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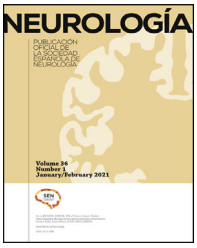

ORIGINAL ARTICLE

Sensitivity and pain in focal dystonia of the hand☆,☆☆

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Abstract
Introduction: A growing body of evidence highlights the importance of understanding both the sensory and the motor pathophysiology of focal dystonia in order to improve its treatment. This study aims to evaluate somatosensory afferences in patients with focal or segmental dystonia affecting the upper limbs, to analyse whether the dominant limb is more frequently affected, to analyse pain tolerance, and to examine the potential association with pain perception in patients with hand dystonia.
Methods: We recruited 24 participants: 12 patients with focal hand dystonia and 12 individuals without dystonia. All participants were evaluated with a digital algometer (Somedic SenseLab AB®, Farsta, Sweden), a Semmes-Weinstein monofilament test, and the visual analogue scale for pain.
Results: According to our data, patients showed greater impairment in surface sensitivity than controls, both in the dominant and the non-dominant hands, as well as greater presence of pain ($P > .001$). Furthermore, the dystonia group showed a negative correlation between perceived pain and pressure pain tolerance threshold (rho = −0.83; $P < .001$).
Conclusions: Patients with focal hand dystonia presented alterations in sensitivity and more severe perceived pain than individuals without dystonia. Future studies with larger samples should aim to analyse the clinical implications and everyday impact of both objective and subjective pain.

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PALABRAS CLAVE
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Sensibilidad y dolor en distonías focales de la mano

Resumen
Introducción: Considerando las evidencias acumuladas actualmente es importante estudiar la fisiopatología tanto sensorial como motora de las distonías focales para comprenderlas y mejorar su tratamiento. Por ello, los objetivos del presente estudio son evaluar las aferencias somatosensoriales de los pacientes con distonía focal o segmentaria con afectación del miembro superior, comprobar si se corresponde con la mano de más uso, analizar la tolerancia al dolor y examinar la posible relación con la percepción del dolor en los pacientes con distonía segmentaria de la mano.
Métodos: Se contó con una muestra total de 24 participantes: 12 pacientes con distonía focal de la mano y 12 sujetos sin distonía. Todos ellos fueron evaluados con un algómetro electrónico (Somedic AB®, Farsta, Suecia), con los monofilamentos de Semmes-Weinstein y con la escala visual analógica.
Resultados: Los datos hallados muestran, en la población estudiada, una mayor afectación en la sensibilidad superficial comparada con el grupo control, tanto en la mano dominante como en la no dominante, así como presencia de dolor ($p > 0{,}001$). Además, el grupo de distonía focal obtuvo una correlación negativa entre el dolor percibido y en el umbral de tolerancia de dolor a la presión ($rho = -0{,}83$; $p < 0{,}001$).
Conclusiones: Las personas con distonía segmentaria de la mano presentan una alteración en la sensibilidad y manifiestan mayor dolor percibido que las personas sin distonía. Se requieren más estudios con una muestra mayor que detecten las implicaciones clínicas y cotidianas, tanto del dolor objetivo como subjetivo.

Introduction

Dystonia is the third most common movement disorder, after essential tremor and Parkinson's disease. It is characterised by sustained or intermittent muscle contractions that cause abnormal, repetitive movements and/or postures.[1] It is often triggered or exacerbated by voluntary action, and is associated with excessive or overflow muscle activation.[2] While the pathophysiology of dystonia is not yet fully understood, 3 mechanisms have been identified that may coexist: loss of neuronal inhibition, irregular sensorimotor integration, and altered synaptic plasticity.[3] Recent publications underline the importance of studying both sensory and motor pathophysiology in order to fully understand focal dystonia and improve the treatment of the condition.[4]

Medical treatment varies according to the type and localisation of dystonia, and currently includes oral drugs for generalised dystonia, intramuscular botulinum toxin (BTX) injections for focal dystonia, and surgery for either type.[5] In addition to medical treatments, other approaches are based on rehabilitation techniques combined with immobilisation of the affected segment, eliminating the repeated sensory stimulation.[6–8]

