Hippocampal Lesion Patterns in Acute Posterior Cerebral Artery Stroke
Clinical and MRI Findings

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Background and Purpose—Reports of ischemic stroke affecting the hippocampus are rare. In this study we used diffusion-weighted MRI (DWI) to characterize patients with posterior circulation stroke involving the hippocampus.

Methods—Fifty-seven consecutive acute stroke patients with hippocampal infarct (HI) on DWI were analyzed with regard to clinical features and ischemic lesion patterns. The last 20 of these underwent additional neuropsychological testing of short-term, working, and episodic long-term memory.

Results—We found unilateral HI in 54 and bilateral HI in 3 patients. Visual analysis identified 4 patterns of DWI lesion affecting (1) the complete hippocampus (15/60), (2) the lateral (19/60) or (3) dorsal (22/60) parts of the hippocampal body and tail, and (4) circumscribed lesions in the lateral hippocampus (4/60), corresponding well to hippocampal vascular anatomy. In all cases DWI showed further ischemic lesions in the posterior circulation. Symptoms from lesions outside the hippocampus were the common leading clinical signs. Whereas mnestic deficits were prominent in only 11/57 patients, neuropsychological examination in 20 patients showed deficits of verbal episodic long-term memory in left and of nonverbal episodic long-term memory in right HI.

Conclusion—Several phenotypic lesion patterns can be distinguished in HI that usually occur as part of multifocal PCA ischemia. A careful neuropsychological examination is necessary to detect resulting memory deficits. (Stroke. 2009;40:2042-2045.)

Key Words: diffusion imaging • ischemic stroke • hippocampus

In 1900, the Russian Neurologist Bechterew described a patient who experienced amnesia related to stroke, while the postmortem study revealed bilateral softening involving the uncus and the Ammon horn.1 In 1961, a likewise postmortem study of a patient with bilateral infarctions in the posterior cerebral artery (PCA) territories established stroke as an etiology of acute and in particular persistent amnesia.2 Postmortem cases reported transient amnesia in unilateral PCA stroke.3,4 Benson et al described 10 patients in whom amnesia was accompanied by hemianopia in PCA territory strokes (6 bilateral, 4 unilateral) on radionuclide brain scans.5 In 1993, Ott and Saver described 3 patients with unilateral PCA stroke with hippocampal involvement causing amnesia.6 The common feature in all unilateral cases was the involvement of the left hippocampus.

Diffusion weighted MRI (DWI) is highly sensitive to even very small ischemic lesions, providing a strong contrast between affected and unaffected tissues7 and offering more detail in stroke syndromes. In this study we examined the morphological findings of DWI in hippocampal infarct (HI) and attempted to detect clinical and neuropsychological changes in acute HI patients.

Methods

Subjects
We studied 57 patients (28 men, 29 women, mean age 68.3 years) consecutively admitted to the stroke unit of our hospital between 1998 and 2007 with acute ischemia in the posterior circulation and DWI proven involvement of the hippocampus (n=60 affected hippocampi). In all patients we performed standardized stroke MRI (T1- and T2-weighted sequences, diffusion-weighted images [b=0 and 1000 s/mm²] parallel to the hippocampal body, and a 3D time-of-flight MR-angiography) within the first 72 hours after symptom onset (mean time from onset to MRI 46.25 hour). The study was approved by the local ethics committee; written informed consent was obtained from all patients.

MRI Analysis
A standardized written protocol for image review incorporating lesion analysis (lesion location, signal characteristics, multiplicity of lesions, and evidence of chronic tissue change) was completed by 2 readers separately, who then compared results and agreed mutually in cases with differing ratings. On coronal and transverse views of 3D MRA reconstruction characteristics of the PCA flow signal were recorded.
State Examination (MMSE), the Clock Drawing Test, and tests of acute ischemic lesions (A–D). The possible vessels involved are the proximal posterior cerebral artery (PCA; A), the longitudinal terminal segments of the hippocampal arteries (B), and the middle or posterior hippocampal artery (C). The small lesions might be explained by distal emboli (D). Note that in right image the anterior hippocampal artery is not shown; it is partly hidden by the PCA and the basal vein and disappears into the uncal sulcus.

Neuropsychological Testing
A standardized neuropsychological assessment was performed in the last 20 patients of this series within 4 days after MRI, including parts of the Aachener Aphasie Test, a line bisection task, the Mini Mental State Examination (MMSE), the Clock Drawing Test, and tests of verbal short-term and working memory. Verbal long-term memory was measured using a subtest of the Rivermead Behavioral Memory Test (RBMT) and a German version of the Auditory Verbal Learning Test (AVLT). Nonverbal long-term memory was measured using the Rey-Osterrieth Complex Figure Test (ROCF). For each test, published normative data were used to evaluate each patient’s performance in terms of percentile ranks relative to the normative samples’ performance. We compared performance of patients with right versus left HI in these tests using independent-samples t tests and 1-tailed probability values.

