

## Case Report

# High-grade Atrioventricular Block Triggered by Spontaneous and Stimulation-induced Epileptic Activity in the Left Temporal Lobe

\*Dirk-Matthias Altenmüller, †Manfred Zehender, and \*Andreas Schulze-Bonhage

\*Epilepsy Center and †Department of Cardiology, University of Freiburg, Freiburg, Germany

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**Summary:** Cardiac bradyarrhythmias may play a pivotal role in the pathophysiology of sudden unexpected death in epilepsy (SUDEP). We describe a patient with left temporal lobe epilepsy in whom high-grade atrioventricular conduction blocks were triggered by both spontaneous and stimulation-induced epilep-

tic activity in the left temporal lobe. Electrophysiological data obtained by surface and intracranial electrodes point to a cerebral cardioarrhythmogenesis in the left amygdala and anterior hippocampus. **Key Words:** Epilepsy—SUDEP—Ictal cardiac arrhythmia—Intracranial electrodes—Cortical stimulation.

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Cardiac arrhythmias are considered a possible mechanism for sudden unexpected death in epilepsy (SUDEP) (1). A limited number of anecdotal case reports have documented a temporal association between focal ictal activity and the occurrence of potentially life-threatening cardiac rhythm disturbances, in particular bradycardia and asystole (2). Little is known about the pathophysiology of ictal bradycardia. We present a patient in whom high-grade atrioventricular (AV) conduction blocks were manifest exclusively during left temporal epileptic activity arising spontaneously or subsequent to cortical electric stimulation.

### CASE REPORT

A 46-year-old right-handed woman with drug-resistant left temporal lobe epilepsy since age 16 years underwent video-EEG monitoring for presurgical evaluation. Seizures were characterized by rare epigastric auras and ictal sensory aphasia, facultatively followed by arrest, impaired responsiveness, and oral as well as gestural automatisms with occasional secondary generalization through head version to the right. Postictally, a marked aphasia and retrograde amnesia were common. High-resolution magnetic resonance imaging (MRI) failed to reveal a

temporal or extratemporal lesion; in particular, no morphologic abnormalities of the hippocampus or amygdala were seen. Positron emission tomography showed a focal hypometabolism in the left temporal lobe. Ictal <sup>99m</sup>Tc-ethyl-cysteine-dimer single-photon emission computed tomography visualized left temporal hyperperfusion. Postoperatively, the histologic diagnosis of a glioneuronal hamartoma in the left temporal lobe was confirmed. No history of cardiac disease was noted. Routine 12-lead electrocardiogram (ECG) and interictal 24-h ECG monitoring showed no abnormalities. To facilitate seizures for video-EEG registration, the antiepileptic drugs (AEDs) were temporarily tapered off [i.e., step-by-step reduction of sodium valproate (VPA) from 900 to 0 mg and of lamotrigine (LTG) from 400 to 50 mg daily].

