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Neuropsychologist's (re-)view: Resective versus ablative amygdalohippocampectomies

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ABSTRACT

Pharmacoresistant mesial temporal lobe epilepsy (mTLE) represents the major indication for epilepsy surgery. Since epilepsy surgery is an elective treatment option, preserving cognition is a high priority. Given the essential role of temporomesial structures in declarative long-term memory formation, surgical treatment for mTLE is primarily associated with a risk of material-specific memory decline, but other cognitive domains may be affected as well. The major determinants for the neuropsychological outcome are the functional integrity of surgically affected tissues, the functional reserve capacities of the remnant brain, the postoperative seizure outcome, as well as the quantitative and qualitative changes of antiepileptic drugs.

Anterior temporal lobectomy has long been the standard procedure for treating mTLE. However, if an exclusive mesial pathology is present, then functional non-pathological tissues of the temporal pole and neocortex are sacrificed. As a result, more selective or tailored surgical approaches have been developed which strive towards minimizing iatrogenic effects. However, whether or not these approaches are equipotential with regard to seizure control is still a matter of debate. The quality of the presurgical diagnostics could also be decisive. Selective surgery should indeed be selective in terms of preventing evitable collateral cortical damage along the approach. Invasivity and risks of collateral damage associated with "open" selective resective surgery are further minimized by stereotactic ablative surgery via thermocoagulation, or eventually even eliminated by gamma knife surgery.

From a neuropsychological point of view, this development is consequent and desirable, but no clear scientific evidence of a superior cognitive outcome after radiosurgery or thermocoagulation currently exists. The studies that are available contain significant methodological limitations. Thus, randomized head-to-head cognitive outcome studies of competing selective procedures are needed, which should meet the minimum requirements for study design and neuropsychological evaluations.

Finally, none of the surgical treatment variants can systematically prevent memory decline when the hippocampus is targeted.

1. Neuropsychological risks of temporal lobe surgery

Hippocampal sclerosis is the leading etiological cause of pharmacoresistant mesial temporal lobe epilepsy (mTLE), and thus represents the most frequent indication for epilepsy surgery. Given the essential role of the hippocampus for declarative long-term memory formation, surgically treating mTLE could result in significant deterioration of anterograde memory functions. The most dramatic postsurgical consequence would be global amnesia, i.e. the complete disruption of long-term memory formation. This anterograde amnesia is often accompanied by retrograde memory deficits. Global amnesia was observed after bilateral mesial temporal lobe resections (Scoville and Milner, 1957) (which is why this procedure is no longer performed), and after unilateral temporal lobe surgery when the contralateral homologue structures were not functional or subsequently lost function due to pathological processes (Dietl et al., 2004). Unilateral temporal lobe surgery can cause or aggravate material-specific memory deficits if contralateral structures are unaffected (Milner, 1972). Resections within the dominant (typically left) hemisphere are primarily associated with deteriorations in verbal memory, whereas right temporal lobe surgery mostly affects non-verbal memory functions. However, the hippocampal system is usually organized bilaterally, and the material-specific preference is due to the hemispheric specialization of the neocortex and not of the hippocampi per se (Helmstaedter et al., 1997). Accordingly, unilateral resections usually do not eliminate verbal or nonverbal long-term memory functions, but instead lead to a decline in

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the performance level. Furthermore, left temporal lobe surgery may also diminish non-verbal memory, and right temporal lobe resections may be accompanied by additional verbal memory declines (Helmstaedter, 2013).

2. Determinants of cognitive outcome

Since epilepsy surgery is an elective treatment option, preserving cognition is a high priority. The major determinants of the postsurgical neuropsychological outcome are: (1) the functional integrity of the resected tissues (Chelune, 1995); (2) the reserve capacities and functional plasticity of the remnant brain, in this case, the contralateral temporomesial structures in particular (Helmstaedter, 1999); and (3) the postsurgical seizure outcome (Helmstaedter et al., 2003). Finally, reducing the antiepileptic drug load and withdrawing antiepileptic agents with unfavorable cognitive profiles can also enhance the postsurgical cognitive status (Helmstaedter et al., 2016).

The functional integrity of the epileptogenic hippocampus to be resected primarily depends on the severity of the underlying pathology and is decisive for memory change after the surgical treatment of mTLE (Chelune, 1995). Thus, resecting a severely sclerotic hippocampus will cause less memory decline than only resecting the mildly affected or even non-lesional hippocampus (Witt et al., 2015).

3. Searching for the optimal surgical procedure

Postoperative neuropsychological deteriorations are not only related to the functional integrity of the targeted epileptogenic lesion, but also to the preservation of adjacent or distant tissues that are intentionally or accidently affected by the surgical procedure. This is the central theme of this article. From a neuropsychological point of view, the best approach would be the most selective surgical procedure with a low risk of collateral damage that provides a high chance of achieving continuous seizure freedom.

