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# Outcome after epilepsy surgery in patients with MRI features of bilateral ammon's horn sclerosis

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Received 29 August 2012; received in revised form 17 December 2012; accepted 11 February 2013

Available online 13 March 2013

## KEYWORDS

All epilepsy/seizures;  
Epilepsy monitoring;  
Epilepsy surgery;  
Hippocampal sclerosis;  
Intracranial electrodes

**Summary** In refractory temporal lobe epilepsy with unilateral ammon's horn sclerosis (uAHS) resective epilepsy surgery is an established treatment option whereas little evidence exists about the consequences of unilateral hippocampal resection in patients with bilateral ammon's horn sclerosis (bAHS). The aim of this study was to evaluate the post-surgical outcome of patients with bAHS after selective amygdalo-hippocampectomy (SAH) in comparison to uAHS patients. For this purpose, all bAHS and uAHS patients, identified at our center between 2003 and 2009 were analyzed retrospectively. Thirty-one bAHS patients and 291 uAHS patients were identified. Only 55% of the bAHS, but 80% of the uAHS patients were referred for formal pre-surgical diagnostics ( $p=0.001$ ). Eleven bAHS and 127 uAHS patients underwent SAH. There was no difference in seizure-free outcome (Engel IA) at 12 months (bAHS 82% vs. 69%,  $p=0.40$ ) and 24 months follow up (bAHS 57% vs. 60%,  $p=0.80$ ). None of the bAHS patients became globally amnesic post-surgically. The favorable outcome in these highly selected bAHS patients suggests that bAHS patients may have a fair chance of becoming seizure-free after SAH. However, due to the large number of bAHS patients not undergoing formal presurgical evaluation, the results cannot be extrapolated to bAHS patients in general.

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## Introduction

In refractory temporal lobe epilepsy (TLE) with unilateral ammon's horn sclerosis (uAHS), unilateral anterior temporal lobectomy (ATL) and selective amygdalo-hippocampectomy

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(SAH) are established surgical treatment options with good chances of postoperative seizure-freedom (Elsharkawy et al., 2009; McIntosh et al., 2004; Thom et al., 2010). There is little evidence regarding surgical outcome for patients with MRI features of bilateral ammon's horn sclerosis (bAHS) so far (Boling et al., 2009; Cukiert et al., 2009). A frequent assumption is that these patients are inappropriate candidates for epilepsy surgery. The reasons for the reluctant use of surgical therapy options in this patient group have not been fully explored. Mainly two causes can be suggested: the expectation of poor seizure outcome (Jack et al., 1992) and the fear of severe memory deficits (Trenerry et al., 1996). The aim of this retrospective study at a tertiary referral center was to evaluate how many TLE patients with bAHS were pre-surgically studied, how many qualified for SAH, which proportion of them became seizure-free after operation in comparison to uAHS patients and whether postoperative memory deficits of bAHS patients differed from those having uAHS. Patient histories and clinical and paraclinical characteristics were used to detect etiological differences between uAHS and bAHS.

## Methods

All inpatients and outpatients of our tertiary referral epilepsy center at the University of Bonn diagnosed with bAHS on the basis of dedicated MR imaging at the Department of Radiology/Neuroradiology of this center from January 2003 to March 2009 were retrospectively identified from the database. As a comparator cohort for seizure outcome and to reveal etiological differences between the groups, all inpatients and outpatients of the same period with the visual MRI diagnosis of uAHS were assessed.

Pre-surgical candidacy selection is integral part of inpatient and outpatient assessment of each patient transferred to this institution. Every patient is evaluated by at least one experienced epileptologist. Performance of in-house high-resolution MRIs is part of the assessment and counseling of the patient with regard to the option of a potential referral to formal pre-surgical evaluation according to commonly accepted principles (Clusmann et al., 2006). In intracranial recordings of the bAHS patients, performed with depth and strip electrodes, the laterality index was calculated separately for clinical and subclinical seizures as the proportion of seizures arising from the predominantly epileptogenic hippocampus. The required number of seizures and judgment of eligibility for surgery according to the laterality index of clinical seizures depended on individual decisions of treating physicians.

Clinical and paraclinical data were retrospectively obtained from the patient records. For all patients with the diagnosis of uAHS and bAHS on in-house MR images, the following data were collected: gender, age at epilepsy onset and disease duration, initial precipitating injuries (IPI) (Mathern et al., 1995), additional potential epileptogenic MRI-lesions and results of formal neuropsychological evaluation. In addition, for the operated patients in both groups, age at operation, non-invasive and invasive EEG data and side of surgery were noted.

## MRI

Brain MRIs were obtained according to a dedicated epilepsy protocol (Urbach et al., 2004) using a 3 Tesla Scanner, Philips, The Netherlands (Department of Neuroradiology). All MRIs were re-analyzed for this study. To confirm the visual radiological diagnosis of bAHS, MRI-T2-relaxometry in bAHS patients was performed as described previously (von Oertzen et al., 2002). Only patients with visual diagnosis of bAHS in terms of bilateral atrophy and signal increase in combination with bilaterally elevated relaxation times were considered as bilaterally affected.

## Neuropsychological assessment

All operated bAHS patients were assessed by clinical impression with dedicated history taking regarding day-to-day memory function as well as standardized neuropsychological assessments pre- and postsurgically (at 12 months) according to previously published protocols (Helmstaedter et al., 2008). Verbal memory was assessed by a list learning design (15 items), and figural memory by a design learning test using 9 items (Helmstaedter et al., 1991, 2000). Memory deficits were defined as performance below one standard deviation of normal, age-matched control persons.

Catastrophic memory outcome which comes close to global amnesia was defined as no correct word recalled out of learned words in verbal free delayed recall plus random recognition performance in delayed verbal and figural memory as well.

## Neuropathological assessment

Biopsy specimens were obtained from all bAHS and uAHS patients with chronic pharmaco-resistant TLE, who underwent surgical treatment in the epilepsy surgery program at the University of Bonn Medical Center. Surgical removal of the hippocampus was clinically indicated in every case. Standardized neuropathological analysis was performed in all patients under study (Blumcke et al., 2007).

## Follow up

Follow up investigations were carried out in operated bAHS and uAHS patients 12 months and, if available, 24 months after surgery. Patients with post-surgical follow up periods less than 12 months were excluded from further analysis. At the 12 months follow up, all patients received a neurological examination including observation of behavior disorders, exploration of seizure outcome, a cerebral 3 Tesla MRI and a neuropsychological reassessment. To avoid bias effects in post-surgical outcome regarding the extent of resections only patients with SAH were compared directly in the bAHS and uAHS groups. Seizure outcome was classified as completely seizure-free since surgery (including auras), i.e. Engel class IA, or not seizure-free (Engel class IB-IV) (Engel et al., 1993).

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