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Subcallosal artery stroke: infarction of the fornix and the genu of the corpus callosum. The importance of the anterior communicating artery complex. Case series and review of the literature

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Abstract
Introduction Despite the variable anatomy of the anterior communicating artery (AcoA) complex, three main perforating branches can be typically identified the largest of which being the subcallosal artery (ScA). We present a case series of infarction in the vascular territory of the ScA to highlight the anatomy, the clinical symptomatology, and the presumed pathophysiology as it pertains to endovascular and surgical management of vascular pathology in this region.
Methods In this retrospective multicenter case series study of patients who were diagnosed with symptomatic ScA stroke, we analyzed all available clinical records, MRI, and angiographic details. Additionally, a review of the literature is provided.
Results We identified five different cases of ScA stroke, leading to a subsequent infarction of the fornix and the genu of the corpus callosum. The presumed pathophysiology in non-iatrogenic cases is microangiopathy, rather than embolic events; iatrogenic SCA occlusion can present after both surgical and endovascular treatment of AcoA aneurysms that may occur with or without occlusion of the AcoA.
Conclusion Stroke in the vascular territory of the ScA leads to a characteristic imaging and clinical pattern. Ischemia involves the anterior columns of the fornix and the genu of the corpus callosum, and patients present with a Korsakoff's syndrome including disturbances of short-term memory and cognitive changes. We conclude that despite its small size, the ScA is an important artery to watch out for during surgical or endovascular treatment of AcoA aneurysms.

Keywords Anterior communicating artery · Subcallosal artery · Fornix · Stroke · Infarction

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Purpose

The anterior arterial circulation is interconnected by the anterior communicating artery (AcoA) in the circle of Willis. Many variations can be found in the AcoA complex [1]. The AcoA harbors several important perforating branches. Serizawa et al. [2] classified them into three main groups according to their vascular territories. First, hypothalamic branches origin from the AcoA, being multiple and of small caliber and ending in the hypothalamic area. The second group of the perforating arteries is the chiasmatic branches. The third and most important vessel is the subcallosal artery (ScA), usually a single vessel and typically the largest of the arteries arising from the AcoA. The ScA mainly supplies the bilateral subcallosal areas but also the bilateral columns of the fornix and the genu of the corpus callosum. The ScA can be recognized in 91 % of the cases in a cadaveric study of the ACoA complex with a mean diameter of approximately 0.5 mm [3]. Lesions of the fornix may lead to severe clinical symptoms [4, 5]. Patients often initially present with acute confusion due to Korsakoff's syndrome, also known as amnesic-confabulatory syndrome. ScA infarction as the cause for a lesion of the fornix is rare with only a few case reports reported in the literature. We reviewed the pertinent literature

Table 1 Cases with ScA stroke confirmed by MRI

Reference, year	Age, sex	Initial presentation	Area of infarction	Presumed pathophysiology	Symptoms
Moudgil et al., 2000	71, F	Acute amnesia	Columns of Fo, genu of CC	Microangiopathy	Anterograde amnesia
Park et al., 2000	60, F	Acute loss of memory	Bilateral anterior Fo, Genu CC	Microangiopathy	Anterograde verbal and visual memory deficits
Moussouttas et al., 2005	61, M	Acute confusion	Bilateral anterior Fo, genu of CC, SP	Microangiopathy	Anterograde amnesia, impairment in word recall
Saito et al., 2006	NA	Sudden apathy	Bilateral anterior Fo, genu of CC	Microangiopathy	Anterograde amnesia
Hattingen et al., 2007	33, F	Incidental finding of AcoA aneurysm	Bilateral anterior Fo, anterior part of CC	Iatrogenic injury after clipping ACoA aneurysm	Anterograde amnesia, amnesic aphasia, personality changes, psychomotor slowing
Renou et al., 2008	68, M	Acute amnesia	Bilateral anterior Fo, genu of CC	Microangiopathy	Acute Korsakoff's syndrome with anterograde and retrograde amnesia
Chen et al., 2008	72, F	Acute stroke	Bilateral Fo	Microangiopathy	Anterograde amnesia, psychomotor retardation
Adamovich et al., 2009	53, F	Acute confusion	Bilateral anterior Fo	Microangiopathy	Anterograde and retrograde amnesia
Korematsu et al., 2010	52, M	Acute Amnesia	Unilateral left anterior Fo	Microangiopathy	Anterograde and retrograde amnesia
Murr et al., 2012	NA	Acute confusion	Bilateral anterior Fo	Giant cell arteritis	Anterograde amnesia
Mosimann et al., 2012	47, M	SAH due to rupture of an ACoA aneurysm	Bilateral anterior Fo, genu of CC, SP	Iatrogenic injury after coiling ACoA aneurysm+closure ACoA	Korsakoff dementia, anterograde and retrograde amnesia, dysphoria, dysexecutive syndrome
Ritzek et al., 2013	56, M	Acute amnesia	Bilateral Fo	Microangiopathy	Anterograde amnesia
Case 1	59, F	Unruptured ACoA aneurysm	Unilateral left anterior Fo	Iatrogenic injury after clipping ACoA aneurysm	Anterograde amnesia
Case 2	62, M	Acute amnesia when awake	Bilateral anterior Fo, genu of CC	Microangiopathy	Anterograde and some retrograde amnesia, MoCA score of 15/30
Case 3	32, F	Unruptured AcoA aneurysm	Bilateral anterior Fo, genu of CC	Iatrogenic injury after clipping ACoA aneurysm	Anterograde amnesia
Case 4	60, M	Unruptured AcoA aneurysm	Bilateral anterior Fo, genu of CC	Iatrogenic injury after clipping ACoA aneurysm	Memory difficulties, significant cognitive deficits in short-term memory
Case 5	71, M	Unruptured AcoA aneurysm	Bilateral anterior Fo, genu of CC	Iatrogenic injury after coiling ACoA aneurysm No closure of AcoA	Korsakoff dementia, attention and concentration difficulties, behavioral troubles

