

Abnormal tactile temporal discrimination in psychogenic dystonia

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ABSTRACT

Objective: Neurophysiologic studies demonstrated that patients with primary torsion dystonia (PTD) and with psychogenic dystonia (Psy-D) share similar abnormalities in the motor system. In this study, we evaluated somatosensory function in Psy-D by testing temporal discrimination threshold (TDT), and compared the results with those obtained in patients with PTD.

Methods: TDT of tactile stimuli was assessed in 10 patients with Psy-D, 10 patients with PTD, and 16 control subjects. The 2 groups of patients were matched for age, gender, disease duration, and distribution of dystonia. Tactile stimuli consisted of pairs of non-noxious electrical shocks delivered to the right or left hand at interstimulus interval increasing from 0 to 400 msec, in 10-msec steps. TDT was defined as the value at which subjects recognized the 2 stimuli as asynchronous.

Results: TDT was higher in Psy-D and PTD compared to control subjects, for both the right and the left hand. In a subgroup of patients with unilateral dystonia (Psy-D = 4, PTD = 5), TDT did not differ between the affected and the unaffected side in both groups of patients. Disease duration was not correlated to the increased TDT value.

Conclusions: Our study suggests an impaired processing of somatosensory inputs in both Psy-D and PTD. These abnormalities might represent a neurophysiological trait predisposing to develop a dystonic posture triggered by psychiatric and psychological factors. *Neurology*® 2011;77:1191-1197

GLOSSARY

ANOVA = analysis of variance; **CRPS** = complex pain regional syndrome; **FD** = fixed dystonia; **ICC** = intraclass correlation coefficient; **ISI** = interstimulus interval; **MDS** = movement disorders; **Psy-D** = psychogenic dystonia; **PT** = perceptual threshold; **PTD** = primary torsion dystonia; **SMA** = supplementary motor area; **TDT** = temporal discrimination threshold; **TMS** = transcranial magnetic stimulation.

The pathophysiology of psychogenic movement disorders (PMDs) is unknown. Most patients with PMDs have an underlying conversion disorder, associated with coexisting depression, anxiety, or personality disorders.¹

Recent neurophysiologic and neuroimaging studies, mainly exploring the motor system, have attempted to define a neurobiological model for PMDs.^{2,3} Transcranial magnetic stimulation (TMS) studies in psychogenic dystonia (Psy-D) have demonstrated alterations of inhibitory circuits at cortical and spinal level, similar to those described in primary torsion dystonia (PTD),^{3,4} whereas sensorimotor plasticity, tested with the paired associative stimulation, was found to be abnormal in PTD but not in Psy-D.⁵ PTD is also characterized by impairment of sensory processing, as revealed by increased spatial and temporal discrimination thresholds (TDT).⁶⁻⁸ Increased tactile TDT has been found in both generalized⁹ and focal dystonia,⁸ including blepharospasm¹⁰ and cervical¹¹ and focal hand dystonia.^{12,13} Tactile TDT is also increased in unaffected body parts in patients with focal dystonia,^{8,10} in nonmanifesting DYT1

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Table 1 Demographic and clinical features of patients with psychogenic (Psy-D) and organic dystonia (PTD)

Psy-D	Age, y	Disease duration, y	Phenomenology	Affected side	Precipitant	Course and clinical features ^a
1	23	1	Upper limb dystonia with tremor and shoulder elevation	Right	Traumatic right wrist fracture	Gradual onset, fluctuating severity ^{2,5,6}
2	49	4	Fixed dystonia of the hands	Left > right	Traumatic cervical whiplash	Sudden onset, spreading to the right hand ^{3,5}
3	23	4	Upper limb dystonia	Right	No clear precipitant	Gradual onset, fluctuating severity ^{2,3,4}
4	44	3	Upper limb dystonia	Right	No clear precipitant	Gradual onset with dystonic postures of the upper limb, fluctuating severity ^{2,3,5}
5	34	1	Upper limb dystonia	Right	Trauma	Gradual onset, worsening at night with sudden awakenings ^{1,2,3}
6	34	1	Neck rotation	Right > left	Trauma, issues with the spouse in the months before wedding	Sudden onset, fluctuating severity ^{2,3,4}
7	52	9	Generalized	Right > Left	Right shoulder trauma	Sudden onset, paroxysmal course, spreading to the left side ^{2,3,6,7}
8	33	12	Generalized fixed dystonia	Left > Right	Exposure to a disease model	Sudden onset, spreading to legs and hands, fluctuating severity ^{1,3,4,7}
9	45	20	Eyes closure	Bilateral	No clear precipitant	Gradual onset, fluctuating severity ^{2,4,7}
10	44	10	Eyes closure	Bilateral	Divorce	Sudden onset, paroxysmal course ^{1,2,3,4,7}
PTD	Age, y	Disease duration, y	Phenomenology	Affected side	Course	
1	32	6	Writer's cramp	Left	Gradual onset, stable course	
2	38	10	Dystonic cramp	Right	Gradual onset, stable course	
3	49	6	Dystonic cramp	Right	Gradual onset, stable course	
4	55	5	Dystonic cramp	Right	Gradual onset, stable course	
5	23	6	Writer's cramp	Right	Gradual onset, stable course	
6	50	10	Cervical dystonia	Right > left	Gradual onset, stable course	
7	34	8	Generalized	Left > right	Gradual onset, stable course	
8	46	4	Generalized	Left > right	Gradual onset, stable course	
9	64	8	Blepharospasm	Bilateral	Gradual onset, stable course	
10	44	5	Blepharospasm	Bilateral	Gradual onset, stable course	

