



Original Article

Clinical outcome of selective amygdectomy in a series of patients with resistant temporal lobe epilepsy

Guive Sharifi¹, Mohammad Hallajnejad¹, Samaneh Sadat Dastgheib², Mahmoud Lotfinia³, Omidvar Rezaei Mirghaed¹, Arsalan Medical Amin¹

¹Department of Neurosurgery, Skull Base Research Center, Shahid Beheshti University of Medical Science, Tehran, Iran, ²Department for General Psychology and Cognitive Neuroscience, Friedrich Schiller University of Jena, Jena, Thuringia, ³Department of Neurosurgery, Klinikum Saarbrücken, University of Saarland, Saarbrücken, Saarland, Germany.

E-mail: Guive Sharifi - guivesharifi@hotmail.com; Mohammad Hallajnejad - hallajnejad@gmail.com; Samaneh Sadat Dastgheib - samanehsadat.dastgheib@uni-jena.de; Mahmoud Lotfinia - mda617@yahoo.com; Omidvar Rezaei Mirghaed - info@drrezaee.ir; *Arsalan Medical Amin - dr.arsalanamin@gmail.com



*Corresponding author:

Arsalan Medical Amin,
Skull Base Research Center,
Shahid Beheshti University of
Medical Science, Tehran, Iran.

dr.arsalanamin@gmail.com

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ABSTRACT

Background: Selective amygdalohippocampectomy is one of the main approaches for treating medial temporal lobe epilepsy (TLE). We herewith describe seven cases of amygdala lesions treated with selective amygdectomy with the hippocampus saving procedure. Furthermore, we explain the trans-middle temporal gyrus transventricular approach for selective amygdectomy.

Methods: We studied patients with TLE who underwent selective amygdectomy with hippocampal saving procedure between March 2012 and July 2018. We preferred the trans-middle temporal gyrus transventricular approach. We adopted pterional craniotomy with extensive exposure of the base and posterior of the temporal lobe. The posterior margin of resection in the intraventricular part of the amygdala was considered the inferior choroidal point. Medially anterior part of the uncus was resected until reaching the ambient cistern. We applied the transcortical transventricular approach for selective amygdectomy in all patients.

Results: We present 11 cases having an amygdala lesion in our series, seven of whom underwent selective amygdectomy with hippocampal sparing. Nine patients had neoplastic lesions, and in two of them, gliosis was evident. Total resection of the lesion was achieved in all cases based on postoperative magnetic resonance imaging. No unusual complication or surgically-related new neurological deficit occurred.

Conclusion: We consider the resection of the amygdala until the inferior choroidal point sufficient for the disconnection of its circuits, which results in more effective control of seizures and reduction of surgery time and complications.

Keywords: Amygdala, Amygdectomy, Case series, Clinical outcome, Medial temporal lobe epilepsy

INTRODUCTION

About 50 million people worldwide have epilepsy, which portrays epilepsy as one of the most prevalent diseases of the brain and is responsible for 0.7% of the global burden of disease. With a rate of 5% in Iran, the prevalence is even higher in developing countries.^[27] Although more than 30 antiepileptic medications are available, nearly one-third of epileptic patients continue to have seizures while using two or more anti-seizure medications, a condition known as intractable or refractory epilepsy.^[23] Surgery is considered the primary therapeutic approach in

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patients who have refractory epilepsy, often done to resect the minimal area of the cortex, which triggers seizures, known as the epileptogenic zone.^[16,27] Among different types of epilepsy, temporal lobe epilepsy (TLE) is the highest target for neurosurgery. The International League Against Epilepsy defines two main subtypes of TLE; one is mesiobasal involving the amygdala and hippocampus, sometimes known as mesial TLE (MTLE), and the other is lateral, which incorporates the neocortex.^[16]

