Thalamic Neuronal and EMG Activity in Psychogenic Dystonia compared with Organic Dystonia

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Abstract

This study is a retrospective analysis of thalamic neuronal and electromyogram activities between subjects with organic dystonia and a subject with psychogenic dystonia, in whom a thalamotomy was carried out before a diagnosis psychogenic dystonia was made.

The electromyogram signal to noise ratio in the lowest frequency band (<0.76Hz, dystonia frequency – DF) in the electromyogram was not significantly different by diagnosis or muscle (Table 1). The coherence at dystonia frequency for wrist flexors X biceps electromyograms was significantly higher in organic dystonia, while the phase was not apparently different from zero for either diagnosis.

In a thalamic pallidal relay nucleus (ventral oral posterior), neuronal firing rates were not apparently different between psychogenic and organic dystonia. The neuronal signal to noise ratio in ventral oral posterior was significantly higher in organic dystonia than in psychogenic dystonia, while both were greater than in controls with chronic pain. Spike X electromyogram coherence was not apparently different between psychogenic and organic dystonia. The proportion of thalamic cells responding to joint movements was higher in the cerebellar relay nucleus (ventral intermediate) of psychogenic dystonia than organic dystonia.

These results suggest that some features, such as firing rates and thalamic reorganization, are similar in psychogenic and organic dystonia. Other features differ, such as the coherence between the electromyograms from different muscles, and the thalamic neuronal signal to noise ratio, which may reflect pathophysiological factors in organic dystonia.

Keywords

Psychogenic Dystonia; Organic Dystonia; Human thalamus; Neuronal activity; Plasticity; Dystonia related activity

INTRODUCTION

The pathophysiology of psychogenic dystonia (PsyD) is not well understood, and some of the same physiological abnormalities identified in organic dystonia have also been found in PsyD [1]. It is possible that some physiological abnormalities do not cause the dystonic movements, but result either from the movements, or from some other common pathophysiological factor. Reorganized forebrain sensory and motor maps have been suggested to result from repetitive movements both in patients with dystonia, and in a monkey model of dystonia [2-4], This concept is consistent with studies demonstrating that repetitive motor activity can lead to reorganization of thalamo-cortical sensory and motor maps in monkeys [5,6]. In addition, the activity of thalamic neurons often show significant peaks of activity at the frequency of dystonic movements (dystonia frequency, DF, <0.76 Hz)[4].

We have previously reported reorganized thalamic maps and altered dystonia frequency activity in patients undergoing thalamotomy for dystonia [4]. Subsequent to surgery, one of these patients was diagnosed as having PsyD. This situation provided a unique opportunity to report descriptively how thalamic neuronal activity in PsyD differs from that recorded in patients with organic dystonia and in 'controls' operated for treatment of chronic pain.

METHODS

Results of surgery in the patient with PsyD were included in a report of nine patients with organic dystonia [4]. At that time, our patient with PsyD was diagnosed with organic dystonia. Thalamic activity in the psychogenic patient could be analyzed only for the first operation because of the poor quality of recordings in the previously operated thalamic nuclei [4]. The electromyogram (EMG) was sampled from myohyoid, deltoid, biceps and wrist flexors in the psychogenic patient, versus flexors and extensors of the elbow and wrist in the other nine patients. Therefore, the thalamic spike X EMG cross-correlation was not previously compared with the other patients [4]. These results were also compared with those in three patients with chronic pain secondary to thoracic spinal cord injury. None of these patients had pain or altered motor function in the upper extremity; clinical details are reported in a previous publication[7].

All the methods used in this study have been previously described in detail [8-10]. Deep sensory cells responded reliably to rapid joint movements and/or squeezing of muscles or tendons, but did not respond to stimulation of the skin deformed by these stimuli. Dystonic movements prevented the sub-classification of deep sensory cells and the identification of cells responding during active movements [4]. Therefore, cells responding to cutaneous stimuli provided our most reliable physiological landmark; putative nuclear location was estimated by moving the atlas maps along the anterior commissure-posterior commissure (AC-PC) line to align the anterior border of Vc with the most anterior cell in the region where the majority of cells respond to cutaneous stimulation [4].