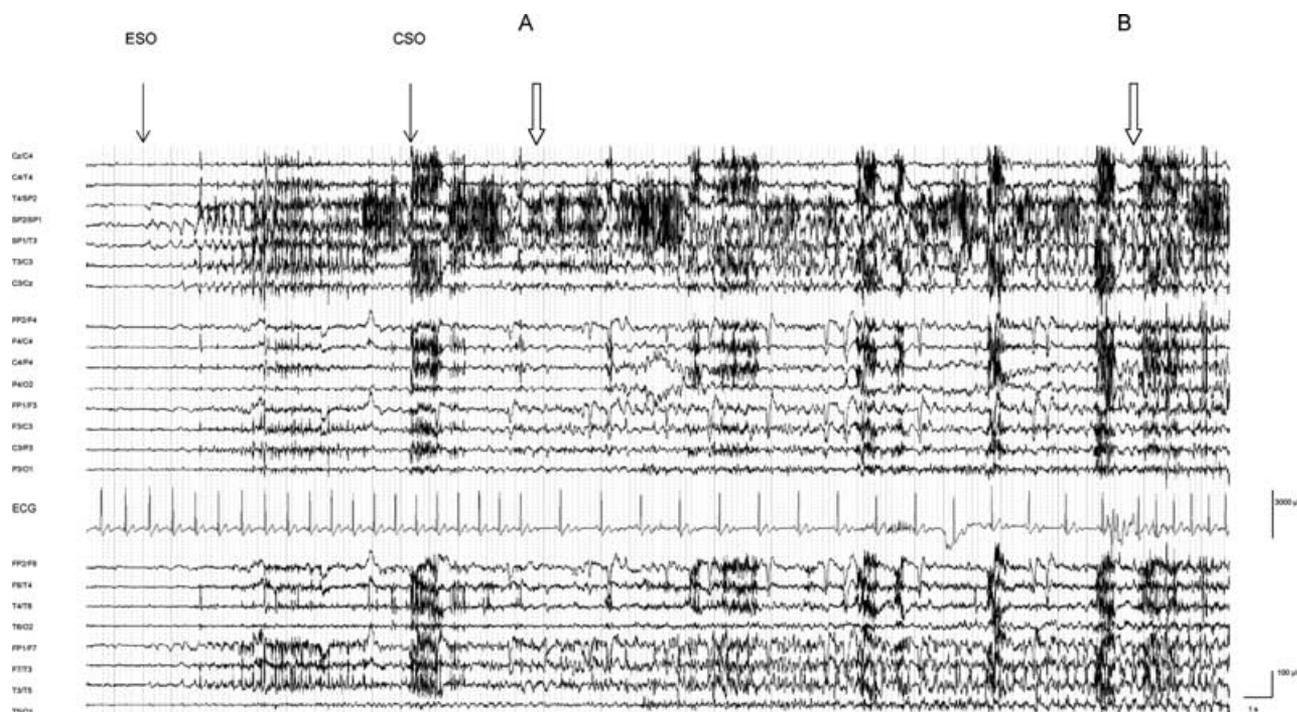
Noninvasive long-term video-EEG monitoring was performed with scalp electrodes placed according to the international 10-20 system and additional sphenoidal electrodes. Continuous two-lead ECG was co-registered. Interictal epileptic activity was seen exclusively over the left temporal region. All of three habitual seizures registered by surface EEG were associated with a left temporal seizure pattern preceding the clinical seizure onset for 1 to 7 s.

During one unprovoked habitual complex focal seizure, 13 s after left temporal EEG seizure onset, a high-grade AV block developed, ceasing spontaneously after 21 s. Thirty-five s later there was secondary seizure generalization (Fig. 1). During the cardiac arrhythmia, ictal surface EEG

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Address correspondence and reprint requests to Dr. D.-M. Altenmüller at Sektion Prächirurgische Epilepsiediagnostik am Neurozentrum Freiburg, Breisacher Strasse 64, 79106 Freiburg, Germany. E-mail: altenm@nz.ukl.uni-freiburg.de



**FIG. 1.** Surface EEG with additional sphenoidal electrodes (SP1/SP2) and electrocardiogram during a spontaneous complex focal seizure with left temporal seizure onset and high-grade AV block (A, onset; B, end). ESO, EEG seizure onset; CSO, clinical seizure onset.

activity was confined to frontocentrottemporal leads on the left side with a maximum over the left temporal lobe. Semiology at this time was characterized by oral automatisms and impaired responsiveness in accordance with seizure activity in the temporal lobe.

For further presurgical investigations, a subdural grid with 64 leads and two subdural strip electrodes with four leads each were implanted. These covered the left lateral and basal temporal lobe, respectively. In addition, a 10-lead intrahippocampal electrode was inserted stereotactically on the left side. The location of the intracranial electrodes is illustrated schematically in Fig. 3A. Exact placement was verified by MRI. Note that the two anterior leads of the "intrahippocampal" electrode were placed within the left amygdala (Fig. 3B).

During postoperative observation at the intensive care unit the day after implantation throughout the course of habitual complex focal seizures not yet registered by EEG, two episodes occurred with increasing PQ prolongation, subsequently increasing AV block up to third degree and a resulting asystole of 35 s (Fig. 2).

Invasive video-EEG monitoring revealed a large epileptogenic area with EEG seizure onset (low amplitude fast activity) at the basal and anterior lateral left temporal lobe 3 to 18 s before clinical seizure onset. None of five spontaneous seizures was associated with cardiac conduction disturbances. Additionally, frequent interictal spiking was noted in the left amygdala.

