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# Electrophysiological Effects of Direct Electrical Stimulations during Awake Brain Surgery: Methodological Considerations

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**D**IRECT electrical stimulation (DES) has long been used to perform real-time functional mapping of the brain. More recently, this technique was introduced in the neurosurgery of slow-growing and infiltrative brain tumors to guide the resection with great success [1]. By generating transient perturbations, this method allows the real-time identification of both cortical areas and subcortical networks that are essential for the function. Thus, as much as possible, non-functional tissue can be removed while minimizing the sequelae. However, the understanding of the electrophysiological effects of DES and, in particular its remote propagation, remains an open and key question. DES can be used to probe on-line and in-vivo the spatio-temporal connectivity and the dynamics of functional networks by associating electrophysiological recordings. Such methodology has been performed using electrocorticography (ECoG) and implanted grids on the surface of grey matter for pre-surgical planning of drug resistant epileptic patients [2, 3]. Some of these results suggest a local cortico-cortical propagation of evoked potentials (EPs) with DES. However, the propagation through subcortical pathways and at distant sites needs more direct evidences. To investigate more remote effects of DES (i.e. cortico-subcortico-cortical EPs), electroencephalographic (EEG) recordings would be of some interest.

Intra-operative EEG recordings were studied to analyze if and how stimulation currents spread at distant sites and more especially if they can be perceptible in the “controlateral” hemisphere. In other words, does DES induce EPs? Does DES modify the frequency contents included in the natural activity of the brain? We also aimed to measure the effects of DES on functional connectivity, i.e. to determine if DES modifies the correlation between the different EEG signals between the pre, intra and post-DES phases. To our knowledge, this approach has never been performed.

Data were collected during an awake brain surgery (without interfering with the surgical routine) for one patient harboring a right frontal hemisphere tumor and under local anesthesia. Neural activity was recorded from the surface of the skull (EEG, sampling frequency of 2048 Hz) on 4 sites (3 controlateral sites: F3, C3 and O1 and 1 ipsilesional site: O2; the lesion was centered on F4, Fp2 and F8). DES was delivered with a bipolar electrode using standard parameters (biphasic square pulse, 60 Hz, ~ 2 mA). First we tried to measure EPs when DES is applied cortically and subcortically. To maximize the EPs while minimizing the noise and the artifacts, EEG signals were synchronized and averaged upon a given time window (500 ms).

The phases when DES is applied can be recognized by the appearance of artefacts on the natural EEG activity. However, whereas EPs have been observed in ECoG [2, 3], no EP was detected in our EEG data. With a 60 Hz frequency, stimulation artefacts can hide EPs. Indeed, the nervous time of conduction is close to the stimulation period, in particular for the interhemispheric transfer (around 20 ms). Choosing a stimulation frequency lower than 60 Hz could limit artefacts and make the detection of EPs easier.

In consequence it is planned to study the time-frequency content of the neural data. To reduce bias and variance problems, multitaper spectral estimation could be used. We will look for modifications of the spectrum for each period of stimulation, before, during and after DES. In addition, functional connectivity also remains to be studied by looking at the correlation between signals from various electrodes, especially between electrodes located in the ipsi vs. controlateral hemisphere.

We will present the setup, the data analysis protocol and the preliminary results.

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