Amygdala is a complex structure in the medial temporal lobe.^[33] Amygdala and hippocampus play a significant role in MTLE, and selective amygdectomy is one of the main approaches for treating MTLE.^[5,38] Although hippocampus resection generally is considered a safe procedure, it can accompany threatening complications.^[19] Whereas the incidence of sclerosis and neoplastic lesions is scarce in the amygdala, there is no clear guideline in literature for decision-making about the best approach for treating MTLE with amygdala lesions without the involvement of the hippocampus. Moreover, the anatomical position of the amygdala is in a delicate area, and essential structures, such as the anterior choroidal artery, optic tract, and oculomotor nerve are in the vicinity; so, the familiarity of every surgeon to the anatomy of this area and technique of surgery is critical to avoid complication.^[7]

We describe 11 MTLE cases associated with amygdala lesions, seven of whom were treated by selective amygdectomy with a hippocampus saving procedure. We also explained the trans-middle temporal gyrus transventricular approach for selective amygdectomy, the standard approach in our hospital.

MATERIALS AND METHODS

We enrolled patients with TLE referred to our service for amygdectomy between March 2012 and July 2018. All patients signed informed consent to take part in this study. The institutional research board and committee approved the protocol of this study of ethics.

A thorough history and physical examination, brain magnetic resonance imaging (MRI) for localization of the probable lesions, and identifying the anatomy, plus the electrodiagnostic and neuropsychiatric tests were performed before the operation. Only patients whose MRI did not indicate hippocampal involvement or hippocampal sclerosis were selected for this specific procedure since hippocampal sclerosis alone could develop an epileptic zone.

The surgeon performed selective amygdectomy using the trans-middle temporal gyrus transventricular approach [Figure 1]. After general anesthesia, the patient is positioned supine with a head rotation of 45°. We adopted pterional craniotomy with extensive exposure of the base and posterior

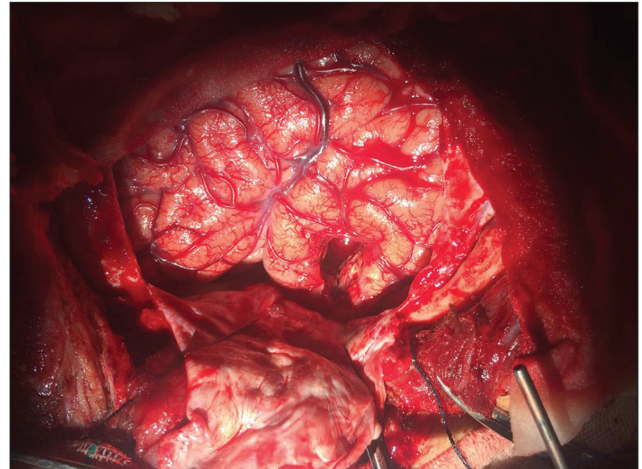


Figure 1: Intraoperative view of the trans-middle temporal gyrus transventricular approach.

of the temporal lobe, and dura matter was opened in a C-type fashion. We preferred to determine the site of corticotomy with navigation. However, if it was not available, a 2 cm corticotomy about 2–3 cm above the middle fossa floor on the middle temporal gyrus could provide direct access to the temporal horn of lateral ventricles.

After opening the ependymal layer of the lateral wall of the temporal horn of the lateral ventricle, the collateral eminence, hippocampus, lateral ventricular sulcus, choroidal fissure, inferior choroidal point, choroid plexus, fimbria of the fornix, and amygdala were exposed. Hippocampus is located between the collateral sulcus laterally and choroidal fissure medially. The lateral ventricular sulcus separates the hippocampus from the collateral eminence, extending anteriorly toward the amygdala-hippocampal junction. The medial border of the hippocampus is the choroidal fissure, and the inferior choroidal point is at the most anterior and inferior point of the choroidal fissure. The anterior choroidal artery passes through the inferior choroidal point to enter into the temporal horn of the lateral ventricle. The amygdala forms the anterior wall of the temporal horn of the lateral ventricle. Superiorly, the amygdala blends into the globus pallidus; inferiorly, the temporal amygdala bulges inferiorly into the most anterior portion of the roof of the temporal horn above the hippocampal head and the uncus recess; medially, it is related to the anterior and posterior segments of the uncus. The uncus recess separates it from the head of the hippocampus. The anterior segment of the uncus, which contains the amygdala, has a close anatomical relationship with the internal cerebral artery (from the origin to bifurcation/trifurcation of the middle cerebral artery) M1 segment of the middle cerebral artery and globus pallidus; therefore, extreme care was taken during the removal of the amygdala. After the borders of the planned resection have been delineated via visual inspection and frameless