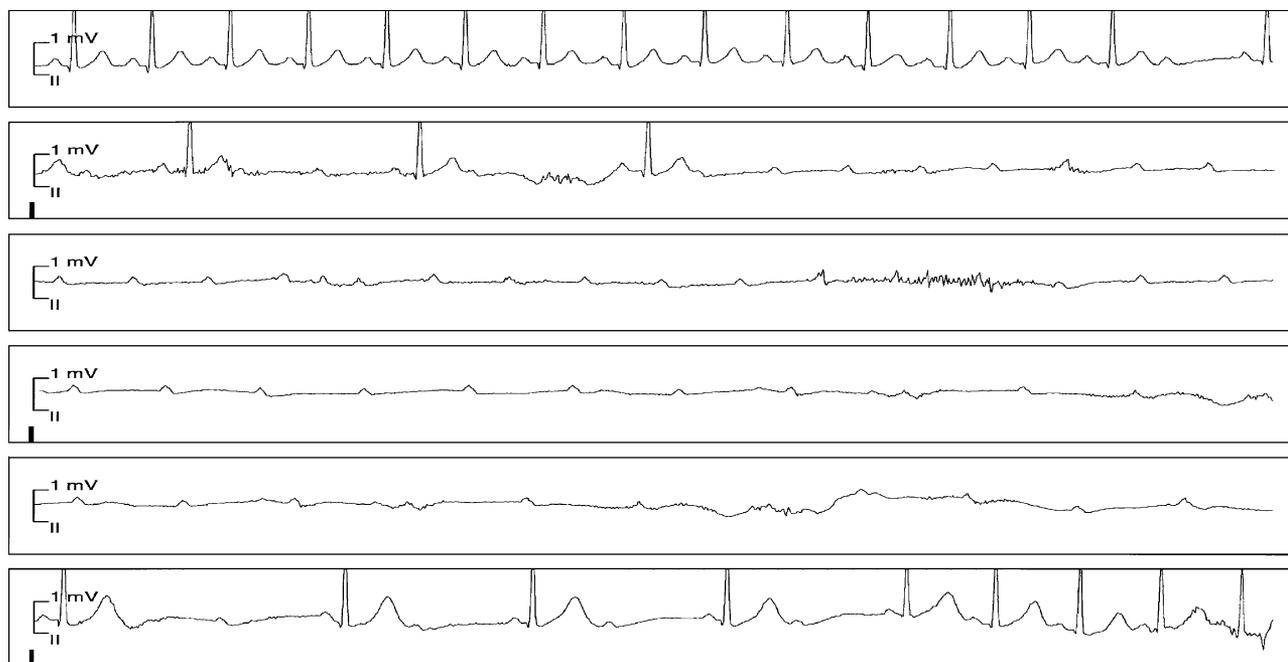
A further high-grade AV block associated with an epigastric aura was triggered by cortical stimulation (3 mA;

frequency, 50 Hz; duration, 7 s) via two subdural electrodes located on the mesial and basal parts of the left anterior temporal lobe (Fig. 3A). During this AV block lasting 5 s, epileptic activity, as recorded by intracranial electrodes, was restricted to the mesial and basal parts of the left anterior temporal lobe, the left amygdala, and the left anterior hippocampus. The leads overlying the posterior and lateral parts of the left temporal lobe showed no ictal EEG activity (Fig. 3A and C). Cortical stimulation via the other subdural and intrahippocampal electrodes did not elicit any AV block.

A cardiac pacemaker was implanted to protect the patient from further conduction blocks.

## DISCUSSION

The combined registrations of video-EEG and ECG in the present case revealed high-grade AV blocks occurring exclusively during left temporal ictal activity. It is noteworthy that in this patient, these potentially life-threatening cardiac arrhythmias were observed in a high percentage of seizures. Overall, consistent evidence for a single epileptogenic area located exclusively in the left temporal lobe allows the conclusion that in the present patient, also the two prolonged asystoles evolving each from a high-grade AV block during habitual, not secondarily generalized seizures, were associated with left temporal epileptic activity, although EEG was not recorded during these episodes.



**FIG. 2.** Electrocardiogram revealing increasing PQ prolongation, subsequently increasing atrioventricular block up to the third degree and long-lasting asystole during habitual complex focal seizure (EEG not recorded).