A two-thirds anterior temporal lobectomy (ATL) is the standard procedure for the surgical treatment of TLE. However, with an exclusively temporomesial pathology (e.g. hippocampal sclerosis), ATL unnecessarily sacrifices non-pathological functional tissue, thus causing otherwise preventable neuropsychological deterioration (Helmstaedter, 2013).

In addition to an individually tailored ATL which minimizes collateral damage to a certain degree, other more selective standard procedures have been developed that strive towards sparing non-pathological tissues. Whether or not selective surgery is equipotential with regard to seizure control is still a matter of debate (Josephson et al., 2013). However, the quality of presurgical diagnostics must be taken into consideration as well. If presurgical diagnostics reveal a clearly localized, circumscribed epileptogenic zone, then selective surgery will most likely be successful. Otherwise, more extensive surgery increases the probability of including relevant epileptogenic tissues. Furthermore, if a selective or superselective surgery is not successful, then more extensive surgery can still be offered to the patient (Grote et al., 2016).

Selective amygdalohippocampectomy (SAH), first introduced by Wieser and Yaşargil (1982) spares the temporal pole and the temporolateral cortex and thus leads to a beneficial neuropsychological outcome when compared to that of ATL (Helmstaedter, 2013). However, the published evidence suggests that the superior cognitive outcome is not univocal and raises the question of just how "selective" selective surgery really is. In particular, the surgical approach to the hippocampus might affect the cognitive outcome. Three major approaches to the temporomesial structures have been established: the transsylvian, the transcortical, and the subtemporal approach. All three variants intentionally sacrifice non-pathological functional tissues along the approach with the additional risk of collateral damage (Table 1). The degree of collateral damage adjacent to the transsylvian or transcortical approach negatively affects postsurgical learning and recognition performance (Helmstaedter et al., 2004). Studies comparing the neuropsychological outcome of at least two different selective approaches are rare and reveal only minor differences in memory outcome (for an overview see Helmstaedter, 2013). One randomized study found a superior outcome in executive function following a transcortical versus a transsylvian SAH (Lutz et al., 2004). At first glance, there appear to be some promising results regarding memory outcome after subtemporal (temporobasal) SAH with almost no verbal memory decline (Hori et al., 2007). However, this approach intentionally sacrifices fusiform gyrus tissue which is critically involved with face recognition (especially within the right hemisphere). Another study (von Rhein et al., 2012) demonstrated a worse outcome after subtemporal (temporobasal) SAH with regard to nonverbal memory and verbal fluency compared to transsylvian SAH. This was attributed to the affection of the fusiform gyrus and the temporobasal language area. Park et al. (1996) developed a transparahippocampal subtemporal approach that spares the fusiform gyrus with preliminary evidence showing a good neuropsychological outcome (Robinson et al., 2000).

Another approach for reaching temporomesial structures is a limited pole resection with subsequent amygdalohippocampectomy. Compared to the transsylvian SAH, this surgical strategy resulted in superior verbal memory outcome after left-sided surgery and inferior nonverbal memory outcome after right-sided surgery (Helmstaedter et al., 2008). These findings were discussed in the light of the disparate relevance of the temporal stem (which is affected by transsylvian SAH) versus the temporal pole with regard to material-specific memory functions.

A further step towards minimizing collateral damage is

Table 1
Overview of surgical variants for treatment of mesial temporal lobe epilepsy.

Surgical procedure	Cranial access	Intended sacrificed tissues	Tissues at risk	Cognitive functions at risk (beyond hippocampus mediated memory)
Standard 2/3 ATLR	Craniotomy	Temporal pole Temporolateral neocortex	–	Language and verbal learning after left-sided surgery
Tailored ATLR	Craniotomy	Temporal pole Temporolateral neocortex	–	?
Pole resection + AH	Craniotomy	Temporal pole	–	Nonverbal memory after right-sided surgery [a]
Transsylvian SAH	Craniotomy	Temporal stem	Superior temporal gyrus Frontal lobe	Verbal fluency [a]
Transcortical SAH	Craniotomy	Middle temporal gyrus	–	–
Subtemporal temporobasal SAH	Craniotomy	Fusiform gyrus	Inferior temporal gyrus	Nonverbal memory, semantic fluency [a]
Subtemporal transparahippocampal SAH	Craniotomy	Parahippocampal gyrus	Inferior temporal gyrus	–
Stereotactic thermocoagulation	Borehole	–	Occipital lobe	–
Gamma knife surgery	–	–	(Radionecrosis)	–

ATLR, anterior temporal lobe resection; AH, amygdalohippocampectomy, SAH, selective amygdalohippocampectomy.
[a] Preliminary evidence based on single studies outlined in Section 3.