Clinical Neurophysiology 129 (2018) 959–966

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Occurrence of thalamic high frequency oscillations in patients with different tremor syndromes

Sarah Schnitzler [a,b], Christian Johannes Hartmann [a,c], Stefan Jun Groiss [a,c], Lars Wojtecki [a,c], Alfons Schnitzler [a,c], Jan Vesper [b], Jan Hirschmann [c,*]

[a] Heinrich Heine University, Medical Faculty, Department of Neurology, Center for Movement Disorders and Neuromodulation, Duesseldorf, Germany
[b] Heinrich Heine University, Medical Faculty, Department of Functional and Stereotactic Neurosurgery, Center for Movement Disorders and Neuromodulation, Duesseldorf, Germany
[c] Heinrich Heine University, Medical Faculty, Institute of Clinical Neuroscience and Medical Psychology, Duesseldorf, Germany

ARTICLE INFO

Article history:
Accepted 18 January 2018
Available online 19 February 2018

Keywords:
High frequency oscillations
Tremor
Thalamus
Local field potentials
Neuronal oscillations
Deep brain stimulation

HIGHLIGHTS

- High frequency oscillations (HFO) occur in the thalamus of patients with different tremor syndromes.
- As in the subthalamic nucleus, we found slow (<300 Hz) and fast HFOs (>300 Hz).
- Slow HFOs were stable across several mm and their detection required macroelectrodes.

ABSTRACT

Objective: To assess whether high frequency oscillations (HFOs, >150 Hz), known to occur in basal ganglia nuclei, can be observed in the thalamus.
Methods: We recorded intraoperative local field potentials from the ventral intermediate nucleus (VIM) of the thalamus in patients with Essential Tremor (N = 16), Parkinsonian Tremor (3), Holmes Tremor (2) and Dystonic Tremor (1) during implantation of electrodes for deep brain stimulation. Recordings were performed with up to five micro/macro-electrodes that were simultaneously advanced to the stereotactic target.
Results: Thalamic HFOs occurred in all investigated tremor syndromes. A detailed analysis of the Essential Tremor subgroup revealed that medial channels recorded HFOs more frequently than other channels. The highest peaks were observed 4 mm above target. Macro- but not microelectrode recordings were dominated by peaks in the slow HFO band (150–300 Hz), which were stable across several depths and channels.
Conclusion: HFOs occur in the thalamus and are not specific to any of the tremors investigated. Their spatial distribution is not homogeneous, and their appearance depends on the type of electrode used for recording.
Significance: The occurrence of HFOs in the thalamus of tremor patients indicates that HFOs are not part of basal ganglia pathophysiology.

1. Introduction

Abnormal oscillatory activity in the basal ganglia plays a pivotal role in the pathophysiology of movement disorders. In particular, an increase of beta activity (15–30 Hz) in the subthalamic nucleus (STN) has been suggested to underlie slowing of movement in Parkinson's disease (PD) (Kühn et al., 2009; Ray et al., 2008). Beta oscillations are modulated by dopaminergic medication (Brown et al., 2001; Levy et al., 2002; Priori et al., 2004) and voluntary movement (Cassidy et al., 2002; Levy et al., 2002). Recently, high frequency oscillations (HFOs, >150 Hz) in STN and globus pallidus internus (GPi) were shown to couple with the phase of beta activity (Connolly et al., 2015; López-Azcárate et al., 2010; Özkurt et al., 2011; Yang et al., 2014). Two distinct bands of HFOs have been identified: slow HFOs (sHFOs) in the range of 200–300 Hz and fast HFOs (fHFOs; >300 Hz). Administration of levodopa led to a shift of HFO-power from sHFOs to fHFOs in the STN, and the power ratio of those two bands was found to be correlated with motor symptoms (Özkurt et al., 2011). Furthermore, recent studies in PD patients revealed tremor-related changes in the subthalamic HFO power ratio (Hirschmann et al., 2016, 2017).

* Corresponding author at: Heinrich-Heine-Universität Düsseldorf, Institut für Klinische Neurowissenschaften und Medizinische Psychologie, Universitätsstr. 1, 40225 Düsseldorf, Germany.
E-mail address: Jan.Hirschmann@med.uni-duesseldorf.de (J. Hirschmann).

https://doi.org/10.1016/j.clinph.2018.01.073
1388-2457/

So far, it is unclear whether the occurrence of HFOs is restricted to basal ganglia nuclei or whether they also occur in thalamic nuclei, especially the ventral intermediate nucleus (VIM), which is an effective target for deep brain stimulation in patients with tremor syndromes (Benabid et al., 1996; Schuurman et al., 2000). Research on oscillatory activity in VIM has focused on frequencies <150 Hz. Elevated theta activity (4–7 Hz) was found in the VIM of Essential Tremor (ET) patients (Kane et al., 2009) and it was demonstrated that many neurons in the VIM are coherent with the electromyogram of upper limb muscles at tremor frequency (Lenz et al., 1994). Pedrosa and colleagues demonstrated that these tremor-associated oscillations are confined to spatially distinct "tremor clusters" (Pedrosa et al., 2012), which may arise due to clustered terminal fields of axons transmitting input from the dentate nucleus (Mason et al., 2000). In addition to theta activity, alpha peaks have been described for patients with different tremor syndromes (Paradiso et al., 2004) and beta activity was found in the VIM of tremor, chronic pain and PD patients (Basha et al., 2014; Paradiso et al., 2004). As in other parts of the motor system, beta power in the VIM showed a movement-related decrease (Basha et al., 2014; Paradiso et al., 2004). In contrast, gamma-power increased during movement (Kempf et al., 2009) and was correlated with reaction time (Brücke et al., 2013).

