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Interictal infraslow activity in patients with epilepsy

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HIGHLIGHTS

- Interictal infraslow activity (ISA) can provide additional information about the epileptogenic process.
- It can be assessed with conventional EEG systems.
- ISA activity is more widely distributed in localisation-related epilepsies than might be assumed.

ABSTRACT

Objective: To evaluate if interictal infraslow activity (ISA), as obtained from a conventional EEG system, can contribute information about the epileptogenic process.
Methods: The entire long-term intracranial monitoring sessions of 12 consecutive patients were evaluated on an XLTEK system for ISA. Three additional patients had long-term scalp recordings.
Results: In intracranial as well as scalp recordings, the ISA background was consistently higher in the waking state than during sleep. From this background emerged intermittently focal changes, which could achieve in intracranial recordings millivolt amplitudes, while they remained in the microvolt range in scalp recordings. Although they were mainly contiguous between adjacent channels, this was not necessarily the case and intermittent build-up could be seen distant from the epileptogenic zone or radiographic lesion.
Conclusions: Interictal ISA can be detected in routine intracranial and scalp recordings, without the need for DC amplifiers, and can provide additional information.
Significance: Since ISA is a separate element of the electromagnetic spectrum, apparently non-neuronal in origin, its assessment should be included not only in the pre-surgical evaluation of epilepsy patients but also in patients with other neurologic disorders and normal volunteers.

1. Introduction

The change from analogue to digital EEG systems and associated improvements in amplifier technology has opened new vistas for the exploration of cerebral electrical activity. Frequencies above the gamma band which required for visualisation films from cathode-ray oscillograph tracings or tape recordings which manipulated data acquisition and playback speeds (Buchwald et al., 1966; Buchwald and Grover, 1970; Rodin et al., 1971a,b, 1977; Rodin and Wasson, 1973; Rodin, 1972, 2005), can now be readily observed in routine clinical recordings when high sampling rates are employed. This frequency range is currently under intense investigation and only some early as well as the latest references will be listed (Allen et al., 1992; Fisher et al., 1992; Bragin et al., 1999; Worrell et al., 2008; Jiruska and Bragin, 2011; Modur et al., 2011, 2012; Wang et al., 2013).

A similar situation pertains to the recording of <0.5 Hz activity. These frequencies had previously required DC amplifiers for display but currently all commercial EEG systems have a lower frequency limit of at least 0.1 Hz, while it is 0.05 Hz for the XLTEK system and 0.016 for the Nihon-Kohden system. Since the signals below these frequencies are not abolished but merely attenuated in amplitude and wave duration, even slower activity is retrievable from routinely obtained clinical data.

Early publications have shown that epileptic seizures can be associated with slow baseline shifts, which can have localising significance (Cohn, 1954; O'Leary and Goldring, 1959; Vanasupa et al., 1959; Gumnit and Takahashi, 1965; Caspers and Simmich, 1966; Chatrian et al., 1968; Gumnit et al., 1970). Inasmuch as these observations required DC amplifiers, they were referred to as 'DC shifts'. Yet Ikeda et al. demonstrated that these shifts were also observed, in intracranial as well as scalp recordings, when

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conventional AC amplifiers with a long time constant were used (Ikeda et al., 1996, 1999). The finding was subsequently verified by several other investigators (Gross et al., 1999; Thordstein et al., 2005; Bragin et al., 2005; Mader et al., 2005; Hughes et al., 2005; Rodin et al., 2006, 2008, 2009; Rodin and Modur, 2008; Ren et al., 2011; Shi et al., 2012; Rampp and Stefan, 2012; Constantino and Rodin, 2012; Modur et al., 2012).

Most of these studies also showed that ictal baseline shifts were not unidirectional but consisted of a series of high-amplitude slow waves of varying durations, involving at times a large number of channels at different time points during the seizure and extending into the post-ictal period. The latter aspect was most marked in the immediate post-ictal state after a tonic–clonic seizure when the conventional EEG frequencies showed attenuation. Figures 6 and 7 of the publication by Rodin and Modur (2008) provided a typical example. When one keeps these observations in mind, two aspects become apparent. One is that the terms 'baseline shifts' or 'DC shifts' are inadequate to describe the phenomenon because one is dealing with a marked increase of continually present infraslow activity (ISA). The other aspect is that ISA follows different laws and therefore must have different generators than the conventionally sampled frequency band.

As mentioned earlier, there are by now several studies which deal with the ictal aspects of ISA, but a review of the literature showed that there appeared to be no publications specifically devoted to the pre- and interictal state in epilepsy patients. Yet, this information could potentially also be important especially with regard to seizure prediction, which is still imprecise. We, therefore, decided to study this problem in a systematic prospective manner. A preliminary report was presented at a symposium on cerebral electromagnetic ISA of the American Clinical Neurophysiology Society and subsequently published (Rodin and Funke, 2012; Constantino and Rodin, 2012). Since the patient number was small and there were no data available on scalp recordings monitored over the long term, the study was continued on a larger patient population which also included scalp recordings.

