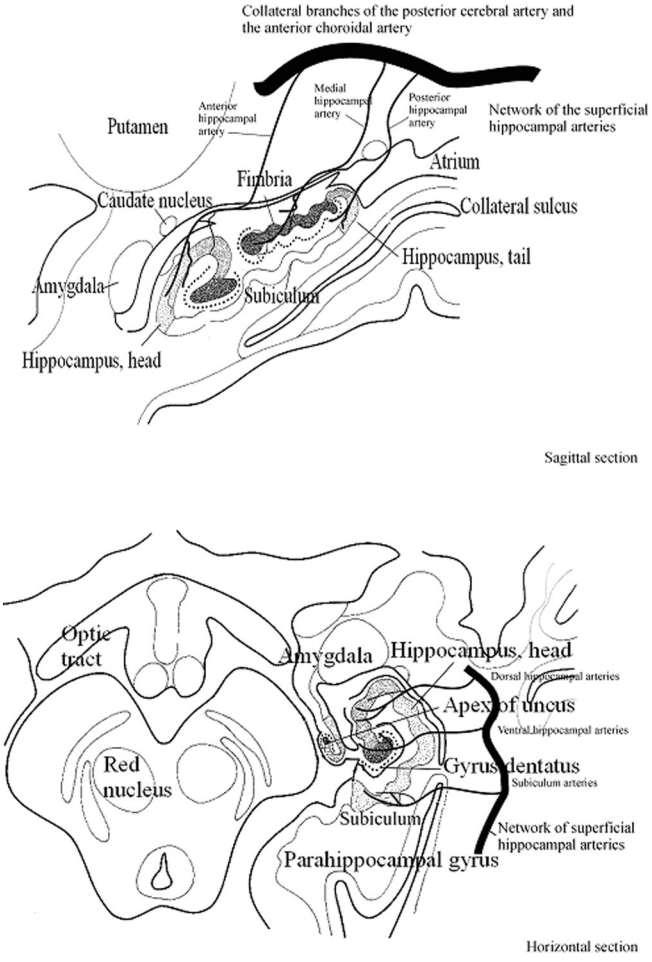

Fig. 1. Illustration of hippocampal vascular complexity and vascular territories, as shown by illustration of Duvernoy. In sagittal section, anterior, medial and posterior superficial hippocampal arteries arose from collateral branches of the posterior cerebral artery and the anterior choroidal arteries. In horizontal section, superficial hippocampal arteries give rise to intrahippocampal vascularization which was named as ventral, dorsal and subiculum arteries.

the Location Learning Test (LTT) in which patients were required to learn the correct placement of 10 everyday objects on a 5 × 5 grid, presented to them on a stimulus card [19]. Motor sequence learning was tested by the Serial Reaction Time Task (SRTT) in which patients were asked to repeatedly respond to visual cues that can appear in one of four positions on a computer screen [20]. This task assessed specific memory for procedural-motor skill. Following neuropsychological tests, the scores below the normal cut-off value indicating impairment in patients are presented in Table 1.

3. Results

Nineteen patients (0.03% of all ischaemic stroke patients in our registry) had unilateral (16 patients) and bilateral (3 patients) lesions inside the classical hippocampal artery territory, and consisted of 10 men (53%) and 9 women (47%). Unilateral lesion was present at the left side in 9 patients (47%) and at the right side in 7 patients (37%) (Figs. **2** and 3). The mean age ± SD was 63 ± 9 years (range 48 to 79 years).

3.1. Anterior Hippocampal Infarcts

Four patients (21% of hippocampal infarcts) had unilateral lesion in the anterior hippocampal vascular territory (Figs. 2 and 3). Mean age ± SD was 63 ± 7 years (range 56 to 72). Infarct of this territory

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