^a 1 = Previous medically unexplained complaints despite appropriate investigations; 2 = obvious psychiatric disturbances; 3 = multiple somatizations; 4 = spontaneous remissions; 5 = nonanatomic sensory loss; 6 = false weakness; 7 = response to placebo.

mutation carriers,¹⁴ and in unaffected relatives of both familial and sporadic adult-onset dystonia patients.¹⁵

Our hypothesis is that in Psy-D patients who developed a dystonic posture secondary to psychiatric and psychological factors there is a somatosensory dysfunction. In order to test this hypothesis, we assessed tactile TDT in patients with Psy-D and compared the findings with those of a group of patients with PTD (matched for age, level of education, disease duration, and distribution of dystonia) and healthy control subjects.

METHODS Subjects. We recruited 10 patients (6 female, 4 male; mean age 38.1 ± 10.2 years) with documented or clinically established Psy-D according to Fahn and Williams criteria,¹⁶ 10 with PTD (6 female, 4 male; mean age 43.5 ± 12.0 years), and 16 age-matched normal control subjects (9 female, 7 male; mean age 36 ± 16.2 years). Demographic and clinical features of Psy-D and PTD are given in table 1.

Patients underwent extensive neurologic examination in order to exclude those with clinical somatosensory abnormalities. Predominant symptoms in Psy-D were localized to the arm ($n = 5$), the face ($n = 2$), the neck ($n = 1$), and one hemibody with secondary involvement of the contralateral side ($n = 2$). Patients with PTD were matched to Psy-D according to the distribution of symptoms: 5 patients had focal hand dystonia, 1 had cervical dystonia, 2 had generalized dystonia, and 2 had blepharospasm. Dystonia in Psy-D was mainly mobile, except for 2 patients with

fixed dystonia but without any sign of complex pain regional syndrome (CRPS). Diagnosis of Psy-D was done at referral centers for movement disorders (MDS) by a neurologist expert in MDS, and then confirmed by videotape review by 2 additional MDS specialists (F.M. and D.M.). All experiments were carried out by 2 neurologists expert in clinical neurophysiology (G.S. and F.M.). Patients undergoing botulinum toxin received the last injection at least 4 months prior to the study.

Standard protocol approvals, registrations, and patient consents. The study was approved by the ethics committee of the recruiting centers and conformed with the Declaration of Helsinki. All subjects gave their written informed consent prior to participation.

Stimuli and procedure. Paired tactile stimuli consisted of square-wave electrical pulses delivered by a constant current stimulator (STM 140, HTL, Udine, Italy) through surface skin electrodes (1 mm in diameter) attached by means of adhesive pads to the volar surface of the distal phalanx of the index finger of the right or left hand.