Postoperative Analysis

The action potentials of single neurons were discriminated and digitized at 10 kHz by a standard shape-fitting package (Explorer, Brainwave, Thornton, Colorado). The spike train was converted into an equivalent analog signal by using the French-Holden algorithm, a standard technique which preserves the time resolution of the action potentials in the spike train [10-12]. The EMG signals were high pass filtered (6 dB) at 20 Hz to eliminate low frequency movement artifact while preserving the raw EMG signal. We had data epochs which were long enough to be analyzed by a standard spectral analysis technique, rather than by a multi-tapper technique which would have been required for shorter epochs [13].

Standard techniques were used to take, process and interpret the spectral analysis of the neuron and EMG signals[4,10,12].

Patient with Psychogenic Dystonia

The patient was a 33 year old woman with a two year history of dystonia at the time of the first surgery. The dystonia involved the left oro-mandibular structures and the left upper and lower extremity. She had failed treatment with trihexyphenidyl (40 mg per day) and with levodopa/carbidopa. Marked post-operative improvement lasted only 2 months. Following a second, right-sided thalamotomy 18 months after the first, dystonia progressed to involve the other side of the body. Six months later she was seen by a movement disorders neurologist. The diagnosis of PsyD was subsequently made based upon: (1) inconsistencies on examination such as severe tongue involvement only when speech was formally assessed, extreme slowness in performing finger-to-nose testing, but normal speed of similar voluntary movements outside of the context of the examination, and (2) incongruities with organic dystonia including marked acute exaggeration of generalized dystonic postures, such as severe axial extension triggered when she was asked to look upward, and the rapid progression to generalized involvement in an adult without other neurological abnormalities. At that time, she had severe generalized dystonia involving her face, all limbs and axial muscles, and required assistance to walk.

The patient was informed that she might improve considerably with admission to hospital, physiotherapy and withdrawal of the anti-cholinergic medication. Within days of hospitalization, the dystonia had almost completely resolved. At the time of discharge, she had only minimal posturing in the left hand and that subsequently resolved. In view of the rapid and sustained remission, the diagnosis of PsyD was clear. She remained stable on further follow-up and so psychiatric assessment and treatment was not actively pursued.

RESULTS

Analysis of EMG was carried out and demonstrated no apparent difference in signal to noise ratio (SNR) between diagnoses of dystonia (Table 1). The EMG X EMG cross-correlation function could only be compared for wrist flexors × biceps (see *Methods*). In patients with organic versus psychogenic dystonia, more synchronous EMG activity was observed between these muscles (Table 1).

Although RF maps were recorded for cells in the ventral intermediate nucleus (Vim), records of activity during involuntary movements were only available for neurons in ventral oral posterior (Vop) in the patient with PsyD. Therefore, analysis of spike trains and spike X EMG functions were limited to Vop, whereas analysis of somatic sensory properties included neurons in both Vim and Vop. The Vop spike SNR at dystonia frequency was significantly higher in organic dystonia than in PsyD and both were greater than in patients with chronic pain (Table 1). Neither firing rates nor ISIs appeared to be different between these diagnostic groups.

The proportion of neurons with spike X EMG coherence > 0.42 and maximum SNR at dystonia frequency did not appear to be different between PsyD versus organic dystonia, for either wrist flexors or biceps. The phase did not appear to differ between dystonia diagnoses.

Figure 1, shows the thalamic map of neuronal location and stimulation sites for the patient with PsyD. It is remarkable for the large number of cells with deep receptive fields, which was significantly greater than in patients with chronic pain. The size of the representations of individual joints in Vim (see Figure 1) did not appear to be different between the dystonia diagnoses, although these lengths were less in chronic pain than in organic dystonia.

DISCUSSION

The patient with PsyD has a secure diagnosis since her dystonia remitted with suggestion and physiotherapy, fulfilling Fahn & Williams' criteria for Documented Psychogenic Dystonia [14]. We believe that it is unlikely that she had organic dystonia originally followed by PsyD post-surgery since the appearance of the dystonia was very similar throughout her clinical course, and since the pattern of clinical remission was consistent with PsyD. The results in this manuscript were obtained from this one patient, and the number of cells studied was limited, so the conclusions must be considered tentative until confirmed.