navigation, the amygdala was resected in a sub-pial fashion to the inferior choroidal point. After hemostasis, the dura is closed in a watertight fashion; the bone flap is replaced, the temporal muscle, fascia, galea, and skin are closed properly.

The patients were then transferred to the neurosurgical intensive care unit and managed according to routine protocols. After transfer to the general ward, a postoperative MRI was performed to investigate the extent of resection. With every event during their admission recorded, the patients were followed up for related events after their discharge.

RESULTS

From 2012 to 2018, amygdalohippocampal lesions based on neuroimaging were diagnosed in 11 MTLE cases; of those, seven underwent selective amygdalectomy. The age range was between 17 and 57 years (mean 31 years). The mean follow-up duration was 3.5 years. The clinical characteristics of the patients are summarized in [Table 1]. Most patients presented with intractable, drug-resistant, MTLE which is defined as “failure of adequate trials of two tolerated, appropriately chosen and used antiepileptic drug schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom.” One patient came with just one episode of the seizure [Figure 2], and one patient presented with complex partial seizures, depression, anxiety, and memory deficits. In one interesting case, the symptoms presented with complex partial seizure with hemiparesis during the seizure [Figure 3]. Aura was oroalimentary in seven patients, and two patients presented with olfactory aura and anxiety before the complex partial seizure. In two cases, the neoplastic lesion of the amygdala expanded to surrounding structures. Magnetic resonance imaging revealed an amygdala lesion with expansion to internal capsule fibers.

The transcortical transventricular approach was applied to perform selective amygdalectomy in all patients. In five patients, neuronavigation was used for localization. In seven patients, selective amygdalectomy was performed [Figure 4], three patients underwent amygdalohippocampectomy plus anterior temporal lobectomy [Figure 5], and in one patient, selective amygdalohippocampectomy was done. Total resection of the lesion was achieved as far as the patient consented in all cases based on postoperative MRI. Regarding seizure control, seven patients who presented with refractory epilepsy achieved Engel Class Ia, and in one patient who came with just one episode of seizure, the attack did not recur. No unusual complications and surgically related new neurological deficit occurred during hospitalization.

In a patient with ependymoma as the etiology of the mesial temporal lesion, extensive recurrence with CSF dissemination occurred 1 year after surgery, and finally, he died due to this complication. The patient who presented with depression and anxiety showed improvements in memory function and mood. Other patients did not have any specific event during follow-up.

DISCUSSION

The amygdala is an evolutionarily ancient structure present even in reptiles. The name, derived from the Greek, denotes an almond-like shape structure in the medial temporal lobe. It is a complex structure where many circuits that correlate affective and social behaviors intertwine.^[17] The regions described as amygdala nuclei encompass several structures with distinct connectional and functional characteristics in humans and other animals. The basolateral complex, the cortical nucleus, the medial nucleus, and the central nucleus are the primary nuclei of the amygdala.

Table 1: The clinical characteristics of the patients are summarized.

S. No.	Age	Side	Presentation	Technique	Seizure outcome	Pathology
1.	25	L	CPS, oroalimentary aura	SA	Class Ia	Gliosis
2.	22	L	Refractory epilepsy	SA	Class Ia	Gliosis
3.	57	L	CPS, depression, memory deficit	SAH+ATL	Symptom-free	Anaplastic astrocytoma
4.	51	L	Refractory epilepsy	SA	Class Ia	FCD type II
5.	20	L	Refractory epilepsy	SA	Class Ia	Ganglioglioma
6.	24	L	One episode of CPS	SA	Symptom free	Low-grade astrocytoma
7.	42	L	CPS, visual aura, right complete hemianopia	SA	Class Ia	Ependymoma
8.	17	R	Refractory epilepsy, hemiparesis, right homonymous hemianopia	SAH	Class Ia	Low-grade astrocytoma
9.	25	R	Refractory epilepsy	SAH+ATL	Class Ia	FCD type II
10.	26	L	Refractory epilepsy	SA	Class Ia	FCD type I
11.	27	L	Refractory epilepsy	SAH+ATL	Class Ia	Oligo astrocytoma

