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Do surface DC-shifts affect epileptic hippocampal EEG activity?

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Summary Despite considerable research on EEG-feedback of slow cortical potentials (SCPs) for seizure control in epilepsy, the underlying mechanisms and the direct effects on intracerebral pathological activity within the focal area remain unclear. Intrahippocampal EEG recordings from four patients with temporal lobe epilepsy and implanted electrodes were analyzed with regard to spike activity and power in 10 frequency bands (0.5—148 Hz) during SCP feedback based on surface recordings (position Cz). Trials with positive, negative and indifferent SCPs were contrasted. Three of the four patients showed changes in spike activity during SCPs, but these were inconsistent between patients, and resulted in increased and decreased activity in both positive and negative SCPs. Spectral analysis revealed that in all patients, positive surface shifts showed a bi-hemispheric higher power in the high-frequency activity above 40 Hz. Two patients showed a higher power also during negative shifts, both in high-frequency activity and one in most other frequency bands. Feedback-related power effects did not differ between focal and non-focal side. The inconsistent change in spiking activity and the lack of decrease of power in pathology associated frequency bands during SCPs show that these SCPs do not decrease pathological activity within the epileptic focus. A possible relation of higher power in high-frequency activity during positive SCPs to cognitive processes, such as memory functions, is discussed.

Introduction

In search for alternative treatment methods for epilepsy, neurofeedback as a means to influence epileptogenic networks and thus prevent seizures has been object to research in the last decades (Walker and Kozlowski, 2005). Following the reinforcement of activity in a specific frequency band in the electroencephalogram (EEG) (Thompson and Baxendale, 1996), more recent research has been directed

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at the general level of excitability of the underlying cortex. This is represented by slow cortical potentials (SCP or DC-shifts) recorded from the surface (Rockstroh et al., 1989) and has been closely linked to epileptic activity. SCP recordings reach a large negative amplitude imminent to a seizure (Birbaumer et al., 1990; Speckmann et al., 1999). They have gained importance in the noninvasive lateralization and localization of the seizure focus, e.g. during presurgical workup (Miller et al., 2007; Vanhatalo et al., 2003) and may also be recorded intracranially in order to correctly localize the region of seizure onset (Ikeda et al., 1996). Slow positive potentials may also reflect sustained decreases of cellular activity (e.g. Schmitt et al., 2000). In hippocampal slices, DC-shifts may induce or enhance seizure activity (Gluckman et al., 2001). After analyzing penicillin-induced seizures in the hippocampus (Dichter and Spencer, 1969; Gloor et al., 1964), Dichter and Spencer as well as Gloor and colleagues suggested that seizures may be prevented from spreading widely by recurrent inhibitory action in the periphery (Gumnit, 1974).

These findings from basic research have initiated clinical research on the feedback of SCPs, reinforcing the patient's ability to increase or decrease the cortical excitability. The intention is to enable patients to reduce their seizure frequency or seizure severity, yet the method is aimed at the single seizure and not at the epileptic condition itself. Clinical studies applying the reinforcement of positive SCPs (i.e. suppression of negativity) in order to achieve seizure control report a decrease in seizure frequency, with some patients with symptomatic as well as idiopathic epilepsy even becoming seizure free (Kotchoubey et al., 2001; Rockstroh et al., 1993; Strehl et al., 2005). In the latest of these studies, Strehl and colleagues reported that patients with left temporal lobe epilepsy had a lesser probability for seizure reduction. To what extent this variability may be influenced by cortical vs. mesial temporal lesions and their susceptibility to changes in excitability recorded from the surface remains unclear. The respective research group has also explored changes in EEG spectral power during 35 sessions of SCP training. Taking into account frequencies from 0.3 to 30 Hz, they found larger power values in the delta, theta and alpha bands when patient were required to produce positive vs. negative SCP shifts. However the effects were too weak and unstable to be regarded as an immediate consequence of SCP dynamics (Kotchoubey et al., 1999).

Despite considerable research on the mechanisms and effectiveness of EEG feedback, the interaction of neocortical DC potentials recorded with scalp EEG and activity in the epileptogenic area in deeper structures is still unclear. In a recent study of four epilepsy patients, we addressed the question whether SCPs recorded from the surface interact with slow potentials recorded intracranially from temporo-mesial structures (Fell et al., 2007). We were able to show that neocortical and hippocampal SCPs were in fact interconnected and occurred with greater amplitude in the temporo-mesial structures. However, the polarity of the slow potentials within the hippocampus was not uniformly coupled to the cortical signals.

The current paper aims to address the following questions: First, are SCP shifts related to changes in interictal electrophysiological pathology recorded in the hippocampus? Based on previous studies on patients with symptomatic as well as idiopathic epilepsy (Kotchoubey et al., 2001; Rockstroh et al., 1993; Strehl et al., 2005), we hypothesized that positive SCPs should be correlated with a decreased incidence of interictal spikes. Furthermore we expected an overall decrease in spectral power during positive SCPs. Second, are changes in specific frequency bands of temporo-mesial EEG activity associated with positive and negative SCPs? We predicted that hippocampal gamma-band activity (>32 Hz), which is closely linked to inhibitory activity in the hippocampus (Whittington et al., 1995) and probably also in the neocortex (Axmacher et al., 2008), correlates with positive DC shifts.

Material and methods

Patients

All four patients (age 34—46 years) suffered from temporal lobe epilepsy and underwent intracranial EEG recording during pre-surgical evaluation (for patient characteristics see Table 1). Multicontact depth electrodes with platinum

Table 1 Patient characteristics.

	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)	46.8	34.5	45.7	36.5
Sex	Male	Male	Male	Male
Temporal pathology	Hippocampal sclerosis	Hippocampal sclerosis	Hippocampal sclerosis	Parahippocampal dysplasia
Side of pathology	Right	Right	Right	Left
Side of implanted electrodes	Bilateral	Bilateral	Bilateral	Left
Number of included electrode contacts in the hippocampus (left/right)	7/5	4/5	3[a]/3[b]	4/-
Number of included feedback trials	126[c]	134	130	139
Mean number of trials with spikes per contact (left/right)	68.7/75.8	2/41	53.3/49.3	103/-

[a] One of the former four electrode contacts was excluded, because it was defect (constant high frequency firing).
[b] Two of the former five electrode contacts had to be excluded because of invariant pathological firing.
[c] Two subclinical seizures during the 140 conducted trials were excluded in all contacts.