The anode was located 1.5 cm distally from the cathode. The intensity of tactile stimulation was determined for each subject, by delivering a series of stimuli at increasing intensity (from 2 mA in steps of 1 mA). The minimal intensity at which electric stimuli were perceived in 10 out of 10 stimuli was used in the experimental test (perceptual threshold [PT]). Care was taken that stimuli induced no pain or discomfort. Subjects were tested in a single experimental session lasting about 60 minutes. In all subjects both left and right hand were tested separately, and the order of presentation was randomized across subjects. For each hand, combination of stimuli was delivered in 4 separate blocks. Pairs of stimuli were delivered starting from simultaneous stimuli (interstimulus interval [ISI] = 0 msec) and progressively increasing the ISI in steps of 10 msec up to 400 msec. The first out of 3 consecutive intervals at which the subjects recognized the 2 stimuli as sequential was defined as the TDT. More precisely, when the subject recognized the stimuli as separated at 1 ISI, the following ISIs were increased until the stimuli were recognized as separated for at least 3 consecutive ISIs. The TDT was defined as the first ISI at which the subject started to discriminate the stimuli as separated. In this way, TDT represented a stable index of performance. For each hand, averages of 4 values were entered in the data analysis.

To maintain subjects' attention throughout the whole task and to avoid possible perseverative responses, 3 catch trials, consisting of simultaneous stimuli (ISI = 0 msec), were interspersed in the ascending and descending series. More precisely, in catch trials the tactile stimulus was delivered with an ISI of 0 msec and it was intermixed in-between 2 trials in which the tactile stimuli were clearly separated. Catch trials were not included in the analysis. Subjects were allowed to pause between each block. Verbal instructions about the experimental task were also provided before each testing session, as well as examples of single or double tactile stimuli.

Control experiments. To assess the reproducibility of TDT measurement, the experiment was repeated in 6 patients with Psy-D (patients 1–4 and 6–7, table 1) after a mean interval of 12 ± 1.5 months (experiment 1). In these patients dystonia did not vary between the 2 assessments.

To rule out the possible effect of muscle contraction on TDT measurement, normal subjects underwent the experiment twice, under 2 different conditions: at rest (with both hands lying quietly in resting position) and during contraction (main-

taining their right wrist flexed at 90° in order to mimic a dystonic posture, while the left hand was in resting position) (experiment 2).

Finally, in order to assess interrater reliability, in a subgroup of 7 healthy subjects (5 female, 2 male; mean age: 38 ± 14.5 years) TDT was tested independently by 2 investigators who were blinded to each other's findings (experiment 3).

Statistical analysis. The Kruskal-Wallis test was used to compare the 3 groups for age and education level. Disease duration in Psy-D and PTD was compared using the Mann-Whitney *U* test.

Differences in PT and TDT among the 3 groups of subjects were explored by repeated-measures analysis of variance (ANOVA) with group as between-subjects factor (3 levels: Psy-D, PTD, and healthy subjects) and side (2 levels: right, left) as within-subjects factor. Conditional on a significant *F* value, post hoc unpaired *t* tests were performed to demonstrate differences between groups.

A separate factorial ANOVA was performed in the subgroup of Psy-D (4 patients) and PTD group (5 patients) with unilateral dystonia, in order to compare TDT values between the affected and unaffected hand (group as independent variable: Psy-D affected side, Psy-D unaffected side, PTD affected side, PTD unaffected side). For control experiments, repeated-measures ANOVA was conducted with side (2 levels: right, left) as within-subjects factor and time (2 levels: baseline, T12) (experiment 1) or contraction (2 levels: resting, contracting) (experiment 2) as between-subject factor. Post hoc Bonferroni-Dunn test was performed to demonstrate differences between groups, correcting for multiple comparisons (significance was set at $p < 0.008$). For the other statistical tests, significance level was set at $p < 0.05$.

Interrater reliability was expressed by means of intraclass correlation coefficient (ICC). The following ranges of reliability values were used as reference¹⁷: 0.00–0.10, virtually none; 0.11–0.40, slight; 0.41–0.60, fair; 0.61–0.80, moderate; 0.81–1.00, substantial.

A threshold TDT value discriminating between patients and control subjects was determined as the mean TDT (calculated on all right and left hand values) from the control group plus 2 SD; TDT values exceeding this value were considered abnormal. Correlations in the patients' group between disease duration and TDT values were tested using Spearman rank correlation. Unless otherwise stated, data are given as mean $\pm$ SE.