Results
According to our Stroke Unit data bank during the study period, a mean of 800 patients per year with acute ischemic stroke or TIA were treated at our institution. Approximately 5.25% of all patients had an acute ischemic lesion in the PCA territory (n=378), and of these the hippocampus was affected in 21%.

MRI Analysis
Of the 57 HI patients, 3 had bilateral hippocampal lesions and 54 had unilateral lesions (right: 22, left: 32). We identified 4 different patterns of acute ischemic lesions of the hippocampus (Figure 1): (1) involving nearly the complete hippocampus (15/60; 25.0%) with extensive extrahippocampal involvement (complete or subtotal PCA stroke); (2) lesions confined to the lateral aspect of the hippocampus along the complete length of the hippocampal body and tail (19/60; 31.7%); (3) partial lesions in the dorsal part of the hippocampal body (22/60; 36.7%), or (4) small, dot-like lesions in the lateral border of the hippocampus (4/60; 6.7%). In all patients with HI multiple acute ischemic lesions were found involving extrahippocampal tissue in the PCA territory, with their total number ranging from 2 to 17. When subdividing the PCA territory the additional lesions were located in the ipsilateral thalamic-peduncular region in 33 (55%) and in the occipital lobe in 42 cases (70%). In 9 (15%) cases the complete PCA territory was affected. Additional DWI lesions were seen in either the posterior inferior cerebellar artery (PICA), the superior cerebellar artery (SCA), or the middle cerebral artery (MCA) territory (n=8). In 2 patients with occlusion of the basilar artery (BA) as well as both PCA acute ischemic lesions were scattered in the vertebrobasilar territory. In 50% either proximal or distal (P1 or P2 segment) occlusion of the PCA was present, whereas in 16.7% a focal stenosis of the PCA, and in 3.3% asymmetrically low flow signal of the entire PCA was found.

Clinical Aspects
The mean NIHSS in the series was 4.6 (range 0 to 20). In most patients the acute presenting clinical symptoms arose from functional loss through lesions outside the hippocampus. The most common deficits were visual field defects in 40/57 (70.2%), followed by motor weakness and sensory loss in 18/57 (31.6%), and hemisensory deficit 16/57 (28.1%). Apparent clinical acute amnestic syndromes—identified by testing of orientation and a 3-item memory test as part of the routine neurological examination—were present in 11/57 (19.3%) patients only, including 2 of the 3 patients with bilateral HI (Figure 2). One patient with bilateral HI could not be assessed because of the severe neurological deficit with coma. One patient presented with an initial seizure.

Neuropsychological Testing
Of the 20 patients, 11 and 9 patients had lesions within the left and right hippocampus, respectively. The 2 groups did not differ in age, years of formal education, or gender distribution.

Tests of repetition, comprehension, naming, and writing indicated no signs of aphasia. There were no significant differences in the language tests between groups, t<sub>18</sub>=1.81, P<0.089. Only 1 patient with right PCA infarction showed unilateral neglect in the line bisection task. In the MMSE, the patients reached a score of 24.30±3.91 (lying in the mildly impaired range), with no difference between groups, t<sub>18</sub>=1.33, P=0.202. In the Clock Drawing Test, the patients reached a score of 2.84±1.26 (at the border of the normal range), with no difference between groups, t<sub>17</sub>=0.51, P=0.618. With regard to verbal short-term and

Figure 1. We identified 4 different patterns of acute ischemic lesions of the hippocampus corresponding to the vascular anatomy and affecting either the complete hippocampus (A), the lateral (B) or dorsal (C) parts of the hippocampal body and tail, and small circumscribed lesions in the lateral hippocampus (D). The lesion patterns are presented as schematic drawings (1–4) and as DWI hyperintense acute ischemic lesions (A–D). The possible vessels involved are the proximal posterior cerebral artery (PCA; A), the longitudinal terminal segments of the hippocampal arteries (B), and the middle or posterior hippocampal artery (C). The small lesions might be explained by distal emboli (D). Note that in right image the anterior hippocampal artery is not shown; it is partly hidden by the PCA and the basal vein and disappears into the uncal sulcus.
working memory, the patients reached a forward and backward digit span of 5.00±1.11 and 3.11±0.74, respectively, with no difference between groups, \( t(17) < 0.41, P > 0.690 \).