CPS: Complex partial seizure, SA: Selective amygdalectomy, SAH: Selective amygdalohippocampectomy, ATL: Anterior temporal lobe resection, FCD: Focal cortical dysplasia

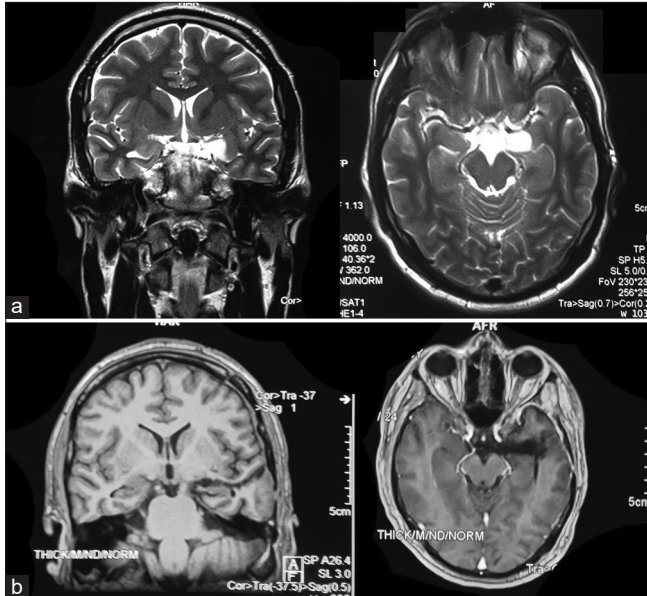


Figure 2: (a) Preoperative MRI of a 24-year-old man presenting with one episode of complex partial seizure. The lesion can be seen in the left amygdala. He underwent selective amygdectomy. Pathology was low-grade astrocytoma. (b) Postoperative MRI of the same patient.

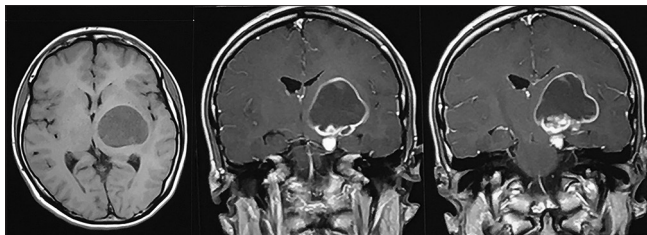


Figure 3: A 17-year-old man with refractory seizures and progressive hemiparesis and right homonymous hemianopia. The origin of the tumor was left the optic tract.

Knowledge about amygdala connections is critical to understand the semiology of its lesions. The amygdala received many input fibers from different subcortical structures in the brain, such as the hypothalamus, basal ganglia, septal region, and autonomic centers of the brainstem. The input fibers are mainly sensory, and the amygdala receives input from modalities such as olfactory, somatosensory, gustatory, visceral, auditory, and visual.^[28-30,35,36] The output fibers of the amygdala are mainly through two efferent fiber systems: Stria terminals and ventral amygdalofugal pathway, by which it connects to variable structures such as the cerebral cortex, limbic system, mediodorsal of the thalamus, and hypothalamus.^[2,11,31]

In our series, among 11 cases having amygdala lesions, seven patients underwent selective amygdectomy. Electrodiagnostic indicated the medial temporal lobe as

the epileptogenic zone, and semiology of seizure such as oroalimentary, visual, and olfactory aura seems to relate to the amygdala involvement.^[13] Amygdala-related seizures may have atypical manifestations, such as panic and anxiety attacks, which were the main seizure presentation in one of our cases.^[4] Accordingly, having the amygdala in mind as an epileptogenic zone is of diagnostic importance in these patients.