The latest studies establish different theories on the pathophysiology of dystonia, though none is conclusive. Some authors suggest that dystonia may be caused by an alteration of cortical-subcortical sensorimotor maps, which are usually segregated, in the putamen; this would lead to a loss of functional selectivity of muscle activation.[9] However, Herath et al.[10] observed no significant differences in MRI studies of the sensorimotor cortex or basal ganglia of patients with dystonia. Other researchers focus on impaired modulation patterns in patients with writer's cramp, which may reflect deficiencies in the integration of proprioceptive afferent inputs and reduced inhibition of cortical and spinal levels during writing.[11] The 2019 study by Battistella and Simonyan[12] suggests that abnormal hyperexcitability of the premotor-parietal-putaminal circuitry may be explained by alterations in information transfer between these regions secondary to an underlying deficiency in connectivity. Regarding pain tolerance, pain pressure thresholds are reported to be 2 times lower in patients with dystonia than in individuals without the disorder[13,14]; according to Stamelou et al.,[13] pain is correlated with quality of life, which is not the case for motor symptoms.[15,16] These studies indicate that much remains to be understood about sensitivity, its processing, and its relationship with pain in these patients. Thus, we conducted a study into dystonia symptoms and their association with sensitivity.

This study aims to evaluate somatosensory afferents in patients with focal or segmental dystonia affecting the upper limbs, to determine whether the hand affected is the dominant one, to analyse pain tolerance, and to examine the potential relationship with pain perception in patients with dystonia.

Patients and methods

We conducted a descriptive cross-sectional case-control study. We included a sample of 24 individuals: 12 patients with dystonia and 12 controls without the condition. Cases were recruited by non-probability sampling of consecutive patients at the neurology department of Hospital Ramón y Cajal (Madrid, Spain). Patients had been diagnosed at the hospital's movement disorders unit, which established a diagnosis of occupational or continuous isolated focal or segmental dystonia of the upper limb, according to the clinical consensus criteria of the Movement Disorder Society. Controls were selected by convenience sampling of individuals close to the research team and from the university setting. In the selection of controls, we excluded all individuals presenting any disease or pro-

Table 1 Sociodemographic characteristics of the sample.

	Patients with dystonia (n = 12)	Controls (n = 12)
Type of dystonia: focal/writer's cramp/segmental, n (%)	3 (25)/7 (58.3)/2 (16.7)	
Age, years: mean ± SD (range)	51.50 ± 16.80 (25-76)	50.08 (12.25) (25-65)
Sex: women/men, n (%)	3 (25)/9 (75)	4 (33.3)/8 (66.7)
Level of schooling: basic/medium/high, n (%)	2 (16.7)/5 (41.7)/5 (41.7)	0 (0)/0 (0)/12 (100)
Disease progression time, years: mean ± SD (range)	14 ± 13.88 (2-50)	0 (0) (0-0)
Dominant hand: right/left, n (%)	12 (100)/0 (0)	11 (100)/0 (0)
Most affected side: right/left, n (%)	12 (100)/0 (0)	0 (0)/0 (0)
Burke-Fahn-Marsden scale score, median (q1—q3)	4.50 (4-7.86)	
Musculoskeletal problems; neck/R shoulder/lumbar spine/none, n (%)	2 (16.7)/3 (25)/2 (8.3)/6 (50)	0 (0)/0 (0)/1 (9.1)/10 (90.9)
Psycho-emotional problems: anxiety/frustration/combination/none, n (%)	4 (33.3)/1 (8.3)/1 (8.3)/6 (50)	1 (8.3)/0 (0)/0 (0)/11 (91.7)
VAS, median (q1-q3)	0 (0-5.75)	0 (0-0)
QUICKDASH general score, median (q1-q3)	18.27 (6.81-33.52)	1.13 (0-7.95)
QUICKDASH work module, median (q1-q3)	50 (18.75-62.5)	0 (0-0)
IMPACT-S, median (q1-q3)	89.5 (69-94)	99 (97.25-99)

IMPACT-S: ICF-Measure of Participation and Activities Screener; SD: standard deviation; VAS: visual analogue scale.

cess related to dystonia or any disease or lesion that may affect the upper limbs.

Inclusion criteria for the patient group were as follows: aged between 18 and 75 years; right-handed; diagnosed at least a year previously with occupational dystonia/focal dystonia of the hand/segmental dystonia with upper limb involvement.

Exclusion criteria were: combined or secondary dystonia or pseudodystonia, and other neurological diagnoses or musculoskeletal alterations or lesions affecting the upper limbs.

The study was approved by the ethics committee of Universidad Rey Juan Carlos and Hospital Ramón y Cajal, and complies with the principles of the Declaration of Helsinki on medical research involving human subjects, adopted at the 18th World Medical Assembly (Helsinki, Finland, June 1964), and the latest amended version, updated at the 64th World Medical Association General Assembly (Fortaleza, Brazil, October 2013). Participants gave written informed consent for inclusion in the study.