The questions to be answered were: (a) Does interictal ISA contain additional information which is not readily available from the conventional frequency band? (b) If this were to be the case, does it have potential clinical relevance with regard to the patient's seizure disorder? (c) Can interictal, and especially pre-ictal, ISA contribute to the prediction of the occurrence of a seizure?

2. Materials and methods

The methodology was the same as in the previous report (Constantino and Rodin, 2012) but seven additional patients with intracranial and three with scalp recordings were added. Of these 12 patients with intracranial data, 11 also had scalp recordings at our laboratory. However, these had been obtained earlier and contained only samples rather than the complete monitored sessions. The samples consisted, apart from seizures, of an initial 35-min epoch, subsequent 35-min samples of what the XLTEK program regarded as an "event" and hourly 1-min epochs of interictal data. The three new patients with long-term scalp recording sessions have not yet had further intracranial investigations. The clinical characteristics of the patients are shown in Table 1. It should be emphasised that the study was prospective and contained all patients who had been recorded between August 2011 and February 2013.

Scalp, as well as intracranial, recordings were obtained on an XLTEK system. For scalp recordings, EMU40 amplifiers were used (40 channels; low-frequency cut-off at 0.05 Hz–6 db/octave), while the intracranial data were recorded with 128SF amplifiers (128 channels; low-frequency cut-off at 0.03 Hz–6 db/octave). After de-identification, the data were transferred to an external drive before they were sampled for storage purposes. For intracranial recordings, the sampling rate was 512 Hz while it was 256 Hz for scalp recordings. The intracranial strip and grid electrodes were platinum (Ad-Tech Medical Instruments, Racine, WI, USA) and for scalp recordings Ag/AgCl electrodes were used. For intracranial recordings, the electrode coverage ranged from 20 to 88 electrodes and, except for two cases, was unilateral in areas of suspected seizure origin. The scalp electrodes were placed according to the 10/20 system but infraorbital and at times T1/T2 and/or sphenoidal electrodes were added. For intracranial recordings, the reference electrode was a needle electrode inserted into the temporalis muscle.

For data analysis, the software package BESA® (BESA Research version 6; BESA GmbH, Gräfelfing, Germany) was used. Initially, the data were reviewed on the conventional frequency band (0.5–70 Hz), and when muscle artefact contaminated the scalp recordings, the low-pass filter was set to 15 Hz. The program allowed for removal of eye blinks as well as lateral eye movements and this module was used when indicated. For better visualisation

Table 1
Clinical profile of patients.

Patient	Age/sex	MRI	Resection performed	Latest operative result
1	48/F	Cerebellar atrophy and white matter changes	L A T lobectomy with hippocampectomy	Seizure free since surgery 9/2011
2	20/F	Normal	R A T lobectomy with hippocampectomy	Seizure free since surgery 8/2011
3	33/M	Previous L T lobectomy	L STG resection	Seizure free since surgery 9/2011
4	32/F	L F encephalomalacia; multiple cav mal	L insular cav mal lesionectomy	Seizure free since surgery 10/2011
5	29/M	Small L hemisphere and hippocampus	L A T lobectomy with hippocampectomy	Seizure free since surgery 11/2011
6	54/M	Multple cav mal; bifrontal encephalomalacia	R insular cav mal lesionectomy	Seizure free since surgery 01/2012
7	49/M	Normal	R A T lobectomy with hippocampectomy	Seizure free since surgery 02/2012
8	32/M	R F encephalomalacia	Partial R F lobe resection	1 seizure since surgery 5/2012
9	23/F	R F encephalomalacia	R F lobe resection	Occasional seizures
10	41/M	Normal	None[b]	N/A
11	32/F	Normal	R T lobectomy	Died of SUDEP after surgery
12	13/F	L T dysplasia	L T lobectomy (Frontal focus not resected)	Still having seizures
13[a]	24/M	Normal	None[b]	N/A
14[a]	48/F	L parahippocampal hemosiderin c/w trauma	None[b]	N/A
15[a]	20/F	L P tumor resected; additional mass L F and L T	None[b]	N/A

All patients had temporal seizure semiology; R, right; L, left; F, frontal; P, parietal; T, Temporal; STG, superior temporal gyrus; Cav mal, cavernous mal formations.
[a] Scalp EEG only.
[b] No surgery was performed in 10 due to discordant Wada, 13 was controlled with medications, 14 had strong memory on the lesion side, and 15 had additional tumor in anatomically critical areas.