RESULTS The 3 groups of subjects (Psy-D, PTD, and controls) did not differ in age and level of education. Disease duration and frequency of fixed dystonia were comparable between Psy-D and PTD. The mean intensity of stimulation did not differ among patients with Psy-D, PTD, and healthy subjects for both sides (table 2). TDT was increased in Psy-D and PTD, in both the right (Psy-D = 105.6 ± 9.9 msec; PTD = 107.3 ± 9.1 msec) and the left hand (Psy-D = 100.9 ± 8.4 msec; PTD = 102.8 ± 8.5 msec), compared to healthy subjects (right hand = 59.8 ± 4.2 msec; left hand = 58.2 ± 3.2 msec). These observations were confirmed by repeated-measures ANOVA that showed a main effect of group ($F = 19.4$, $p < 0.0001$), but no main effect of side ($F = 1.2$, $p = 0.2$) or a side $\times$ group interaction ($F = 0.1$, $p = 0.9$). Post hoc unpaired *t* test demon-

Table 2 Group comparisons for age, level of education, disease duration, frequency of fixed dystonia, and perceptual threshold^a

	Psychogenic dystonia	Primary torsion dystonia	Controls	p Value
M/F ^b	4/6	4/6	7/9	0.9
Age, y ^c	38.1 ± 10.2	43.5 ± 12.0	36.1 ± 11.2	0.2
Level of education, y ^c	10.8 ± 4.4	10.9 ± 4.2	13.6 ± 4.9	0.2
Disease duration, y ^d	6.5 ± 6.2	6.8 ± 2.1	NA	0.3
Fixed dystonia ^e	2/10	0/10	NA	0.4
PT (right hand, ms) ^f	10.2 ± 3.4	10.7 ± 3.6	8.1 ± 6.0	0.6
PT (left hand, ms) ^f	10.3 ± 9.4	10.8 ± 10.3	8.2 ± 5.9	0.5

Abbreviations: NA = not applicable; PT = perceptual threshold.

^a All data are mean ± SD.

^b Chi-square test.

^c Kruskal-Wallis test.

^d Mann-Whitney U test.

^e Fisher exact test.

^f Factorial analysis of variance (independent variable = group).

strated that TDT was higher in Psy-D ($p < 0.0001$) and PTD ($p < 0.0001$) compared to control subjects (figure 1A). A separate factorial ANOVA computed in the subgroup of patients with unilateral dystonia showed no main effect of the factor group ($F = 0.4$; $p = 0.6$), as TDT did not differ between the affected and the unaffected side in both Psy-D (96.6 ± 17.2 vs 97.5 ± 12.7 msec) and PTD (87.5 ± 6.7 vs 80.0 ± 6.8 msec).

The normal upper limit of TDT (mean + 2 SD) for the hand was 85.3 msec. Among the 20 patients with Psy-D and PTD, 4 (patients 3 and 10 in the Psy-D group and patients 2 and 5 in the PTD group, table 1) had normal TDT (figure 1B). Spearman rank correlation analysis did not disclose any correlation between TDT and disease duration in Psy-D (ρ corrected for ties = -0.3 ; tied p value = 0.2) and PTD (ρ corrected for ties = -0.1 ; tied p value = 0.6) (figure 2).

Control experiments. Re-evaluation of TDT in 6 patients with Psy-D after a mean interval of 12 ± 1.5 months disclosed values (right: 104.1 ± 34.6 ; left: 95 ± 28.5) comparable to baseline (right: 109.3 ± 39.6 ; left: 99.5 ± 28.2), as pointed out by no main effect or interactions of the factors time ($F = 0.1$, $p = 0.7$) and side ($F = 0.5$, $p = 0.8$).

Contraction of the right flexor forearm muscles did not modify TDT values in both hands in the subgroup of 7 healthy subjects. This was demonstrated by no main effect or interactions of the factors contraction and side for both raters (table 3). Finally, interrater reliability was substantial for the 2 examiners according to ICC values (>0.9 ; table 3).

DISCUSSION We found a higher TDT for tactile stimuli in both hands of patients with Psy-D, most of

them manifesting dystonia in the upper limbs. We therefore suggest that somatosensory processing is impaired in Psy-D.

Our data of a higher TDT in Psy-D do not confirm a recent study¹⁸ investigating somatosensory function in patients with the fixed dystonia (FD) syndrome, a condition fulfilling criteria for Psy-D in 37% of cases.¹⁹ Indeed, TDT values did not significantly differ from healthy subjects, although they were higher in patients with FD.¹⁸ Possible reasons for explaining differences between the 2 studies might be the different methodology employed to test TDT, as stimuli were delivered to the index and middle fingers in patients with FD¹⁸ whereas in our study both stimuli were delivered to the index finger. Moreover, the presence of concomitant pain, the frequent involvement of lower limb, and the different distribution of dystonic symptoms between patients with FD and patients with PTD¹⁸ might have determined dissimilarity in the results. We tried to minimize the possible influence of clinical features and distribution of muscular contraction by enrolling patients with PTD and patients with Psy-D with similar body parts affected by dystonia. Finally, perceptual thresholds were similar among the 3 groups in our study, thus ruling out any methodologic bias due to a different intensity of stimulation.