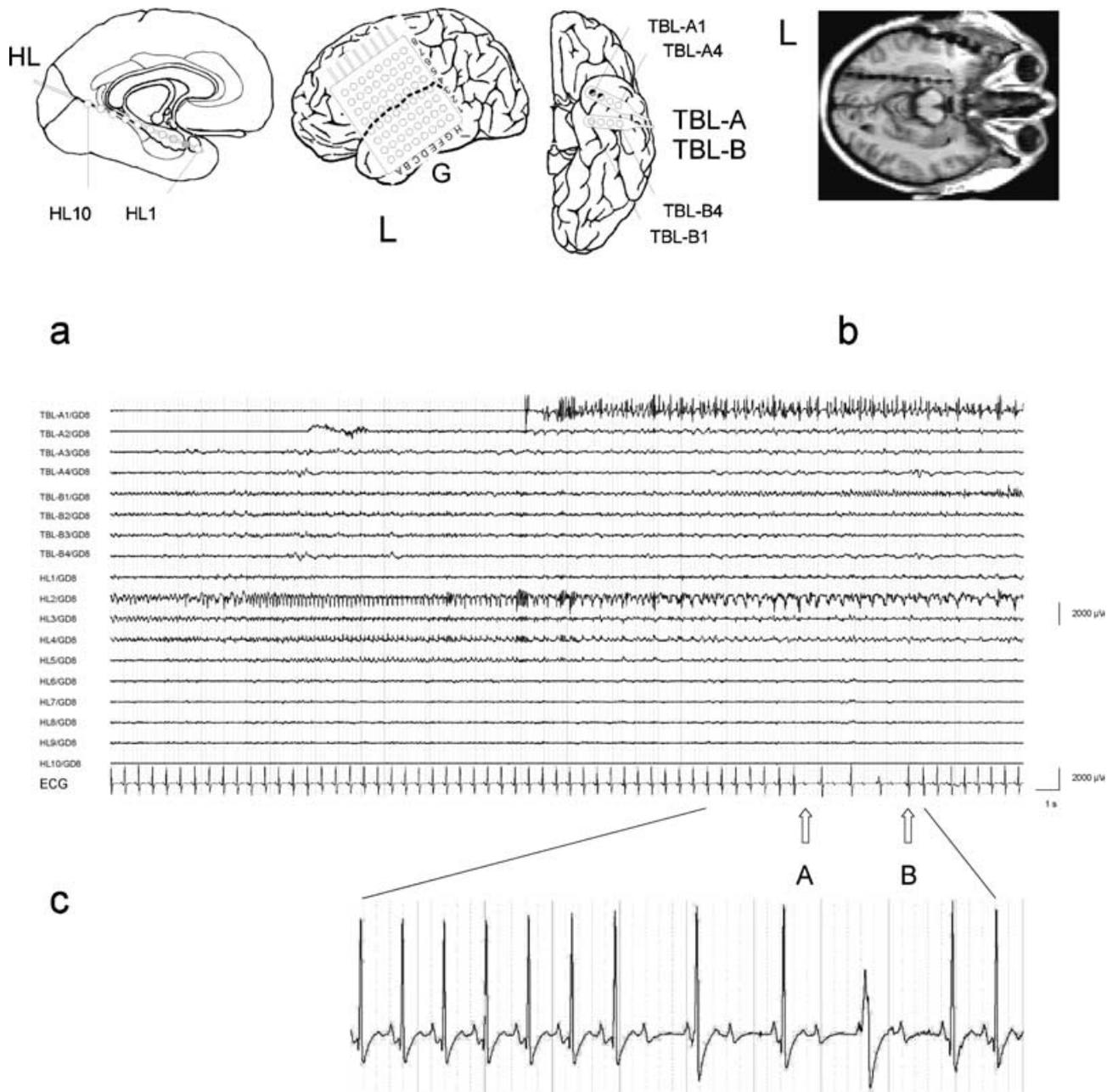
Ictal bradycardia and cardiac asystole throughout the course of focal epileptic seizures are underestimated phenomena that have been documented in several case reports (2). In those with medically refractory epilepsy who underwent simultaneous EEG-ECG monitoring, Zijlmans et al. (3) observed ictal bradycardia (defined as a decrease of  $> 10$  beats/min compared with average baseline heart rate) in 15% of 81 patients, Opherk et al. (4) found first- or second-degree AV blocks during three of 102 seizures (in one of 41 patients), and Rocamora et al. (5) reported that ictal cardiac asystole occurred in five of 1,244 patients. With regard to pathophysiology, evidence exists from animal experiments for a synchronization of the cardiac autonomic (sympathetic and vagal) neural discharge with epileptogenic activity (6). This so-called “lockstep” phenomenon may be a contributing factor for the development of cardiac arrhythmias during seizures in epilepsy patients. Because ictal cardiac arrhythmias may be potentially fatal, it is tempting to discuss them in relation to SUDEP.