The physiological results suggest that Vop neuronal activity is characterized by higher SNR in organic than psychogenic dystonia, while both are higher than in patients with chronic pain (Table 1). This finding suggests that SNR is an abnormal feature in both types of dystonia, which differs in degree between the two diagnoses. The increased SNR in PsyD may be either a consequence of dystonic movements, or a risk factor which predisposes to the development of dystonia during repetitive movements, or both [2,15]. The origin of this change could be related to grouped GPi neuronal discharges in dystonia patients [16,17] which increase with increasing duration and severity of dystonia [16,18]. GPi projects to Vop and lesions of either of these structures may interrupt dystonia [4,19]. Thalamic neuronal activity was often correlated with EMG activity in both diagnoses, and so may drive movement for both whether it is a consequence of dystonic movements or risk factor for the development of these movements.

The large number of deep sensory cells in PsyD may also be due to a plastic change in the sensory representation resulting from dystonic movements. Specifically, cortical plasticity associated with sensory protocols including associative conditioning lead to greater cortical reorganization than do protocols in which sensory stimuli are not related to conditioning [20,21].

The present study also points to differences between the two types of dystonia. EMG coherence between arm muscles has previously been described in organic dystonia [22,23], excepting focal hand dystonia [24]. EMG coherence was lower in PsyD (Table 1). This may be a useful measure to distinguish psychogenic from organic dystonia. Paired associative magnetic stimulation testing of cortical plasticity may also differentiate these conditions [25]. Such non-invasive measures may be practical biomarkers for distinguishing psychogenic from organic dystonia, especially given the difficulty differentiating them on clinical grounds alone.

Acknowledgments

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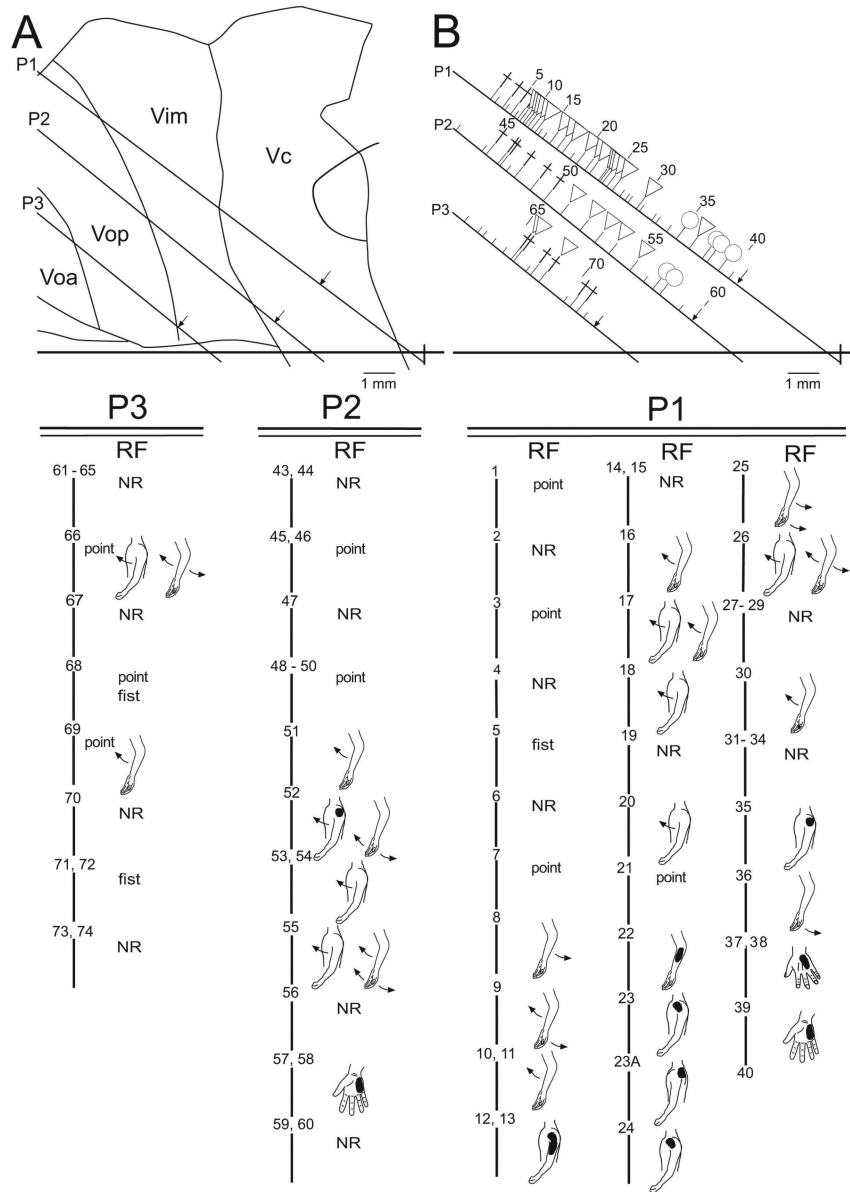
Figure 1.
Sagittal map of thalamic neuronal location relative to the AC-PC line (horizontal line, PC as indicated) and nuclear boundaries, in the patient with psychogenic dystonia. Electrode trajectories (P3, P2 and P1) are shown by the oblique lines. Locations of recording sites are indicated by ticks to the right of each trajectory. Long tics indicate location of a neuron which responded during sensory stimulation, or active movement, or both; short tics indicate unresponsive neurons. The symbol at a long tic indicates the presence of a neuron responding during active movement (cross), cutaneous stimulation (circle), and deep stimulation (triangle), as described in the methods. Sites are numbered sequentially and numbers are indicated for every fifth tick. Scale as indicated.