There are significant controversies regarding the best surgical approach for TLE. Selective amygdalohippocampotomy and anterior temporal lobe resection are the primary surgical approach warranted seizure control and low complication.^[34,39] Because of the paucity of amygdala lesions, there is limited evidence of selective amygdectomy in literature though it has been prompted since 1991.^[12] In cases with nonlesional amygdala with hippocampal sclerosis and failure of the Wada test, corticoamygdectomy is safe and advisable; however, the rate of seizure control is lower than amygdalohippocampotomy.^[25] If the amygdala has a lesion, there is no clear cut for decision-making in the literature, whether to save the hippocampus or not. Usui *et al.* have reported 15 cases of amygdala lesions in 2018.^[40] They achieved acceptable results regarding seizure control using selective amygdalohippocampotomy or anterior temporal lobectomy in their series. Although selective amygdalohippocampotomy is an overall safe procedure, complications, such as damage of fornix fimbria and optic radiation, memory deficit, and neuropsychiatric disorders, can be accompanied by complications. The most threatening complication is vascular events, such as choroidal arteries during coagulation or dissection of choroidal fissure,^[14] so we decided to implement selective amygdectomy with hippocampal sparing. In seven cases for whom we performed selective amygdectomy with saving the hippocampus, patients achieved seizure control; this could provide the rationale for selective amygdectomy in MTLE patients having an amygdala lesion.

From the pathophysiological view, mesial temporal lobe sclerosis is the leading cause of MTLE, with most of the debate regarding the MTLE's etiology favors the loss of net inhibition in the hippocampal structure due to the extensive loss of pyramidal neurons in mainly in the CA3 (cornu ammonis) and CA1 subfields of the hippocampus^[3,9,21] as the main feature of mesial temporal sclerosis. Thus, sclerosis could develop into an active epileptic zone, causing a majority of the seizures. However, the whole scenario MTLE is complex and has other scenes and players, one of which is the amygdala. The extreme susceptibility of the amygdala of several species to electrical kindling, which is a long established animal model of epileptogenesis, could be a shred of evidence that explains the potential role of the amygdala in the initiation of the MTLE.^[18,26]

Interictal spikes, including spike-wave and polyspike complexes, have been seen in the amygdala during epileptic surgery. However, more studies recruiting intraoperative recordings are crucial before jumping to conclusions.^[26]

Previously, Graebenitz *et al.* reported spontaneous discharges in the lateral amygdala recorded from brain slices derived from patients with intractable MTLE, especially in those whose sclerosis was minimal.^[18,26] Basolateral nuclei of the amygdala are the primary output nuclei of it.^[1,32] Anatomically, it is located on the inferior and lateral aspect of the amygdala and projects widely to the temporal neocortex and hippocampus. Another study by the same group showed a directed propagation of synaptic signals in spontaneously active epileptic human brain slices.^[18] It is beyond the scope of this article. However, we consider that resection of only this part during selective amygdalohippocampectomy may be enough for the disconnection of amygdala circuits and control the seizure and reduce the time of surgery and complications.

In the histopathologic evaluation, three patients were diagnosed with low-grade astrocytoma, one with high-grade astrocytoma, two cases with gliosis, one with ganglioglioma, one ependymoma, and three with focal cortical dysplasia (FCD). We want to highlight FCD as one of the most common pathologies in the amygdala. In most cases, it is frequent in MTLE with normal MRI; its differentiation from neoplasm is almost impossible. FCD often causes amygdalar

enlargement, and a volumetric study of the amygdala may help the diagnosis. The surgical outcome of seizure control in a patient with FCD as the cause of MTLE is quite good.^[6,10,22,24]

Before decision-making to remove the amygdala, extreme attention is essential to some rare lesions that could imitate amygdala lesions in neuroimaging. Neoplastic lesions that arose from the optic tract have a closed anatomical relationship with the amygdala. Anatomically, the optic tract is located posteromedial to the amygdala, and sometimes, we can see it after removing the posteromedial border of the amygdala during surgery. It is difficult to differentiate these lesions, but some clues may help the diagnosis. Amygdala tumors usually extend in an anteromedial direction, but optic tract gliomas extension is predominantly posterolateral. Besides, contralateral hemianopia and the absence of seizure are in favor of optic tract lesions. We will discuss the characteristics of these specific types of tumors in another series.

