Clinical Neurophysiology 126 (2015) 2290–2298

Contents lists available at ScienceDirect

Clinical Neurophysiology

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

Signal features of surface electromyography in advanced Parkinson's disease during different settings of deep brain stimulation

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ARTICLE INFO

Article history:
Accepted 21 January 2015
Available online 16 February 2015

Keywords:
Surface electromyography (EMG)
Parkinson's disease (PD)
Deep brain stimulation (DBS)
Nonlinear dynamics

HIGHLIGHTS

- Efficacy of deep brain stimulation (DBS) treatment was quantified here by using surface EMG and acceleration measurements.
- EMG signal features differed between different DBS settings for biceps brachii muscles.
- EMG features pointed to previously defined optimal settings in most of patients.

ABSTRACT

Objective: Electromyography (EMG) and acceleration (ACC) measurements are potential methods for quantifying efficacy of deep brain stimulation (DBS) treatment in Parkinson's disease (PD). The treatment efficacy depends on the settings of DBS parameters (pulse amplitude, frequency and width). This study quantified, if EMG and ACC signal features differ between different DBS settings and if DBS effect is unequal between different muscles.
Methods: EMGs were measured from biceps brachii (BB) and tibialis anterior (TA) muscles of 13 PD patients. ACCs were measured from wrists. Measurements were performed during seven different settings of DBS and analyzed using methods based on spectral analysis, signal morphology and nonlinear dynamics.
Results: The results showed significant within-subject differences in the EMG signal kurtosis, correlation dimension, recurrence rate and EMG–ACC coherence between different DBS settings for BB but not for TA muscles. Correlations between EMG feature values and clinical rest tremor and rigidity scores were weak but significant.
Conclusions: Surface EMG features differed between different DBS settings and DBS effect was unequal between upper and lower limb muscles.
Significance: EMG changes pointed to previously defined optimal settings in most of patients, which should be quantified even more deeply in the upcoming studies.

1. Introduction

Several parts of the brain participate in controlling the posture, force and movements in humans. These parts include the premotor and primary motor cortex, cerebellum and basal ganglia (Moritani et al., 2004). In Parkinson's disease (PD), there is a progressive degeneration of dopaminergic neurons in the substantia nigra in the basal ganglia. This leads to abnormalities in the basal ganglia function and finally to the primary symptoms of PD: resting tremor, rigidity (increased muscle tone) and bradykinesia (slowness of movements) (Wichmann et al., 2008). PD cannot be cured but the symptoms can be relieved with medication that aims either

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http://dx.doi.org/10.1016/j.clinph.2015.01.021
1388-2457/

to increase the amount or to inhibit the breakdown of dopamine in the brain (Gárdián and Vécsei, 2010). Deep brain stimulation (DBS) can be used to treat advanced PD, when optimal oral medication fails to sufficiently control motor symptoms. The most common target is subthalamic nucleus (STN), although Globus Pallidus Interna (GPi) stimulation has also been used as treatment option in advanced PD (Malhado-Chang et al., 2008). DBS delivers high frequency current to stimulate the STN in the basal ganglia resulting in a complex pattern of excitatory and inhibitory effects that modulate the entire network between basal ganglia, thalamus and cortex. It is thought that DBS regularizes neuronal patterns preventing the transmission of pathologic bursting and oscillatory activity in the brain. This results in improved processing of the sensomotor information and alleviation of motor symptoms (Miocinovic et al., 2013). Often there is a significant reduction in the daily levodopa dose, when STN is stimulated (Benabid et al., 2009; Malhado-Chang et al., 2008).

Efficacy of DBS treatment depends significantly on the correct placement of stimulation electrodes, and on the optimal settings of stimulation parameters. In constant-voltage mode (which is the most common mode used), the controllable stimulation parameters are the amplitude, frequency and width of the stimulation pulse. By choosing active electrode contacts and their polarity, the electrical current can be targeted to correct neural elements (Volkmann et al., 2006; Montgomery, 2010). In some cases, the optimization of DBS treatment is not straightforward because the stimulation parameters are set by subjective evaluation of symptoms and the symptoms may respond to DBS with a variable delay (Levin et al., 2009; Groiss et al., 2009). Rigidity and tremor respond usually within a few minutes and they require only little co-operation from the patient. The tremor may, however, be influenced by the emotional state in some patients. Bradykinesia may respond to DBS in several hours or even days. Therefore, the changes in bradykinesia may not be observed during the DBS adjustment session in all patients (Malhado-Chang et al., 2008; Volkmann et al., 2006). With a careful adjustment of stimulation parameters also the unpleasant adverse effects such as dyskinesia, dystonia (involuntary muscle contractions), dysarthria (speech problems) and abnormal eye function (e.g. diplopia), may be eliminated (Malhado-Chang et al., 2008; Miocinovic et al., 2013).