Two main pathophysiologic interpretations arise from our findings: TDT alteration in Psy-D might be the consequence of muscular contraction, as suggested by previous studies exploring the motor system,³ or alternatively might be a neurophysiologic trait predisposing to development of involuntary dystonic postures. Regarding the first hypothesis, it has been demonstrated that abnormal sensory feedback from involuntary contracting muscles is associated with short and long-term changes in the human brain.^{20,21} Moreover, distorted finger maps in the somatosensory cortex were reported in a primate model of focal dystonia trained to repetitively open and close a hand grip.^{22,23} Therefore, increased TDT might be caused by repetitive dystonic postures. Although we cannot rule out the long-term effects of muscular contraction, the observation that TDT did not change in healthy subjects performing a voluntary contraction of the hand makes unlikely the hypothesis that TDT is influenced by muscular contraction per se. Moreover, the subgroup of Psy-D and PTD patients with unilateral symptoms showed TDT abnormalities even in unaffected body parts. However, given the few patients considered in this subanalysis, the issue of affected vs unaffected sides needs to be further studied in the future. Accordingly, sensory abnormalities in Psy-D could represent a neurobiological substrate contributing to the ex-

Figure 1 Temporal discrimination threshold (TDT) in psychogenic and primary torsion dystonia

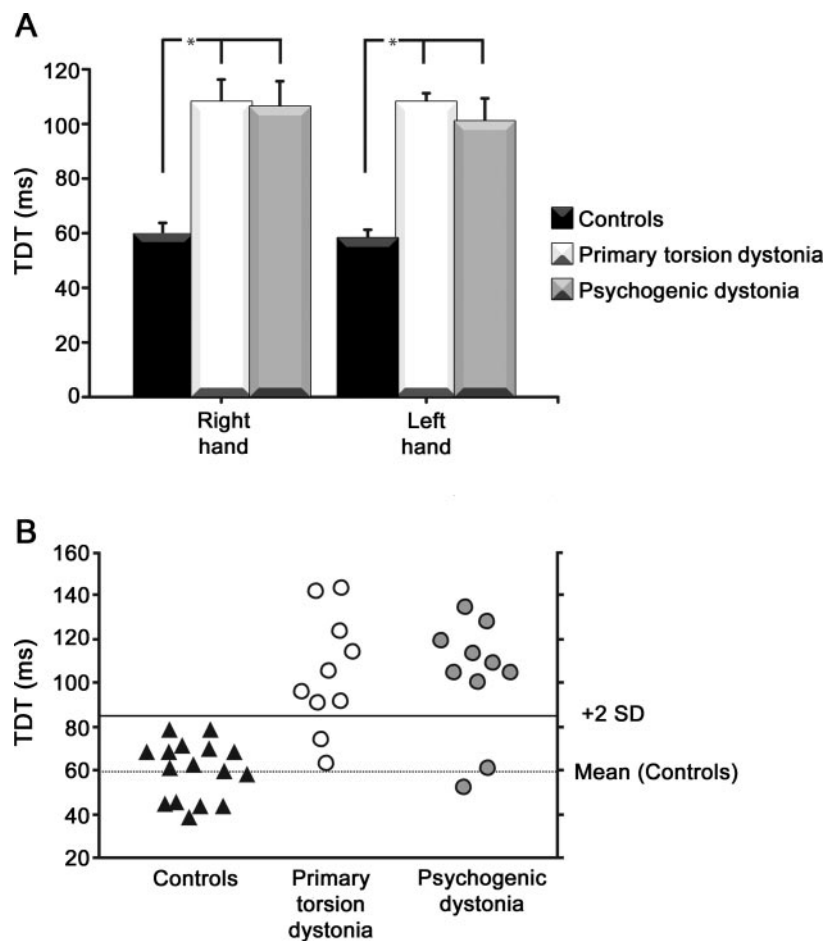
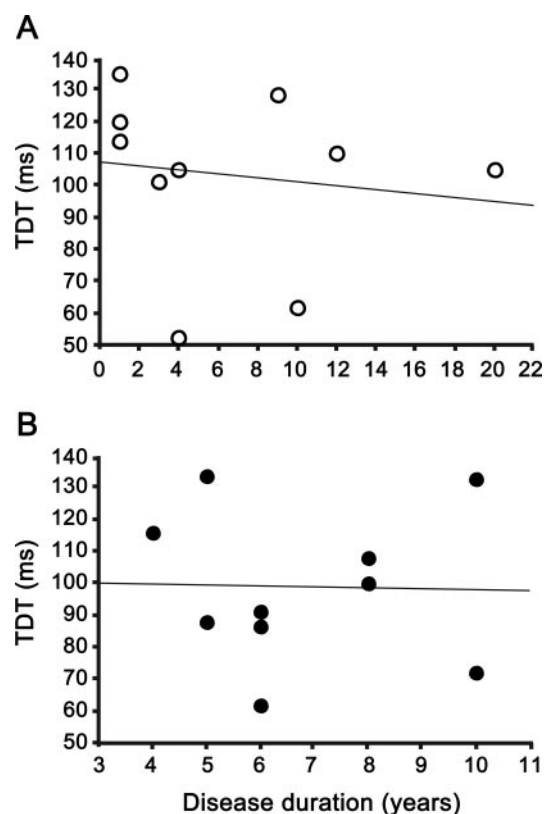