Participants were assessed at Universidad Rey Juan Carlos (Madrid, Spain). Data were recorded on sociodemographic variables, dominant hand, and clinical variables. We subsequently conducted algometry and Semmes-Weinstein monofilament testing.

Semmes-Weinstein monofilaments (Touch Test Sensory Evaluators)[17,18] are used for non-invasive evaluation of skin sensitivity. This test provides objective, reproducible results. Sensitivity was examined in several areas innervated by different nerves. In the hand, we tested 7 points on the palmar face of the thumb and index finger to explore the function of the median nerve, the fifth finger and hypothenar eminence to evaluate the ulnar nerve, and the back of the hand to evaluate the radial nerve.

For algometry testing, we used a digital algometer (Somedic AB®, Farsta, Sweden),[19] which is able to objectively measure the pain threshold and pain tolerance. The tip of the rod is placed perpendicular to the muscle fibre and progressive stimulation is applied (increase of 1 kg per second) until the patient indicates that the sensation changes from pressure to pain. Stimulation is applied 3 times in each location, with a rest period of 30 seconds between readings. The pressure applied corresponds to the mechanical nociceptive threshold or pain pressure threshold.[20,21] Measurements are taken bilaterally at the major occipital, median, ulnar, radial, and tibial nerves, which are identified by manual palpitation. The major occipital nerve was located lateral to the occipital protuberance, at a mean distance of 4 cm. The median nerve (C5) was identified by palpation over the medial part of the cubital fossa, adjacent to the biceps tendon. The radial nerve (C6) was evaluated across the lateral intermuscular septum between the medial and lateral heads of the triceps to reach the middle third of the humerus. The ulnar nerve (C7) was located between the sulcus of the medial epicondyle and the olecranon. The tibial nerve was localised approximately 4 cm below the tibial tuberosity, above the tibialis anterior muscle.[19]

The visual analogue scale (VAS)[22] is a subjective instrument in which the patient scores their perceived pain from 0 (no pain) to 10 (worst possible pain).

Statistical analysis

We initially collected descriptive data from the whole sample, recording data on functional status, and personal and sociodemographic variables. We calculated the frequency of categorical variables and the mean or median for continuous variables. We determined whether the sample was homogeneous by testing for normal distribution of all variables with parametric and non-parametric tests.

Secondly, we tested for correlations between different variables using the non-parametric Spearman test and the parametric Pearson test.

Statistical analysis was performed using the SPSS statistics software (©2013, version 22.0; IBM SPSS Corp.).

Results

We studied 12 patients with isolated dystonia of the upper limb and 12 age- and sex-matched controls. Table 1 shows descriptive data from the tests performed and participants' personal and sociodemographic data.

Monofilament testing identified no significant differences between groups, except in the palmar face of the right thumb (P = .04) and the proximal phalanx of the fifth finger of the left (non-dominant) hand (P = .05). This may indicate that patients with

dystonia are more sensitive to superficial touch than controls, as they were able to feel/locate stimulation from 0.07 g of pressure, compared to 0.20 g in controls.

Algometry testing identified no statistically significant differences between groups, except at the left nerve point of the neck (C5/C6) (P = .02). At this location, patients with dystonia identified pressure as pain earlier than controls (1.34 kg vs 2.18 kg).

Significant differences between groups were found for VAS scores (P = .001).

The patient group displayed a significant negative correlation between VAS scores and algometry results, except in the right neck, left radial and median nerves, and bilateral ulnar nerve and hand. This negative correlation is explained by the fact that VAS scores and algometry results are inversely proportional: patients able to tolerate fewer grams of pressure report more intense pain in the VAS. Table 2 shows the correlations identified in the patient group and in the sample as a whole.

Discussion

We evaluated somatosensory afferents in patients with isolated upper limb dystonia and verified whether these corresponded to the dominant hand. Our results for the evaluation of tactile sensitivity show that patients with focal dystonia present hypersensitivity in both hands: the palmar face of the thumb (C6 dermatome) in the right hand, and the proximal phalanx of the fifth finger (C8 dermatome) in the left (non-dominant) hand. These findings stand in contrast with those reported by Sanger et al.,[23] who observed a significant reduction in tactile spatial sensitivity in the dominant hand in patients with writer's cramp. Contarino et al.[24] conducted a study using somatosensory evoked potentials, finding no evidence of alterations in somatosensory integration, although this method may present lower sensitivity than subjective methods for detecting anomalies in sensory discrimination.

