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# Modulation of central thalamic oscillations during emotional-cognitive processing in chronic disorder of consciousness

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ABSTRACT

We report on thalamic recordings in a patient with chronic disorder of consciousness (DOC). Implantation of central thalamic deep brain stimulation (CT-DBS) electrodes was chosen, as this treatment has been reported to display beneficial effects with respect to behavioural responsiveness in DOC. Local field potential (LFP) oscillations were recorded from central thalamic electrodes and their changes elicited by speech stimuli consisting either of familiar voices addressing the patient or unfamiliar non-addressing phrases were studied. In response to familiar-addressing speech we observed modulation of oscillatory activity in the beta and theta band within the central thalamus accompanied by an increase in thalamocortical coherence in the theta band. Furthermore, the theta phase was coupled to the amplitude of gamma locally in the thalamus. These findings indicate a local and long-range cross-frequency response which is not only indicative of the principle involvement of the central thalamus in processing emotional and cognitive information, but also point towards intact physiological functions that may serve as a marker in diagnosing DOC patients and determining novel targets and parameters concerning therapeutic efforts.



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## 1. Introduction

Assessment of consciousness is still a major issue in the field of clinical neuroscience, both concerning basic research, as well as clinically relevant applications. Recently, it has been suggested to extend established clinical routines in the evaluation of patients displaying diverse disorders of consciousness (DOC) by determining changes in brain activity towards externally applied stimuli (Menon et al., 1998; Monti et al., 2010; Owen et al., 2006). In this context, a differential response in electrophysiological (Cruse et al., 2011) and/or neuroimaging (Eickhoff et al., 2008) derived signals may indicate distinct residual functions of processing emotional and cognitive information and could, thereby, contribute to a more appropriate and sophisticated estimation of a patient's individual state of consciousness, regardless of individual (clinically determined) responsiveness (Fins & Schiff, 2010). Identifying neurophysiological correlates of such residual capacities may, moreover, reveal new and promising targets for novel therapeutic interventions. There is evidence that invasive neuromodulation by means of electrical deep brain stimulation (DBS) of the central thalamus is associated with improvements in behavioural responsiveness after traumatic brain injury (Schiff et al., 2007; Yamamoto & Katayama, 2005; Yamamoto et al., 2005). This is thought to reflect the principle involvement of the thalamus in providing excitatory projections to wide-spread cortical areas and, in turn, facilitating sensory processing. In this context, emphasizing patterns of activity elicited by sensory stimulation via DBS may promote information processing and, thereby, help to re-establish functional integrity in DOC patients.

We examined in a case of chronic DOC distinguishable patterns of central thalamic activity in response to emotionally and cognitively relevant sensory stimulation, i.e., the addressing voices of her children, as compared to unfamiliar voices. The patient was shown before to exhibit specific patterns of cortical and subcortical activity towards these stimuli as revealed by functional magnetic resonance imaging (MRI) (Eickhoff et al., 2008). With respect to these findings, we subsequently assessed electrophysiological measures by means of combined surface EEG recordings and local field potentials (LFPs) from the central thalamus (Ncl. reticularis thalami and internal medullary lamina) to determine modulations in oscillatory activity within these areas.

There are recent publications of LFP recordings from various thalamic regions in different diseases in humans and animals. They report theta, alpha and beta thalamocortical coherence. Especially reports about theta-coherence (Sarnthein & Jeanmonod, 2007, 2008), beta–gamma cross-frequency coupling in memory retrieval (Staudigl et al., 2012) and alpha–gamma coupling based on attention demands (Saalmann, Pinsk, Wang, Li, & Kastner, 2012) supported our hypothesis that (though recorded from a different thalamic site) stimulus-elicited coupling and maybe also local changes in lower frequency power (theta, alpha and/or beta) might occur. We proposed that theta coupling might be a signature of long-range thalamocortical communication and theta might show local entrainment with gamma activity by means of cross-frequency coupling.

## 2. Methods

### 2.1. Patient and procedure

A 45-year-old woman sustained a closed head injury at the age of 38 resulting in a massive subarachnoid haemorrhage and right-hemispheric, space occupying parenchymal haematoma associated with a chronic DOC. Except for stereotypic movements of the left arm she never showed any spontaneous motor activity nor did she respond to environmental stimuli. In the initial assessment following the trauma she was diagnosed with a Glasgow coma scale (GCS) of 4 in the beginning and failed to respond to pharmacotherapeutical intervention (for details of the clinical status see Eickhoff et al., 2008). Since there is evidence for beneficial effects of central thalamic DBS in patients with DOC on behavioural parameters (Schiff et al., 2007; Yamamoto & Katayama, 2005; Yamamoto et al., 2005), after obtaining an ethical vote of the local ethic committee the patient was designated to undergo implantation of bilateral DBS electrodes in the internal medullary lamina and the Ncl. reticularis thalami (Fig. 1A). Target localisation was defined based on atlas coordinates using the atlas by Mai and colleges (Mai, Assheuer, & Paxinos, 2004). Targeting was achieved with neuroimaging by fusion of stereotactic cranial computed tomography (CT) and high-resolution MRI. Furthermore, intraoperative microelectrode recordings using the INOMED MER system (INOMED Corp., Emmendingen, Germany) were performed to obtain some information about the occurrence of bursting activity e.g., of the reticular thalamus. During the operation final macroelectrodes (model 3387 quadripolar DBS lead, Medtronic Inc., Minneapolis, MN, USA) were connected to sterile percutaneous extension wires (model 3550-05, Medtronic), which were led out through the scalp and could be connected postoperatively to EEG amplifiers (BrainAmp, Brain Products GmbH, Gilching, Germany) via external cable connectors (twist lock cable model 3550-03, Medtronic and custom made connector to DIN 428092 touch proof connectors). Thus, postoperative recordings of LFPs from the central thalamus were achieved. Postoperative electrode localisation was visualized on a 3D atlas (Yelnik et al., 2007) by fusion of preoperative MRI and postoperative CT scans with the atlas (Bardinet et al., 2009).

### 2.2. Recordings

Recordings of intrathalamic LFPs were conducted two days after initial implantation of the DBS electrodes and prior to internalization of the corresponding leads and impulse generator. Electrodes provided four distinct contacts along the dorsoventral axis, which provided post-hoc bipolar referencing of adjacent contacts to ensure the local origin of the recorded potentials. Electrical activity of the cortex was measured applying surface EEG-electrodes that were mounted according to the 10-20-System and consisted of the fronto-central (Fz), centro-central (Cz), parieto-central (Pz), occipito-central (Oz) temporal 4 (T4) and temporal 3 (T3) site with a frontopolar reference (Fpz). Signals were recorded with a sampling-frequency of 5 kHz, amplified, low-pass filtered (1000 Hz) and