Figure 2 Lack of correlation between temporal discrimination threshold (TDT) and disease duration



TDT values were not correlated to disease duration in (A) psychogenic dystonia and (B) primary torsion dystonia.

(A) Increased TDT of tactile stimuli in psychogenic and primary torsion dystonia in both the right and left hand, compared to control healthy subjects. $p < 0.0001$, post unpaired *t* test. (B) Normal upper limits of TDT for the hand. This value was determined as the mean TDT (calculated on all right and left hand values) from the control group plus 2 SD.

pression of motor symptoms including dystonia, in presence of an underlying psychopathology. This concept is further supported by evidence of increased TDT in unaffected body regions of patients with different forms of focal dystonia⁸ and in nonmanifesting carriers of the DYT1 mutation.¹⁴

TDT of tactile stimuli is a complex task relying upon several cortical and subcortical areas, such as pre-supplementary motor area (SMA), anterior cingulate cortex, and basal ganglia, in addition to the primary sensory areas.^{24–26} The pre-SMA and anterior cingulate cortex seem to be involved in the temporal processing of somatosensory events, as their activation was found to be specific for the temporal discrimination task.²⁵ Interestingly, functional imaging studies performed in patients with psychogenic sensorimotor loss²⁷ have demonstrated activation in limbic regions, such as the anterior cingulate or orbitofrontal cortices, and also reduced neural activation in brain areas involved in motor planning and

execution, such as the thalamus, basal ganglia, and parietal cortex. Finally, a recent fMRI study using an affective task, conducted in patients with conversion disorder and a movement disorder, has demonstrated greater functional connectivity between the right amygdala and the right SMA during fearful vs neutral, and happy vs neutral stimuli compared with healthy volunteers.² Overall, these neuroimaging studies suggest a link between limbic and motor control areas of the brain, possibly underlying the pathophysiology of motor conversion symptoms. In focal hand dystonia TDT is inversely correlated to suppression of the P27 component of somatosensory evoked potentials in a paired pulse paradigm,²⁸ suggesting that somatosensory abnormalities are related to a dysfunction of cortical inhibitory interneurons. We speculate that TDT increase in Psy-D might be linked to impaired intracortical temporal inhibition in primary sensory cortex.

Our study has a few limitations. The small sample size and the cross-sectional design might have affected the interpretation of the results. However, previous pilot studies on TDT in PTD were successively replicated on larger samples, demonstrating that

Table 3 Temporal discrimination threshold (TDT) values recorded from 7 healthy subjects by 2 different raters, blinded to the other examiner findings

	Right hand TDT		Left hand TDT		R-ANOVA factors (p value)		
	Rest	Contraction	Rest	Contraction	Contraction	Side	Contraction × side
Rater 1	55.1 ± 15.5ms	56.7 ± 16.3ms	54.9 ± 11.2ms	58.3 ± 12.8ms	0.1	0.9	0.5
Rater 2	55.6 ± 11.4ms	54.9 ± 18.2ms	52.3 ± 10.1ms	55.7 ± 14.8ms	0.5	0.8	0.3
ICC (95% CI)	0.94 (0.71–0.99)	0.98 (0.90–0.99)	0.92 (0.59–0.98)	0.91 (0.63–0.98)	NA		

Abbreviations: CI=confidence interval; ICC = intraclass correlation coefficient; R-ANOVA = repeated measures analysis of variance; NA = not applicable.