NA not available, *AA* arterial aneurysm, *ACoA* anterior communicating artery, *CC* corpus callosum, *Fo* fornix, *MoCA* Montreal Cognitive Assessment, *SAH* subarachnoid hemorrhage, *SP* septum pellucidum, *F* female, *M* male

and add five cases demonstrating the typical MRI pattern of ScA stroke leading to infarction of the fornix and the anterior part of the corpus callosum. Special emphasis is given in the discussion to the role of the ScA in the treatment of ACoA aneurysms.

Methods

We performed a retrospective multicentric case series study and identified five cases that were diagnosed with ScA stroke as confirmed by MRI. Cases were identified following retrospective review of the institutional database RIS PACS search

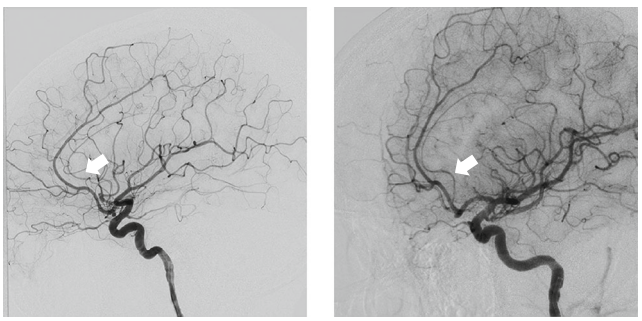

Fig. 1 **a**, **b** DSA of a left ICA injection. **a** Lateral view and **b** oblique view show the small-sized but visible ScA (*arrows*) originating from the AcoA complex

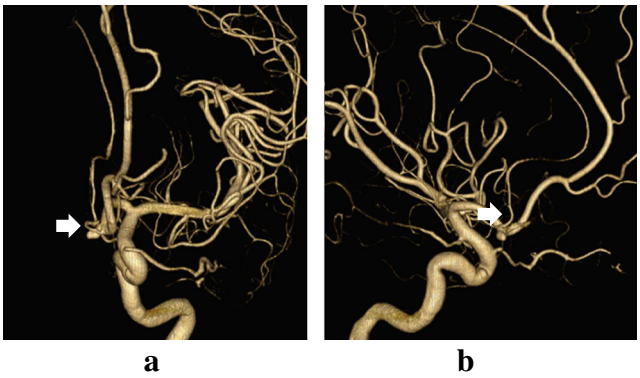

Fig. 2 3D rotational angiography ap and lateral projection allowing a better visualization of the typical course of the ScA (*arrows*) ending in this particular case in the median callosal artery. Note the proximity of the ScA origin to the AcoA aneurysm

engine (Montage TM) that allows for searching of specific terms in any part of the final radiologist's report. Specific search terms were fornix infarction, subcallosal artery, callosal infarction, and arterial ischemia in various permutations. Cases from 2000 to 2013 were searched. A PubMed literature research employing the same search terms in various permutations was used. IRB approval was obtained from the local hospitals' institutional review board. All available data were reviewed with respect to the patient's age, sex, clinical history, associated underlying pathomechanism, and symptoms as well as the location of the infarction and the imaging appearance. ScA stroke was defined as infarction of the uni or bilateral anterior columns of the fornix and the genu of the corpus callosum, with edema on T2 MRI and diffusion restriction. Additionally, a review of the literature is provided.

