



## A right amygdalohippocampectomy: A diagnostic challenge

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### ABSTRACT

**Objective:** Amygdalohippocampectomy (AHE) is the resective surgery for medically intractable mesial temporal lobe epilepsy. To date no study has investigated a wide range of neuropsychiatric symptoms in right AHE outpatients.

**Patients and methods:** Three patients with right AHE participated in this study. The control group are patients with cognitive complaints with no history of epilepsy or neurological impairment and no structural abnormalities on the MRI/CT. We expected no difference in verbal memory compared to the controls. Concerning affective Theory of Mind (ToM) we expect a difference between controls and AHE patients. In terms of behavior it is expected that coping and behavioral questionnaires do not significantly differ between AHE and controls, but that proxies of AHE patients do report more behavioral/psychiatric symptoms.

**Results:** No significant difference was found between groups concerning the cognitive functions. For affective ToM we did find a significant difference ( $p = 0.044$ ). A significant difference for the use of more reassuring thoughts ( $p = 0.006$ ) and a trend for less passive reactions on the coping questionnaire, suggesting an 'active coping style'. Overall, AHE patients report fewer problems the self-reported questionnaires. Proxies of the AHE patients reported a trend for more behavioral disinhibition compared to proxy ratings of the control group.

**Conclusion:** Right AHE patients underestimate their behavioral and emotional changes due to self-awareness deficits. Ratings of significant others are of immense importance for the detection of psychiatric and behavioral problems. Lesions in the amygdala- orbitofrontal cortex connection disrupt the emotional network, which might explain our results.

### 1. Introduction

One of the most successful treatments for medically intractable mesial temporal lobe epilepsy is resective surgery, an amygdalohippocampectomy (AHE), resulting in seizure freedom for more than 70% [1]. Verbal memory problems are most commonly (22–63%) seen in left-sided AHE due to the crucial role of the hippocampus for verbal memory [2,3]. In addition, reduced language comprehension and fluency have also been observed [4]. After AHE a good outcome after 1 year for attention, verbal memory and a composite of total neuropsychological performance has been reported [5,6]. Overall, patients with a right AHE show better improvement on cognitive tests [7–10]. Some suggest that this improvement on cognitive function after right AHE is due to the activation of the left hippocampus [11]. This is in line with studies that suggest a lateralization of the amygdala-hippocampus

complex in processing both cognitive and affective information, where the left side processes verbal information and the right side visually stimuli [12,13].

The assumption is that the cognitive and affective deficits as a result of AHE are related to behavioral changes, e.g. inflexible behavior, upbeat mood [14,15]. The most commonly reported psychiatric disorders after AHE are recurrent depression, anxiety, and sexual changes [16–18]. In contrast, recent studies show a decrease of postsurgical psychiatric symptoms (e.g. anxiety and depression) after AHE [19–21]. In a large study on postsurgical psychiatric symptoms after Temporal Lobe epilepsy (TLE), both left and right, a decrease was found for depressive symptom and anxiety and an increase for hypomania [17]. Postsurgical psychiatric disorders do not worsen postsurgical [17]. The severity of depressive symptomatology appears to be more evident in left sided AHE patients compared to right [22]. Right AHE patients are

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less precise in their perception and interpretation of emotional cues [19]. Some suggest that ratings of significant others, in absence of psychiatric symptoms, are therefore of great importance for the detection of psychiatric and behavioral problems following an AHE [23].

Recently, studies have focused on the social – emotional dysfunctions after a AHE in relationship to psychiatric symptoms and behavior [8,24]. The amygdala has been associated with processing affective and socially emotionally relevant information, including Theory of Mind (ToM) [25,26]. ToM refers to mentalizing about thoughts and beliefs of others ('cognitive ToM'), as well as mentalizing about feelings and emotional states of others ('affective ToM') [27]. Lesion studies provide evidence for an involvement of both amygdala in affective-ToM [15]. In a rare case study of a right AHE patient with 'hyper-empathy' showed an increased ability to read the mental states of others, reflected in normal to higher (e.g. better) scores on a test of affective-ToM. Of note, the patient did not experience any emotion [8]. The authors suggests that this hyper ability to understand the feelings of another person is based on cognitive empathy due to the absence of the emotional- affectively laden interference of the amygdala. A right AHE disrupt the emotional empathy cerebral network, including the orbital and medial prefrontal cortex, which allows us to 'feel' the emotions of others [8]. In reaction to emotionally salient stimuli patients with right amygdala lesion show lower skin conductance and have an reduced startle response compared to left [28]. In line with these findings, a recent study found that lesions of the right uncinate fasciculus, a white matter connection between, among others, orbitofrontal cortex (OFC) and amygdala, disrupts the emotional empathy network [29]. This might suggest that the AHE patients are not hindered by a somatic marker in making empathic reactions (affective ToM) [30]. A somatic marker is induced by potentially harmful decisions, a peripheral autonomic response (e.g. skin conductance, heartrate, smooth muscle contraction), which is experienced as a feeling and used to guide decisions in a positive direction [31]. It has been suggested that damage to the OFC and amygdala connection is associated with deficits in emotional processing and aberrant behavior [32].