For verbal long-term memory as measured by the RBMT, patients with left HI scored significantly lower than patients with right HI in immediate recall of the story, \( t(18) = 2.23, P < 0.05 \), and in delayed recall of the story, \( t(18) = 1.82, P < 0.050 \). Compared to normative samples, the scores of patients with left HI were within the mildly impaired range, whereas the scores of patients with right HI were only slightly below the mean of the normative sample. For verbal long-term memory as measured by the AVLT, patients with left HI scored significantly poorer than patients with right HI with regard to the Learning Score, \( t(17) = 3.22, P < 0.01 \), the Delayed Recall Score, \( t(17) = 5.31, P < 0.001 \), and the Recognition Memory Score, \( t(17) = 4.06, P < 0.01 \). Patients with left HI also forgot significantly more words over time, \( t(17) = 1.94, P < 0.050 \). Compared to normative samples, performance of patients with left HI was clearly in the impaired range, whereas performance of patients with right HI was only in the mildly impaired range. For nonverbal long-term memory, patients with right HI scored significantly poorer than patients with left HI in the recall of the figure after 3 minutes, \( t(14) = 2.38, P < 0.050 \), and after 30 minutes, \( t(14) = 1.92, P < 0.050 \), although there was no difference between the two groups in copying the complex figure, \( t(14) = 0.46, P = 0.651 \) (2-tailed). Compared to normative samples, the scores of patients with right HI were within the impaired and those of patients with left HI in the mildly impaired range (Figure 3).

**Discussion**

Stephens and Stilwell\(^ {15} \) described the hippocampal vascular supply in humans as mainly arising from the PCA and to a lesser degree from the anterior choroidal artery (AChA). Although in general the occipital two thirds of the hippocampus are supplied by PCA branches arising from the P2-segment, namely the anterior, middle and posterior hippocampal arteries, the rostral third of the hippocampus is dominated by branches form the AChA. The middle and posterior hippocampal arteries supply the hippocampal body and tail, whereas the anterior hippocampal artery vascularizes the hippocampal head and uncus. The contribution of the AChA to the vascular supply of the hippocampal head is highly variable.
and may be preponderant in some cases. The distal part of the hippocampal arteries are longitudinally connected in the lateral sulcus of the hippocampus via the so-called longitudinal terminal segments of the hippocampal arteries that run parallel to the course of the hippocampal body (Figure 1).\textsuperscript{15,16}

From the analysis of HI lesions we suggest to differentiate 4 main patterns that correspond to the vascular arterial network: Cases involving large parts of the hippocampus including the rostral aspect, frequently with extensive affection of the PCA territory (pattern 1) are possibly explained by proximal vessel pathology of the PCA. Ischemic lesions affecting the dorsal and lateral part of the hippocampus are most likely explained by occlusion of more distal PCA branches: the middle or posterior hippocampal artery (pattern 3) and the longitudinal terminal segments of the hippocampal arteries (pattern 2). In 3 cases we saw circumscribed small lesions, likely to indicate small embolic lesions in the most distal segments (pattern 4).

Possibly our most important finding is that we did not see patients with isolated infarct of the hippocampus. This contrasts with other diseases like herpes simplex encephalitis, paraneoplastic limbic encephalitis, or primary brain tumors which may predominately or exclusively involve one or both hippocampi as visualized with conventional T2-weighted MRI. Characteristic DWI lesions patterns limited to the hippocampus have also been described for transient global amnesia and complex-partial status epilepticus.\textsuperscript{17,18}

In contrast to these pathologies in acute HI additional extrahippocampal lesions in the PCA territory are highly likely. One previous MRI study evaluated hippocampal involvement in PCA stroke in 14 patients. In 7 of these with left or bilateral HI an amnestic syndrome was reported. In this retrospective study conventional T2-weighted sequences were analyzed, and no detailed neuropsychological data were available.\textsuperscript{19} By contrast, only 19% in our series showed obvious signs of hippocampal dysfunction on standard neuropsychological examination at presentation despite DWI lesions in the hippocampus. This difference could be attributable to the higher sensitivity of DWI for small acute ischemic lesions compared to T2-weighted MRI. Standardized neuropsychological examination in our study, however, revealed mildly or moderately impaired verbal long-term memory in patients with left HI, and nonverbal long-term memory deficits in patients with right HI. These memory deficits are in line with other temporal lobe pathologies, as described by lesional studies,\textsuperscript{20} functional studies with transient unilateral hippocampal electric stimulation in epilepsy patients,\textsuperscript{21} or functional MRI studies.\textsuperscript{22} These are cognitive areas that may well escape a standard neurological examination in acute stroke patients, which focuses on the most common items defined in the NIH stroke scale. This underlines the necessity of a detailed neuropsychological assessment. A recent study suggests that stroke lesions in the hippocampus may become even more relevant in the presence of a second pathology like Alzheimer dementia. The combination of the 2 pathologies may lead to the unmasking and decompensation of a fragile compensated functional state and may thereby be important in the physiopathology of mixed vascular dementia and Alzheimer’s disease.\textsuperscript{23}

Diffusion weighted MRI depicts the exact detail of ischemic lesions in HI. Several phenotypic lesion patterns can be distinguished, which tend to follow the vascular supply of the hippocampus usually in combination with additional acute lesions in extrahippocampal brain regions. Only a careful neuropsychological examination may be able to detect resulting memory deficits.

Disclosures

None.

References

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