Results

We identified five different cases of ScA stroke confirmed by MRI in our centers. In four cases, both the fornix and the genu of the corpus callosum were affected. One case presented only with a unilateral fornix infarction. In four out of five cases, iatrogenic injury after surgical or endovascular treatment of AcoA aneurysms led to the infarction. Stroke occurred in one case without accidental or intentioned closure of the AcoA. The presumed pathophysiology in the non-iatrogenic case was microangiopathy. All our cases presented with amnesia and other memory deficits. Our literature review revealed 12 other cases of ScA stroke as confirmed by MRI [6–17]. In most of these cases the presumed pathophysiology was microangiopathy (n=9), except of two cases with iatrogenic injury of the AcoA complex and one case with a giant cell arteritis. All the previously published cases presented among others with anterograde amnesia as in our series. The results are summarized in Table 1.

In the following, we will highlight salient features of the ScA anatomy, the course of the ScA, its relationship to the fornix and the corpus callosum, and their stroke pattern on the basis of illustrative cases with different stroke etiologies.

Anatomy of the ScA in a patient with an AcoA aneurysm

The following figures (Figs. 1 and 2) show the anatomy of the ScA in a patient with an AcoA aneurysm.

Illustrative cases

Case 2

A 62-year-old male awoke with sudden onset of persisting anterograde amnesia and was admitted to our hospital. There were no other neurological defects on clinical examination. His memory did not improve and his cognition was impaired with a Montreal Cognitive Assessment (MoCA) score of 15/30. Initial CCT showed no evidence of intracranial hemorrhage or mass effect. Remote lacunar infarctions involving the basal ganglia on both sides were noted. MRI revealed an acute stroke affecting the bilateral anterior columns of the fornix and the genu of the corpus callosum with swelling on T2 and diffusion restriction (Fig. 3). Follow-up MRI of the brain revealed persistent diffusion restriction in the swollen fornices bilaterally with slight extension to the septum pellucidum and in the left side of the genu corpus callosum associated with T2 and FLAIR hyperintensity (Fig. 4). In addition to the previous MRI scan, there was subtle contrast enhancement of the fornices due to brain-blood barrier breakdown. The diagnosis of an infarction in the fornices bilaterally and left side genu of

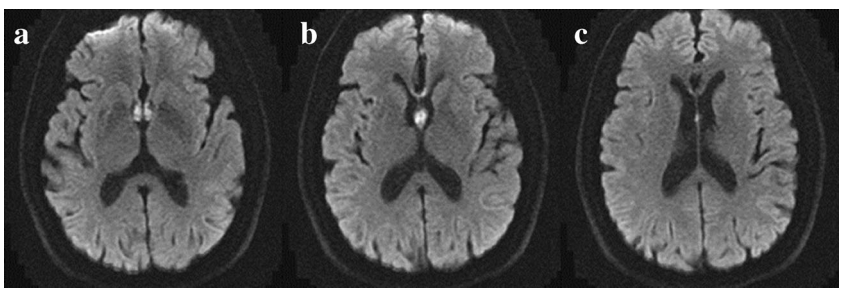

Fig. 3 **a**–**c** DWI MRI axial slides from caudal to cranial showing diffusion restriction in both columns of the fornix and the left side of the genu of the corpus callosum

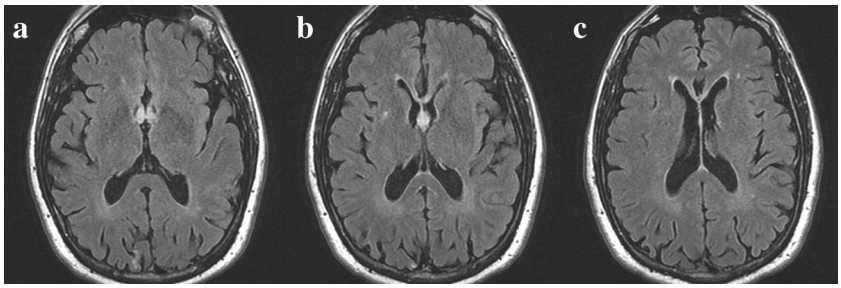

Fig. 4 **a**–**c** FLAIR MRI axial slides from caudal to cranial showing edematous swollen, hyperintensive both columns of the fornix and the left side of the genu of the corpus callosum

the corpus callosum likely related to small vessel atherosclerotic disease with occlusion of the ScA was made. At discharge, clopidogrel and atorvastatin expanded the patients' daily medication.