Different approaches are defined as selective amygdalohippocampectomy.^[7,8,15,20] In our institute, we prefer the trans-middle temporal gyrus transventricular approach for selective amygdalectomy. In seven out of 11 patients, we saved the hippocampus and performed selective amygdalectomy. The posterior margin of resection in the intraventricular part of the amygdala was considered the inferior choroidal point. Medially anterior part of the uncus was resected until reaching the ambient cistern. Superior extension of resection was less specified, and it depends on the extension of the lesion, but care must be taken to avoid injury to globus pallidus. Tan and Byrne defined anterior temporal sulcus (ATS) as the superior border of the amygdala during surgery.^[37] They defined the ATS as a pia-arachnoid fold located near the temporal pole (usually within 2 cm) at the junction of the superior and medial surfaces of the temporal lobe. It can be readily identified on coronal MRI and often with temporal arterial branches of the middle cerebral artery traversing within.

Our studies have several limitations, including the few numbers of participants. Other limitations are the study's

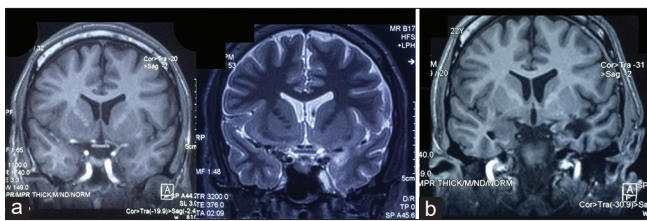


Figure 4: (a) Preoperative MRI of a 22-year-old man with a history of 3 years of epilepsy. The lesion can be seen on the left amygdala. (b) Postoperative MRI of the same patient. The lesion is totally resected. The superior border of resection reached the inferior border of globus pallidus.

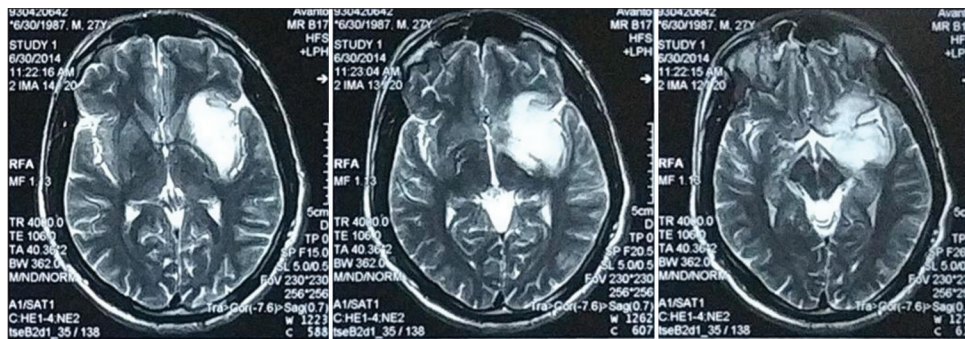


Figure 5: A 27-year-old man with refractory seizures. The involvement of internal capsule fibers and the insular lobe can be seen on MRI.

retrospective nature and the lack of EEG video monitoring after the operation. As a suggestion, some solutions will be designing multicentric studies with a control group and an extended follow-up period.

CONCLUSION

More extensive studies are required to determine both the role of the amygdala in the pathophysiology of MTLE and the long-term outcome of selective amygdectomy in patients with resistant MTLE. We consider the resection of the amygdala until the inferior choroidal point sufficient for the disconnection of amygdala circuits, seizure control, and, accordingly, reduce the time of surgery and complications.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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