We identified sensory alterations in the non-dominant side of the body; this contradicts the hypothesis of Byl and Ilar,[25] who suggest that dystonia may be caused by degradation of topographical representations of the hand in the sensorimotor cortex due to repetitive movements. Our data indicate bilateral tactile hypersensitivity, which suggests the presence of a central alteration; this seems to be unrelated to the specialisation or repetition of movement, as sensitivity is altered both in the dominant arm, which performs more specialised movement, and in the non-dominant arm, whose movements are less precise and which performs fewer movements per day.

Another objective of our study was to analyse pain tolerance and the possible relationship with pain perception in patients with dystonia; our data suggest that these patients present a greater subjective sensation of pain. This is consistent with the results reported by Novaretti et al.[26] on the prevalence of and correlation between non-motor symptoms in patients with idiopathic focal or segmental dystonia: these researchers found pain and discomfort to be common symptoms in this patient group. Similarly, Pekmezovic et al.[27] identified disease-related pain in up to 70% of patients with cervical dystonia and 30% of those with focal hand dystonia and writer's cramp.

Our results on pain tolerance suggest that the mean pain threshold is lower in patients with dystonia than in controls; this is consistent with the findings of a previous study,[28] although we only identified this decreased threshold in one of the muscles studied. However, given that all participants in our study were right-handed and the reduced pain threshold was found on the left side of the neck, our findings support the hypothesis of a central alteration unrelated to specialised or repeated movement, and contrast with the results of other researchers, who relate increased pain sensitivity with the regions of the body that present dystonic movements.[13,29]

Table 2 Correlations between different variables among patients and in the sample as a whole.

VAS	Algometry R neck	Algometry L neck	Algometry R radial	Algometry L radial	Algometry R median	Algometry L median	Algometry R ulnar	Algometry L ulnar	Algometry R hand	Algometry L hand	Algometry R tibial	Algometry L tibial
Patients	rho = −0.42; .14	rho = −0.62*; .03	rho = −0.60*; .04	rho = 0.17; .59	rho = −0.59*; .04	rho = −0.47; .13	rho = −0.53; .08	Rho = −0.51; 0.09	Rho = −0.47; 0.13	Rho = −0.52; 0.09	Rho = −0.83**; 0.00	Rho = −0.69*; 0.01
Whole sample	r = −0.40*; .03	r = −0.48*; .01	r = −0.47*; .01	r = 0.09; .67	r = −0.36; .07	r = −0.34; .08	r = −0.40*; .03	r = −0.43*; 0.02	r = −0.35; 0.08	r = −0.38; 0.05	r = −0.45*; 0.02	r = −0.48*; 0.01

L: left; r: Pearson correlation coefficient; R: right; rho: Spearman rank correlation coefficient; VAS: visual analogue scale.
* Significant correlation with P < .05.
** Significant correlation with P < .001.

The correlation between subjective perception of pain and the pain pressure threshold points to a negative association between these variables: patients with dystonia could tolerate fewer grams of pressure and reported more intense perceived pain. This phenomenon was observed both in the dominant and the non-dominant side, in different regions of the body. Kutvonen et al.[30] present similar findings to our own; they assessed the pain pressure threshold, and found that dystonia was associated with variable pain originating not only in the affected muscles but also, possibly, in the system responsible for pain perception and modulation.

Our results suggest the presence of an alteration affecting somatosensory afferents, and that patients with focal or segmental dystonia present hypersensitivity in both hands and a lower mean pain pressure threshold than controls on both the dominant and non-dominant sides of the body, as well as a more intense subjective sensation of pain.

Our study presents several limitations. Due to the small sample size, our results cannot be extrapolated and we are unable to draw robust conclusions. However, as hand dystonia is classified as a rare disease, recruiting larger patient samples is challenging. Furthermore, as all participants were from the same region, the sample lacks geographical diversity. Despite these limitations, our results have relevant clinical implications with regard to sensitivity and the importance of treating both subjective and objective pain. While in other recent studies, expert recommendations for the diagnosis of focal dystonia establish that sensory symptoms constitute a negative characteristic for the diagnosis of the condition,[31] we believe that, in the light of our findings and the evidence from other current studies, there is a need for complementary research with larger patient samples to examine sensitivity and pain processing in focal dystonia involving the arm.

Conflicts of interest

The authors have no conflicts of interest to declare.

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