Case 1

A 59-year-old female presented to our hospital with multiple intracranial meningiomas and unruptured intracranial arterial aneurysms. A right-sided olfactory groove/planum sphenoidale meningioma enlarged impressively on follow-up MRI scan compared to 6 months ago. Progressive edema in the frontal lobe and the lesion enlarging over time prompted neurosurgical removal. At the same session, a 6-mm unruptured AcoA aneurysm was clipped via the same surgical interhemispheric trajectory (Fig. 5a). Baseline postoperative MRI demonstrated a small acute infarct within the left anterior column of the fornix with diffusion restriction (Fig. 5b, c). On clinical examination, she presented with a temporary anterograde amnesia. No other clinical or neurological deficits were noted.

Case 5

A 71-year-old man presented with an 8-mm unruptured AcoA aneurysm with a large 5-mm neck. He underwent uncomplicated elective coil embolization under full heparinization. The AcoA could be preserved (Fig. 6), and given the large size of the aneurysm, intravenous heparinization was continued for 24 h. When the patient woke up from anesthesia, he presented with a typical Korsakoff's syndrome with acute amnesia and a confabulatory state. Immediate MRI revealed an infarction of the bilateral columns of the fornix and the genu of the corpus callosum (Fig. 7). The AcoA remained patent. We hypothesized that the ScA arose in very close proximity to the sac, less likely from the sac proper, or that the sac had compressed the ScA. A dissection of the ScA origin due to complicated catheterization could not be ruled out but was deemed unlikely given that the aneurysm could be catheterized easily and no balloon remodeling was required. On clinical follow-up, 6 months later, attention and concentration difficulties as well as behavioral troubles remained.

Discussion

In this retrospective multicenter case series study with literature review, we analyzed patients with symptomatic ScA stroke as confirmed by MRI. Stroke in the vascular territory of the ScA leads to a characteristic imaging and clinical pattern. Ischemia involves the anterior columns of the fornix and the genu of the corpus callosum, and patients present with a Korsakoff's syndrome including disturbances of short-term memory and cognitive changes. The presumed pathophysiology in non-iatrogenic cases is microangiopathy, rather than embolic events; iatrogenic SCA occlusion can present after both surgical and endovascular treatment of AcoA aneurysms that may occur with or without occlusion of the AcoA.

Vascular anatomy

The anterior cerebral artery (ACA) is typically described as consisting of the following segments: the precommunicating (A1) segment, the communicating artery system (AcoA), the

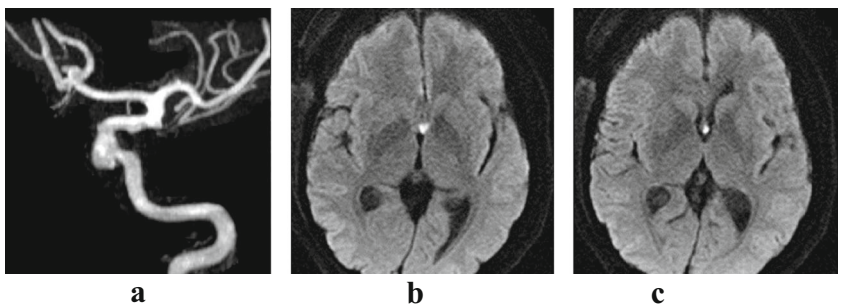

Fig. 5 **a** The pre-operative TOF MRA with an irregular bilobulated, saccular AcoA aneurysm. **b**, **d** The immediate postoperative DWI MRI demonstrating a tiny little infarction within the left anterior column of the fornix with diffusion restriction