^a Recordings were obtained under 2 experimental conditions: rest (both hand resting); contraction (right hand performing a voluntary flexion at the wrist, left hand relaxing).

TDT testing fulfills criteria for a reliable endophenotype with a high sensitivity in dystonia.^{8,29} An important issue to be addressed when studying PMDs is the possibility of misdiagnosis.³⁰ This bias was minimized by recruiting patients with documented or clinically established Psy-D¹⁶ in whom diagnosis was confirmed by 2 neurologist experts in MDS from videotaped clinical examination. The possibility that TDT was abnormal for the presence of the involuntary muscle contraction can also be reasonably excluded, as in our control experiment performed in healthy subjects, TDT did not change when healthy subjects performed a voluntary flexion of the right forearm muscles in comparison to the rest condition. Finally, the substantial level of agreement between the 2 examiners and the observation that, in patients with Psy-D, TDT findings when tested twice over time showed similar abnormalities, demonstrate that tactile TDT is a consistent and reproducible measure.

As for the abnormalities of inhibitory circuits in the motor system,^{3,4} TDT is equally impaired in psychogenic and primary torsion dystonia. Nevertheless, neurophysiologic differences have been described between PTD and Psy-D, such as the alteration of sensorimotor plasticity characterizing only PTD.⁵ Future research should clarify which neuronal networks are involved in inducing a Psy-D phenotype in presence of an underlying psychopathology and of predisposing neurophysiologic abnormalities in the motor and sensory system.

AUTHOR CONTRIBUTIONS

Dr. Morgante: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, acquisition of data, statistical analysis, study supervision. Dr. Tinazzi: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, acquisition of data, statistical analysis, study supervision. Dr. Squintani: analysis or interpretation of data, acquisition of data. Dr. Martino: drafting/revising the manuscript, acquisition of data. Dr. Defazio: drafting/revising the manuscript, acquisition of data. Dr. Romito: drafting/revising the manuscript, contribution of vital reagents/tools/patients, acquisition of data. Prof. Albanese: analysis or interpretation of data, acquisition of data, study supervision. Dr. Di Matteo: drafting/revising the manuscript, acquisition of data. Dr.

Quartarone: drafting/revising the manuscript, analysis or interpretation of data, study supervision. Dr. Giralda: drafting/revising the manuscript, study concept or design, analysis or interpretation of data. Dr. Fiorio: drafting/revising the manuscript. Prof. Berardelli: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, study supervision.

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REFERENCES

1. Feinstein A, Stergiopoulos V, Fine J, Lang AE. Psychiatric outcome in patients with a psychogenic movement disorder: a prospective study. *Neuropsychiatry Neuropsychol Behav Neurol* 2001;14:169–176.
2. Voon V, Brezing C, Gallea C, et al. Emotional stimuli and motor conversion disorder. *Brain* 2010;133:1526–1536.
3. Espay AJ, Morgante F, Purzner J, Gunraj CA, Lang AE, Chen R. Cortical and spinal abnormalities in psychogenic dystonia. *Ann Neurol* 2006;59:825–834.
4. Avanzino L, Martino D, van de Warrenburg BP, et al. Cortical excitability is abnormal in patients with the “fixed dystonia” syndrome. *Mov Disord* 2008;23:646–652.
5. Quartarone A, Rizzo V, Terranova C, et al. Abnormal sensorimotor plasticity in organic but not in psychogenic dystonia. *Brain* 2009;132:2871–2877.
6. Molloy FM, Carr TD, Zeuner KE, Dambrosia JM, Hallett M. Abnormalities of spatial discrimination in focal and generalized dystonia. *Brain* 2003;126:2175–2182.
7. Tinazzi M, Frasson E, Bertolasi L, Fiaschi A, Aglioti S. Temporal discrimination of somesthetic stimuli is im-

