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Alterations of EEG rhythms during motor preparation following awake brain surgery

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ABSTRACT

Slow-growing, infiltrative brain tumours may modify the electrophysiological balance between the two hemispheres. To determine whether and how asymmetry of EEG rhythms during motor preparation might occur following "awake brain surgery" for this type of tumour, we recorded electroencephalograms during a simple visuo-manual reaction time paradigm performed by the patients between 3 and 12 months after surgery and compared them to a control group of 8 healthy subjects. Frequency analyses revealed imbalances between the injured and healthy hemispheres. More particularly, we observed a power increase in the δ frequency band near the lesion site and a power increase in the α and β frequency bands. Interestingly, these alterations seem to decrease for the two patients whose surgery were anterior to 9 months, independently of the size of the lesion. Reaction times did not reflect this pattern as they were clearly not inversely related to the anteriority of the surgery. Electrophysiology suggests here different processes of recovery compared to behavioral data and brings further insights for the understanding of EEG rhythms that should not be systematically confounded or assimilated with cognitive performances. EEG monitoring is rare for these patients, especially after awake brain surgery, however it is important.

1. Introduction

Low-Grade Gliomas (LGG – World Health Organization grade II gliomas) are slow-growing primary brain tumours that develop at the expense of glial cells. Because of their infiltrative and diffuse nature, maximizing the resection of tumoural tissue bordering or merging with functional areas brings important risks of neurological impairments (Duffau and Capelle, 2004). It is therefore crucial to distinguish the eloquent cortex and preserve structures supporting essential cognitive processes such as language or motor control from surgical injury (Plaza, Gatignol, Leroy, & Duffau, 2009; Schucht, Moritz-Gasser, Herbet, Raabe, & Duffau, 2013). In this context, direct electrical stimulation (DES) is used during wide-awake brain surgery for online mapping of brain functions (Duffau, 2015; Mandonnet, Winkler, & Duffau, 2010). The neurosurgeon applies DES with a bipolar stimulator on the surface of the brain and along underlying white matter tracts while the patient is asked to perform a set of motor, language, and cognitive tasks. If the patient consistently fails neuropsychological tests during the stimulation, this means that the region remains functional despite the invasion of the lesion and should be preserved. Conversely, if the stimulated region does not cause deficits in appropriate tasks, this means that its function is taken over by another region. This surgical routine allows the progressive identification and optimal resection of the tumour up to the functional limits (Duffau, 2015).

Tumour discovery mostly relies on first epileptic seizure or incidental detection rather than neurological complaints from patients. It has been suggested that the slow progression of LGG contrasts with more acute lesions, allowing the central nervous system to ensure functional homoeostasis while the tumour disseminates to other brain areas (Desmurget, Bonnetblanc, & Duffau, 2007; Duffau, 2013). This very unique physiopathological model and associated neuroplasticity phenomena were investigated in several works, which have suggested

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various patterns of functional redistribution with progressive involvement of both ipsi- and contra-lesional areas in the compensation of gradually damaged neuronal circuits (Bonnetblanc, Desmurget, & Duffau, 2006; Duffau, 2014a,2014b).

After surgical resection, patients only present transient impairments despite massive exeresis volumes, and recover within 3 months showing no clinical deficits in almost all cases. These deficits are hardly detectable using classical neuropsychological evaluations (Duffau et al., 2003; Herbet, Lafargue, Bonnetblanc, Moritz-Gassers, & Duffau, 2013). Regarding, visuo-spatial and motor cognition, preliminary studies proposed dedicated paradigms for the assessment of recovery kinetics. Sallard, Duffau, and Bonnetblanc (2012a) and Charras et al. (2014) both used standard line bisection tests to reveal transient hemispatial neglect and neglect-like symptoms in the acute post-operative phase preceding fast and substantial recovery in all patients. Sallard, Barral, Duffau, and Bonnetblanc (2012b) also proposed a visuo-manual reaction time paradigm to evidence longer reaction times for the contralesional hand. These results clearly suggest some degree of functional asymmetry during the postoperative period, and were hypothesized to represent more global physiological and functional imbalance between brain hemispheres, including subcortical structures (e.g. Thalamus and cerebellum), induced by tumour resection (Boyer et al., 2015a,2015b).

Apart from behavioural aspects, little is known regarding the consequences of awake brain surgery on postoperative brain dynamics. In order to clarify the role of each hemisphere in compensation processes and possible electrophysiological imbalances, Bonnetblanc et al. (2014) measured the electroencephalographic (EEG) activity of 5 patients performing an analogous visuo-manual reaction time task between 3 and 12 months after surgery. The experiment consisted of combinations of visual stimulus location and responding hand to supposedly recruit each hemisphere to a different extent. The study focused on the amplitude of event-related potentials (ERPs) to probe asymmetries of cortical excitability. Surprisingly, they found that excitability was increased in the injured hemisphere but for patients with the smallest lesions and independently of the anteriority of the surgery. Neither behavioral scores nor excitability changes were illustrative of the time passed from the operation.