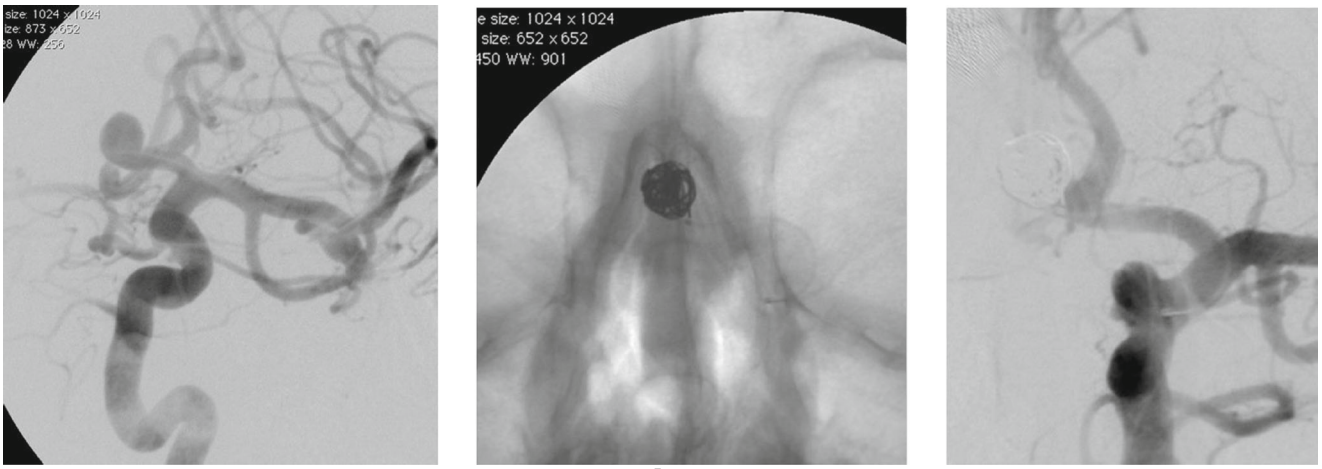

Fig. 6 **a** Pre-embolization DSA selective left ICA injection ap view showing the berry-type, saccular AcoA aneurysm. **b** Nonsubtracted ap view showing the coils and the microcatheter. **c** DSA ap view demonstrating the closure of the aneurysm

A2 segment distal to the AcoA and the branching between the callosomarginal and pericallosal artery (i.e., below the genu of the corpus callosum), and the A3 segment around the genu of the corpus callosum and the distal segments of A4 and A5. This proposed classification was introduced by Fischer in 1938 [18]. The branches originating from the most proximal aspects of the ACA were classified by Lasjaunias et al. [1] into two groups based on the findings of Lang [19]:

1. The hypothalamochiasmatic branches or the anteroinferior diencephalic arteries as called by Lang. These branches feed the infundibulum, optic chiasm, subcallosal area, the fornix, and the preoptic areas of the hypothalamus.
2. The striatocortical branches or the posterolateral inferior "diencephalic" group of Lang. One of the most important arteries from this group is the recurrent artery of Heubner.

Figure 8 shows a schematic drawing of the AcoA complex and its branches, modified after Serizawa et al. [2].

Fornix Papez circuit and clinical presentation

The fornix is a white matter tract bundle which acts as the major output of the hippocampus, arcing around the thalamus and connecting the medial temporal lobes to the hypothalamus [4]. It plays an important role in the formation and consolidation of declarative memories and is an important component of the classic Papez circuit [20]. Aggleton and Brown [21] suggested that the fornices are thought to contribute to the efficient encoding and normal recall of new episodic information. Input to the hypothalamus comes from various areas of association cortex that converge on the entorhinal and parahippocampal cortices in the temporal lobe. These feed into the dentate gyri of the hippocampus, which then converge on the hippocampus proper via the perforant and alvear pathways [4].

Yamada et al. described in 1998 that the hippocampal output is largely via the fornix, ending in the mammillary bodies of the hypothalamus. Fibers from the mammillary bodies pass backward into the anterior thalamic nuclei via the mammillothalamic tract and then on to the cingulate gyrus. The cingulum is then connected with the association cortices and also with the hippocampus [22].

Our series with the review of the literature showed clearly that almost all reported patients presented with very similar symptoms. First, an acute phase of confusion occurred together with subsequent anterograde amnesia. This is clearly related to the arterial supply of the ScA to the bilateral anterior columns of the fornix. The involvement of the genu of the