Lower panels P1, P2, and P3 show the site number, and receptive field (RF). RF is indicated to the right and below the site number. Note that many cells responded to movement of two joints. For example, one cell responded to extension of both shoulder and elbow. Shading on the figurine indicates the part of the body where mechanical stimulation-evoked cellular

activity. All shaded figurines indicate cutaneous stimulation, except for neurons 22 - 24, 35, at which cellular activity was evoked by manipulation of muscle but not by manipulation of the overlying skin. The maximum size of the representation of a part of the body was estimated from the lengths of single electrode trajectories along which all RFs included a single joint, as in a previous study [7]. For example, in electrode trajectory P2, passive shoulder movements were represented by neurons 52 to 55, a distance of 2.5 mm.

Table 1

Summary of results.

Group	Psychogenic	Organic	Pain
Segments with EMG peak < 0.76Hz among segments per epoch.	85%, ND Mann Whitney.	81%	--NA
Wrist Flexor x Biceps EMG coherence	0.23, P<0.01 Mann Whitney.	0.39	--
EMG phase	5.3, ND, Mann Whitney.	-7.9	--
Vop neuron firing rate	14.2 Hz, ND, Mann Whitney.	15.1 Hz	18.3 Hz, ND to both groups
Vop neurons SNR	2.1, P <0.01, Mann Whitney.	3.8	1.2, P<0.001 for both groups
Proportion of Vop neurons with high spike × EMG coherence	59% for WF. 32% for biceps ND for both muscles, Chi square.	25% for WF 58% for biceps	--
Proportion of Vop neurons with phase lead	69% for WF 43% for biceps ND for both muscles, Chi square.	100% for WF 43% for biceps	--
Proportion of cells in Vim and Vop responding to joint movement	26/50 lumped, P<0.00001 23/31 Vim, P<0.00001 3/19 Vop, ND. Chi square.	74/334 lumped 62/222 Vim 12/112 Vop	--
Vim and Vop sensory reorganization	0.7 mm, ND, Mann Whitney.	1.1 mm	0.6 mm, P <0.05 Mann Whitney for the Organic Group only

Grey shading indicates significant results. P values in the Psychogenic column indicate differences to the Organic group. P values in the Pain column indicate differences to one or both of the other groups. ND indicates that the variable is not significantly different by patient group, but does not in any way prove that the two groups are the same. Abbreviations: EMG – electromyogram, SNR - Signal noise ratio, Vim and Vop – thalamic nuclei Ventralis intermedius and oralis posterior. Other conventions as in the text.