Where most studies focus on the relationship between cognitive decline and social cognitive deficits after AHE postsurgical psychiatric symptoms, the nature of behavioral functioning have not yet been described in empirical studies. In particular we have chosen to study right AHE patients because it is clear from literature that they show less cognitive deficits, show more affective-ToM deficits and therefore might show more behavioral problems (e.g. inflexible behavior, cheerful). In the present study, three chronic right-AHE outpatients, and 20 controls, were subjected to a broad neuropsychological test battery and several behavioral-psychiatric questionnaires, including proxy ratings. All patients were referred to our neuropsychiatric department of the Mental Health Institute Altrecht by a proxy because they could no longer cope with the profound changes in their behavior. As far as we know this is the first explorative study that compared right AHE patients to controls on cognitive measures, social cognition tasks, behavioral and psychiatric questionnaires, including proxy rating. Our main goal is to define the characteristics of the behavioral problems and whether cognitive deficits, if present, are associated with behavioral problems.

## 2. Patient and methods

### 2.1. Participants

Three patients (two female, one male) with right AHE participated in the present study. All had focal Temporal Lobe Epilepsy (TLE) and were right handed. Preoperative cognitive and psychiatric

information is lacking. In order to in- or exclude additional cerebral causes for the neuropsychiatric symptoms an MRI was made (see Fig. 1). The control group (nine females, eleven males) are patients with cognitive complains and were randomly selected based on no structural damage and a complete neuropsychological battery. None of the controls met the criteria of mild traumatic brain Injury (mTBI), no posttraumatic amnesia (PTA) or loss of consciousness (LOC). The control group had no history of psychiatry, epilepsy or neurological impairment and had no structural abnormalities on the Magnetic resonance imaging (MRI) or Computed tomography (CT). This gave us 20 controls. See Table 1 for an overview of the demographic data. Patients and controls were recruited via the Mental Health Institute Altrecht (Neuropsychiatry, Vesalius). Patients were subjected to an extensive diagnostic procedure including brain imaging, psychiatric evaluation, extensive neuropsychological assessment, social cognition tasks and behavioral and psychiatric questionnaires. Written informed consent was obtained from participants and caregivers according to the Declaration of Helsinki, and local ethics committee approved the study. During the diagnostic procedure the patient's wellbeing and request for help always outweighed the collection of data.

### 2.2. Psychiatric evaluation

#### 2.2.1. Patient 1

She was referred to the neuropsychiatric department of Altrecht for impulsive, rigid, disinhibited and suspicious behavior. Psychiatric evaluation (2014); no psychotic symptoms, no depression, no suicidal tendencies, cognitive complaints (memory), no obsessive-compulsive behavior, no anxiety. She acknowledges having a somatic disease but indicates not to have changed in behavior due to the AHE. Behavioral problems (e.g. aggression) after her first epileptic seizures for which she had psychiatric treatment. The years before her surgery there were no psychiatric problems.

**MRI:** Status post-amygdalo-hippocampectomy right, characterized by a porencephalic cavity anterior temporal right. There is some gliosis in the adjacent structures.

#### 2.2.2. Patient 2

Psychiatric evaluation (2012); no psychotic symptoms, no depression, no suicidal tendencies, cognitive complaints (memory), no obsessive-compulsive behavior, no anxiety. Is very optimistic and cheerful, rigid in thinking. Husband indicates that she is disinhibited, easily aggressive en agitated, has become very associative. No pre-morbid psychiatric disorders, she was a friendly and cheerful woman.

**MRI:** Status post-amygdalo-hippocampectomy right. Some gliosis along the edge of the resection cavity.

#### 2.2.3. Patient 3

Psychiatric evaluation (2012); no psychotic symptoms, no depression, no suicidal tendencies, cognitive complaints (memory), no obsessive-compulsive behavior, talkative, no anxiety. Wife indicates that her husband is disinhibited, easily aggressive en agitated. Reduced self-awareness concerning his behavior. No pre-morbid psychiatric disorders or psychological distress. Patient has its own business (hairdresser), epileptic seizures never led to problems at work.

**MRI:** Status post-amygdalo-hippocampectomy right. The hippocampus is completely removed. There is minimal gliosis.

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