In this study, we recorded intraoperative local field potentials (LFPs) from the VIM of patients with different tremor syndromes to investigate thalamic HFOs.

2. Materials and methods

2.1. Patients and surgery

The protocol was approved by the local ethics committee (No. 2459) and all patients gave written informed consent.

16 patients with Essential Tremor, 3 patients with Parkinsonian Tremor, 2 patients with Holmes Tremor and 1 with Dystonic Tremor underwent surgery for therapeutic deep brain stimulation (DBS). Of the 22 patients, 18 underwent bilateral, and 4 unilateral electrode implantation. Thus, we recorded 40 hemispheres in total. Clinical details on patients are given in Table 1. Because tremor syndromes might differ with respect to HFO properties, such as spatial distribution or the frequencies of HFO peaks, we chose to restrict all group analyses to ET patients, which constitute the largest, clinically homogenous subgroup of this study. Results for patients with other tremor syndromes are described on the individual level only.

Implantation was performed at the Department of Functional Neurosurgery and Stereotaxy, University Hospital Düsseldorf. Stereotactic surgery was performed using a Leksell frame (Elekta Instruments). For targeting, preoperative stereotactic cranial computed tomography (CT) and high resolution 3 T MRI scans were fused. Targeting of the VIM was based on the position of the anterior (AC) and the posterior commissure (PC) and the size of the third ventricle. The VIM target was located in the axial AC-PC plane, 33% of the AC-PC distance in front of the PC and 11.5 mm lateral to the wall of the third ventricle. The stereotactic target was adjusted according to microelectrode recordings and intraoperative test stimulation if necessary. Following intraoperative test stimulation, final implantation of the DBS macroelectrode in the VIM was performed. DBS-electrode location was confirmed intraoperatively by X-ray and postoperatively by stereotactic CT.

2.2. Intraoperative recordings

We recorded LFPs intraoperatively using electrodes with a microelectrode tip and a macroelectrode contact (Inomed ISIS MER system). The macroelectrode contact was located 1.5 mm superior to the tip. Maximally 5 electrodes were simultaneously

Table 1
Patient details. SD, standard deviation; LA, local anaesthesia; GA, general anaesthesia.

Subject	Sex	Age (y)	Disease	Disease duration (y)	Medication	Hemisphere	Number of recording depths (left/right)	Number of trajectories (left/right)	Anaesthesia
et01	F	46	ET	45	–	Left/right	8/8	2/4	LA
et02	F	55	ET	16	–	Left/right	8/8	5/5	GA
et03	F	61	ET	7	–	Left/right	8/8	2/3	LA
et04	M	58	ET	4	–	Left/right	8/8	4/3	GA
et05	M	75	ET	~50	Primidone 125 mg 0-0-1	Left/right	7/8	3/3	GA
et06	M	59	ET	53	Propranolol 20 mg 1–0-0	Left/right	8/8	3/4	LA
et07	M	68	ET	10	–	Left/right	8/8	4/3	LA
et08	M	74	ET	7	–	Left/right	8/7	3/3	LA
et09	M	71	ET	11	Propranolol 160 mg 1-0-0 Primidone 250 mg 0-0-1	Left/right	8/8	2/2	GA
et10	F	69	ET	11	–	Left/right	8/7	4/4	GA
et11	M	75	ET	22	–	Left/right	8/8	5/4	LA
et12	M	75	ET	~50	–	Left/right	8/8	4/3	GA
et13	M	78	ET	~50	–	Left/right	8/8	2/2	LA
et14	F	55	ET	36	Propranolol 80 mg 1-1-1 Primidone 31.25 mg 1-1-1	Left/right	8/8	5/5	GA
et15	F	75	ET	~40	–	Left/right	8/7	2/3	GA
et16	M	75	ET	61	Primidone 62.5 mg 1-0-0	Left/right	8/8	2/3	GA
ht01	F	42	HT	2	–	Left	7	5	LA
ht02	M	26	HT	5	–	Left	8	5	LA
dt01	M	42	DT	5	–	Left/right	7/7	4/5	GA
pd01	F	77	PD	20	Levodopa/benserazide 100/25 mg 1-1-1-1 Primidone 125 mg 0-1-0	Left/right	8/8	3/3	LA
pd02	F	77	PD	18	Levodopa/Carbidopa/ Entacapone 150/37.5/200 mg 1-1-1-1 Quetiapin 25 mg 0-0-0-1	Right	8	3	GA
pd03	M	78	PD	3	–	Right	7	3	LA
Mean		64.1		23.9			7.9/7.8	3.4/3.5	
SD		14.6		20			0.31/0.4	1.1/1.0	