- paired in dystonic patients. *Neuroreport* 1999;10:1547–1550.
8. Scontrini A, Conte A, Defazio G, et al. Somatosensory temporal discrimination in patients with primary focal dystonia. *J Neurol Neurosurg Psychiatry* 2009;80:1315–1319.
 9. Aglioti SM, Fiorio M, Forster B, Tinazzi M. Temporal discrimination of cross-modal and unimodal stimuli in generalized dystonia. *Neurology* 2003;60:782–785.
 10. Fiorio M, Tinazzi M, Scontrini A, et al. Tactile temporal discrimination in patients with blepharospasm. *J Neurol Neurosurg Psychiatry* 2008;79:796–798.
 11. Tinazzi M, Fiorio M, Bertolasi L, Aglioti SM. Timing of tactile and visuo-tactile events is impaired in patients with cervical dystonia. *J Neurol* 2004;251:85–90.
 12. Bara-Jimenez W, Shelton P, Sanger TD, Hallett M. Sensory discrimination capabilities in patients with focal hand dystonia. *Ann Neurol* 2000;47:377–380.
 13. Fiorio M, Tinazzi M, Bertolasi L, Aglioti SM. Temporal processing of visuotactile and tactile stimuli in writer's cramp. *Ann Neurol* 2003;53:630–635.
 14. Fiorio M, Gambarin M, Valente EM, et al. Defective temporal processing of sensory stimuli in DYT1 mutation carriers: a new endophenotype of dystonia? *Brain* 2007;130:134–142.
 15. Bradley D, Whelan R, Walsh R, et al. Temporal discrimination threshold: VBM evidence for an endophenotype in adult onset primary torsion dystonia. *Brain* 2009;132:2327–2335.
 16. Fahn S, Williams DT. Psychogenic dystonia. *Adv Neurol* 1988;50:431–455.
 17. Shrout PE. Measurement reliability and agreement in psychiatry. *Stat Methods Med Res* 1998;7:301–317.
 18. Katschnig P, Edwards MJ, Schwingenschuh P, et al. Mental rotation of body parts and sensory temporal discrimination in fixed dystonia. *Mov Disord* 2010;25:1061–1067.
 19. Schrag A, Trimble M, Quinn N, Bhatia K. The syndrome of fixed dystonia: an evaluation of 103 patients. *Brain* 2004;127:2360–2372.
 20. Chen R, Corwell B, Yaseen Z, Hallett M, Cohen LG. Mechanisms of cortical reorganization in lower-limb amputees. *J Neurosci* 1998;18:3443–3450.
 21. Chen R, Anastakis DJ, Haywood CT, Mikulis DJ, Manktelow RT. Plasticity of the human motor system following muscle reconstruction: a magnetic stimulation and functional magnetic resonance imaging study. *Clin Neurophysiol* 2003;114:2434–2446.
 22. Byl N, Wilson F, Merzenich M, et al. Sensory dysfunction associated with repetitive strain injuries of tendinitis and focal hand dystonia: a comparative study. *J Orthop Sports Phys Ther* 1996;23:234–244.
 23. Byl NN, Merzenich MM, Cheung S, Bedenbaugh P, Nagarajan SS, Jenkins WM. A primate model for studying focal dystonia and repetitive strain injury: effects on the primary somatosensory cortex. *Phys Ther* 1997;77:269–284.
 24. Lacruz F, Artieda J, Pastor MA, Obeso JA. The anatomical basis of somesthetic temporal discrimination in humans. *J Neurol Neurosurg Psychiatry* 1991;54:1077–1081.
 25. Pastor MA, Day BL, Macaluso E, Friston KJ, Frackowiak RS. The functional neuroanatomy of temporal discrimination. *J Neurosci* 2004;24:2585–2591.
 26. Harrington DL, Haaland KY, Knight RT. Cortical networks underlying mechanisms of time perception. *J Neurosci* 1998;18:1085–1095.
 27. Nowak DA, Fink GR. Psychogenic movement disorders: aetiology, phenomenology, neuroanatomical correlates and therapeutic approaches. *Neuroimage* 2009;47:1015–1025.
 28. Tamura Y, Matsushashi M, Lin P, et al. Impaired intracortical inhibition in the primary somatosensory cortex in focal hand dystonia. *Mov Disord* 2008;23:558–565.
 29. Bradley D, Whelan R, Walsh R, et al. Comparing endophenotypes in adult-onset primary torsion dystonia. *Mov Disord* 2010;25:84–90.
 30. Voon V, Lang AE, Hallett M. Diagnosing psychogenic movement disorders-which criteria should be used in clinical practice? *Nat Clin Pract Neurol* 2007;3:134–135.

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