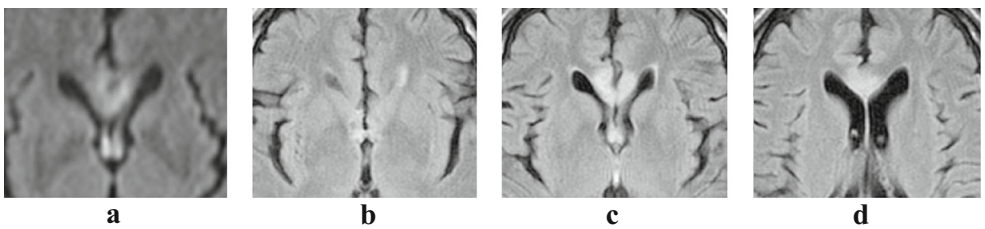

Fig. 7 **a**–**d** Immediate postembolization MRI. **a** Axial DWI MRI, **b**–**d** axial FLAIR from caudal to cranial demonstrating infarction with diffusion restriction and edema on FLAIR within the bilateral anterior columns of the fornix and the genu of the corpus callosum

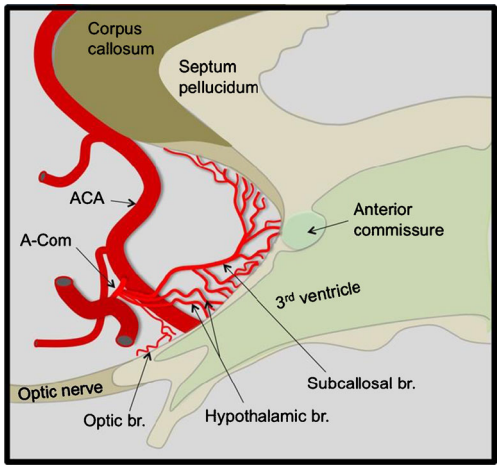

Fig. 8 Schematic drawing of the AcoA complex with its branches, modified after Serizawa et al. [2]. *A-Com* anterior communicating artery, *ACA* anterior cerebral artery, *br.* branches

corpus callosum, as seen in most of the cases, is not very likely to contribute to the presentations of the sudden-onset Korsakoff's syndrome.

Presumed pathophysiology

In 10 out of 17 cases, the presumed pathophysiology is microangiopathy due to small-vessel disease rather than arterial or cardio-embolism. The second most common and presumably underestimated cause is iatrogenic vascular injury after treatment of AcoA aneurysms. In this context, it does not matter if the injury occurs after surgery, coiling, thrombosis, or other ischemic complications during a procedure.

Differential diagnosis

Various different pathologies may affect the fornix. In most of the cases, midline tumors such as gliomas or lymphoma can infiltrate it. Herpes encephalitis may affect the fornix, as a part of the limbic system. Metabolic conditions such as Wernicke encephalopathy might be another differential diagnosis. The most common other causes of fornix affection are surgery and/or trauma [4]. However, diffusion restriction on MRI, and the acute patient's history, will lead to the right diagnosis.

Significance for the treatment of ACoA aneurysms

Gade reported already in 1982 amnesia in patients after operations on aneurysms of the AcoA [23]. Memory impairment following a ruptured aneurysm of the AcoA was demonstrated by Parkin et al. [24] in a single case. They concluded that their patient's symptoms were similar to those found in Korsakoff's syndrome, which is in accordance with our findings. The present review of 17 patients indicates a rather clinical presentation with anterograde amnesia due to fornix infarction, as confirmed by MRI in all cases. As the supply of the fornix is mainly fed by the ScA, one has to be very cautious regarding this perforating branch originating from the AcoA. Matsuoka et al. [25] reported of two cases they have treated with surgical clipping of AcoA aneurysms with both having a perforating artery branching from the top of the dome. In one case, the patient had permanent memory impairment postoperatively, and the other patient did not show any neurological deficit. In the first case, memory impairment was considered as the natural outcome due to the interruption of blood flow of the ScA by the clipping of the aneurysm. On the other hand, in the second case, sufficient collateral blood flow from A2 to the subcallosal area might have prevented damage. However, until now, only one case has been reported that demonstrated a fornix infarction and Korsakoff's dementia after coiling of a large AcoA aneurysm. In this particular case, the cause might have been the accidental closure of the AcoA, thus leading to closure and stroke of the ScA with subsequent fornix infarction. We add one case to the literature and present for the first time that this might even occur without accidental or intentioned closure of the AcoA. As not all patients do receive a standard post-embolization MRI in daily practice, the here underlying pathomechanism might be underestimated in the treatment of AcoA aneurysms but is, however, crucial. We conclude that despite its small size, the ScA is an important artery to watch out for during surgical or endovascular treatment of AcoA aneurysms.

Ethical standards and patient consent We declare that this manuscript does not contain clinical studies or patient data.

Conflict of interest We declare that we have no conflict of interest.

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