The DBS parameters have a therapeutic range, inside which the clinical efficacy is maximal while the current consumption stays reasonable. It has been observed that an increase in the stimulation amplitude leads to increase in the distance of the stimulated neural elements and usually to a reduction in motor symptoms (Volkmann et al., 2006). On the other hand, amplitude increase may give rise to unwanted side-effects by stimulating adjacent elements besides STN (Groiss et al., 2009). Therapeutic amplitudes range between 1 and 3.5 V, above which the electrical current consumption may rise abruptly (Volkmann et al., 2006). The adjustment of pulse amplitude is usually done in 0.3–0.5 V steps (Montgomery, 2010). If needed, the pulse width (60–90 μs) can be increased in order to compensate reduction in the stimulation amplitude (Malhado-Chang et al., 2008). It is known that low DBS frequencies (<10 Hz) may increase parkinsonian symptoms and high frequencies reduce them. The therapeutic pulse frequencies are thought to be above 100 Hz and usually maximal benefit of DBS is around 130 Hz (Volkmann et al., 2006). However, it has been noticed that high-frequency DBS (130 Hz) may worsen gait and speech while low-frequency DBS (60 Hz) may improve them in some patients (Xie et al., 2012; Montgomery, 2010; Moreau et al., 2008). System Oscillations theory (Montgomery, 2010) has been suggested as one explanation for that.

Surface electromyography (EMG) enables the objective quantification of neuromuscular function. Therefore, it may be useful in quantifying treatment efficacy in PD. Previous EMG-based studies have shown that DBS may change the EMG signal characteristics by increasing the dominant tremor frequency in the EMG spectrum (Blahak et al., 2007; Sturman et al., 2004) and by reducing the EMG–acceleration coherence during a resting condition and with backward counting (Sturman et al., 2004, 2007). DBS may also increase the size of the first agonist burst and the number of agonist bursts during rapid point-to-point movements of the elbow and ankle (Vaillancourt et al., 2004, 2006). Rissanen et al. (2011) have presented previously a principal component (PC)-based tracking method for quantifying the effects of DBS in PD by using EMG and kinematic measurements and analysis. The presented method was capable of detecting differences in the surface EMG and acceleration (ACC) signal features between the DBS on- and DBS off-states. However, it stays unclear, if muscle activation and surface EMG are unequal between different settings of the DBS parameters. If surface EMG was unequal between different settings of DBS treatment, it could work in helping the optimal adjustment of DBS treatment. It is also unclear, if surface EMG is changed similarly in upper and lower extremity muscles during the adjustment of DBS settings.

This study aims answer to three questions: What happens to the surface EMG signal characteristics of arms and legs:

- when the stimulation amplitude is increased or decreased with 0.3 V?
- when the stimulation frequency is increased or decreased with 30 Hz?
- when the stimulation pulse width is increased with 30 μs?

In this study, surface EMGs were measured from the biceps brachii (BB) and tibialis anterior (TA) muscles of 13 PD patients with previously implanted DBS during seven different settings (varying stimulation amplitude, frequency or pulse width) of the DBS treatment. The selected DBS settings were supposed to be safe for the patients and causing minimal side-effects. The measured signals were analyzed using different EMG signal parameters.

2. Methods

2.1. Subjects

Thirteen patients with advanced PD participated in this study after giving their informed consent. All patients had been treated with bilateral STN-DBS (Kinetra or Activa PC Neurostimulators, Medtronic Inc., Minneapolis, MN, USA) for 2–34 months. The details of patients, clinical scores (total scores of UPDRS III Motor Examination), STN-DBS details and medications are given in Table 1. The study was approved by the local human ethics committee of the Kuopio University Hospital. The EMG measurements were performed during seven different stimulation settings which are detailed in Table 2. The setting state *S0* refers to the previously (less than 6 months ago) defined optimal parameter values that each patient had used for DBS treatment. Because of severe symptoms, the patients were on-medication during the measurements. If the patient suffered from difficult adverse effects with some stimulation settings, the measurement was canceled and the analysis was not performed with those settings. One patient could not be measured with $A+$ and one patient with DBS OFF. Four patients could not be measured with $W+$. The order of setting states $A+$, $A-$, $F+$, $F-$ and $W+$ was randomized between patients in the measurements. However, the first setting state was *S0* in all patients, which corresponds to typical adjustment session of previously implanted DBS. From that state we got the reference values for clinical scores. The last setting state studied was *OFF* in all patients, because the symptoms were quite severe in many patients when