Simultaneous recordings of surface EEG and ECG pointed in most reported cases of ictal bradycardia to a temporal or frontal seizure onset. With regard to focus lateralization, literature review shows a preponderance of the left hemisphere (2,5). Previous reports on ictal bradycardia during intracranial EEG monitoring are rare and yielded controversial results. With bilateral subdural grid and strip electrodes, Devinsky et al. (7) found a left temporal seizure onset. However, sinus arrest and bradycardia occurred only after seizure activity had spread to the right

temporal lobe. Performing stereo-EEG in a patient with a hypothalamic hamartoma, Kahane et al. (8) observed ictal bradycardia in seizures originating from the right frontal and temporal neocortical areas. At the time heart rate began to decrease, however, widespread bilateral epileptic discharges involving also mesial temporal structures were recorded. Moreover, with regard to lateralization, interpretations must be made with caution because the patient was left-handed.

Our noninvasive and invasive recordings support the hypothesis that ictal bradycardia is triggered by epileptic activity in left temporal structures. In addition, electrophysiological data obtained from simultaneous application of extended left temporal subdural and left intrahippocampal electrodes allow a further localizing differentiation, favoring a cerebral cardioarrhythmogenesis in the left amygdala or in the left anterior hippocampus. This finding is in accordance with experimental studies showing consistent bradycardia responses and cardiac rhythm disturbances including intermittent heart block as a result of electrical stimulation of the amygdaloid region in monkeys (9). The authors did not differentiate between the left and the right side.

Because we did not insert additional intracranial electrodes in the left insula or frontal region and because surface EEG showed ictal involvement of left frontal and central electrodes during cardiac arrhythmia, we cannot definitively rule out that spread of left mesiotemporal epileptic discharges via functionally interconnected anatomic pathways activated more anterior areas, in



**FIG. 3. A:** Implantation scheme. HL, left intrahippocampal electrode with the two anterior (HL1/HL2) of 10 leads within the left amygdala. G, subdural grid with 64 leads (A, anterior/H, posterior; 1 inferior 8 superior) left temporal lateral. TBL-A and TBL-B, subdural strip electrodes with four leads (1 mesial 4 lateral) left temporal basal anterior and posterior, respectively. L, left. *Black*, stimulating leads; *grey/dotted*, leads with maximum (HL2, TBL-A1) or minor (TBL-A2, TBL-B1, HL3, HL4) ictal activity during atrioventricular (AV) block provoked by cortical stimulation. **B:** Magnetic resonance imaging. Location of the left intrahippocampal electrode. **C:** Intracranial EEG recording and electrocardiogram during electrical stimulation via the subdural leads TBL-A1 and TBL-A2. Initially, stimulation artifacts are still seen. The subdural grid left temporal lateral showed no ictal activity (not shown). The patient reported an epigastric aura and terminology, see A. A/B, onset/end of high-grade AV block.

particular left insular structures known to induce bradycardia after intraoperative stimulation in the human brain (10). However, our data are in line with the lateralization effect described by Oppenheimer et al. (10), attributing negative and positive chronotropic properties to the left and right (insular) cortex, respectively.

To our knowledge, the present case is the first published in which extraoperative stimulation of a circumscribed

cortical region elicited a seizure associated with bradycardia. Our observations support the view that stimulation-induced AV block (as well as AV block induced by spontaneous seizures) is not an unspecific phenomenon but relates to ictal involvement of well-defined cerebral areas known as specific autonomic centers, thus leading to an excessive vagal activity. In our case, this seems to affect specifically the AV node, because, in contrast to a

case report presented by Tigarán et al. (11), no concomitant slowing of the P-wave frequency was seen during AV block. Differences in spatial and temporal seizure propagation patterns might be the reason that not all seizures in our patient were accompanied by cardiac arrhythmias.

Whether the reduction of the AEDs might have facilitated the cerebrogenic arrhythmia additionally in our case remains speculative. However, epidemiologic data identifying frequent adjustments of AED dosage as a major risk factor of SUDEP (12) may point to an increased risk of cardiac complications associated with changes in the AED regimen.

As in the present case, centrally triggered cardiac arrhythmias in epilepsy patients may remain undetected for a long time and can be missed by interictal 24-h ECG registrations. To improve presurgical epilepsy care, ECG monitoring should be applied during both video-EEG recording and cortical stimulation. The efficacy of implanting a cardiac pacemaker to reduce the risk of SUDEP in patients with proven seizure-induced cardiac bradyarrhythmia and asystole has not yet been investigated.

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