In the present work, we complement these investigations focusing on the motor preparation period preceding the hand response to study the stationary EEG signal before the ERP and further document the consequences of tumour resection and functional reorganisation on brain electrophysiological dynamics.

We performed usual spectral analyses and searched for potential differences in the amplitude and spatial distribution of common "Brainwaves". These rhythms typically refer to oscillatory activities recorded over the scalp and commonly grouped into bands depending on their frequency, amplitude, and location (Arroyo et al., 1993; Buzsaki and Draguhn, 2004; Garcia-Rill et al., 2016). Their physiological origins and functional role are still highly debated but emerging evidence from animal and human studies suggests their importance in brain spatio-temporal integration and segregation (Varela, Lachaux, Rodriguez, & Martinerie, 2001). Modifications of brain oscillation patterns have been associated with diseases of the central nervous system and quantitatively assessed in EEG studies as clinical indicators, especially in the context of cognitive disorders, seizure, and more particularly, ischemic strokes (Harpale and Bairagi, 2016; Medeiros Kanda et al., 2009; Rabiller, He, Nishijima, Wong, & Liu, 2015). However, alterations of brainwaves in the presence of a brain tumour remain particularly unclear, leading to inconsistent results even though a few MEG and EEG studies highlighted an overall slowdown in electrophysiological activity of the brain, i.e. increased spectral power in the δ (1–4 Hz) and θ (4–8 Hz) frequency ranges (Decker and Knott, 1972; Jongh et al., 2003; Preuß et al., 2015; Selvam and Devi, 2015; Selvam and Shenbagadevi, 2011; Wijk, Willemse, Peter Vandertop, & Daffertshofer, 2012). None of these studies focused on brain oscillations after awake brain surgery and, to the best of our knowledge, no study confirmed the presence of slow waves after the tumour removal. From a functional perspective, the attentional task preceding motor response offers a constrained environment similar to motor preparation paradigm as seen in Brain Computer Interface studies (Han and Bin, 2014) which may help decipher potential modifications of induced brain oscillatory activity, contrasting with ambiguous resting states EEG studies. Therefore, we placed special emphasis on α rhythms (9–12 Hz) and sensorimotor rhythms (consisting of μ: 9–12 Hz and β: 14–20 Hz bands), potentially emerging in occipital and Rolandic areas respectively. These particular oscillations have been linked to visual processing, motor control, motor imagery, action anticipation, and are therefore likely to be elicited during the motor preparation period (Arroyo et al., 1993; Denis, Rowe, Williams, & Milne, 2017; Han and Bin, 2014; Heinrichs-Graham, Kurz, Gehringer, & Wilson, 2017; Kim and Kim, 2016; Sabate, Llanos, Enriquez, & Rodriguez, 2012). The perirolandic region is of particular interest because of its low inter-individual variability (Mellerio et al., 2016). It contains sensorimotor areas which are direct input/oupout for sensory and motor systems and are thus unlikely to be compensated in other locations (Herbet, Maheu, Costi, Lafargue, & Duffau, 2016).

Using spectral analyses, we aim to study the EEG signal during motor preparation period in the frequency domain to provide complementary information and new insights regarding the consequences of awake surgery on brain electrophysiological activity.

2. Materials & methods

2.1. Participants

Five right-handed patients (P1 to P5; 4 males and 1 female; mean ± SD age, 39 ± 5.34, range = [33–45]) and eight age-matched, right-handed, healthy controls (7 males and 1 female; mean ± SD age, 39.75 ± 4.30, range = [33–45]) participated in the study. None of the controls had a history of neurological disease (including motor, visual hemifield, or visuo-spatial impairments). The study complied with the World Medical Association's Code of Ethics (the 1964 Declaration of Helsinki and its amendments). The patients' socio-demographic and clinical characteristics are summarized in Table 1.

P1 (a 35-year-old male) presented with a tumour at right middle and inferior temporal area (Fig. 1a). P2 (a 38-year-old male) presented with a right temporal tumour (Fig. 1b). P3 and P4 (a 44-year-old female and a 33-year-old male, respectively) presented with a right frontal

Table 1
Patient information*:* Socio-demographic and clinical data of the 5 patients enrolled in this study.

Socio-demographic					Clinical			Time of assessment after surgery (months)
Id.	Age (years)	Gender	Edu. level (years)	Handedness	Grade of the tumour	Surgery	Volume of resection (cm3)	
P1	35	M	17	R	II	Awake	7.1	3
P2	38	M	15	R	II	Awake	79.2	3
P3	44	F	12	R	II	Awake	119.1	3
P4	33	M	17	R	II	Awake	116.8	9
P5	45	M	17	R	II	Awake	11.5	12