Investigation of writer`s cramp muscles using botulinum toxin injections through automatically guided electromyography

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Abstract
In this study we investigated the writer`s cramp muscles experimentally by using the automated electromyograph (EMG) guided system and the botulinum toxin injections based on the detection of dystonic muscles to that of primary dystonia and followed by torsion dystonia. In our study we found that in respect of variability, as reflected in the variances through our computation, and standard deviations(σ), the results were highly significant. In contrary to our previous results obtained and published in the journal, in respect of variability, the situations differ. Variances are considerably different in all patient's muscle. Standard deviations (σ) are considerably different in the right handwriting signals and in left handwriting signals in all muscles of all patients. In most cases, right handwriting signal variability is markedly higher than the corresponding lefthand signal handwriting variability. Based on 29999 degrees of freedom, the discordant group (D-group), the concordant group (C-Group), *p-values* near to 1 indicate that the right-handwriting variance is significantly smaller than the corresponding lefthand writing variance. The Variances of the 5 righthand and 5 lefthand, their f-ratios and their *p-values* are significantly different.

Keywords: B.o.N.T, AAN,

Introduction

Writer`s cramp Dystonia can be classified as focal: single region, and segmental: two or more regions, multifocal: two or more nonadjacent regions or generalized: leg or legs, trunk and one other region, or hemi dystonia: ipsilateral arm and leg, based on the region involved.[1-5] Writer's cramp is a task specific focal dystonia. Approximately 5% of patients have a positive family history of a similar condition. Patients together with D.Y.T.1 gene-mutation may initially present in conjunction with the writer's cramp before developing generalized dystonia and may have a history of writer's cramp among their family members. In EMG dystonic writer`s cramp, most cases are idiopathic.[6-14]

a. Abnormal electro physio logical stimulation

The finding of abnormal co-contraction of agonists and antagonists is the underlying feature of all dystonia and suggests abnormal motor control and muscle selection by the basal ganglia.[15]

The exact pathophysiology of dystonia is still unclear. There are three proposed mechanisms –loss of inhibition, abnormal plasticity, and abnormal sensory activation, which individually or together has been noted in dystonia.

Malfunction of reticence

A principal finding in focal dystonia is that of loss of inhibition. The abnormally long bursts of EMG activity, co-contraction of antagonist muscles, and overflow of activity into muscles not intended for the task may be explained by the loss of inhibition. Various studies have demonstrated loss of inhibition at spinal, brainstem, and cortical level.

1. Trials demonstrating efficacy of botulinum toxin

In the design of double-blinded, randomized, prospective study, cohort size was - 17 limb dystonia through which 10 occupational cramp patients, 3 idiopathic, 2 post-stroke, and 2 Parkinson disease patients with the treatment serotype brand/dose: serotype/ and brand not specified but 3 active doses: individualized, half, normal or double. For which the outcome measures /Results (1-primary, and 2-secondary) 1.blinded scoring of videos and handwriting analysis, and 2.subjective patient rating (however, 1 patient was dropped out, i.e., drop out was 1.). adverse events: Focal weakness with 53% injections, more common with higher dose, lasted 6 weeks; muscle stiffness, pain, malaise, muscle twitching, paresthesia, nausea.

Outcome/ results and the size of the effects: No significant change in blinded rating: 59% improved with B.o.N.T vs. 38% with placebo, Subjective patient rating improved in 82% with botulinum toxin injections (B.o.N.T.), versus 6% in conjunction with placebo.

In another study, blinded, randomized, prospective, placebo-controlled cross-over study, with no dropouts, based on 1.writing speed, accuracy, and writing samples and 2. patients' subjective report, the adverse events are: 100% had weakness in injected muscles; pen control worse in 1 patient injected with B.o.N.T, the findings are as follows:

Speed and accuracy improved in 35% with B.o.N.T; Gibson maze improved; pain improved in 67% with pain, No improvement with placebo, NNT for significant improvement in writing is equivalent to 5

In an another blinded, randomized, prospective, placebo controlled cross-over study, ten 10 patients with focal hand dystonia and the Botox used was individualized. 1. Patient subjective rating, patient subjective rating, 2. Objective writing accuracy and speed, and physician rating. Patients

dropped outs were nil. Treatment: Focal weakness in 80% of B.o.N.T.-treated muscles, and the results were subjectively 90% had at least mod improvement, and scientifically/ objectively 6 better with B.o.N.T and 1 patient improved with placebo but none of the patients were dropped out.

As per the guidelines issued by American Association of Neurology (AAN), botulinum toxin remains the currently available best treatment for Writer's cramp (Level B recommendation).[16] (Based on the above trials AAN has issued a Level B recommendation for the use of botulinum toxin in patients with writer's cramp.)[17]

1. Choice of muscles for botulinum toxin injections

Selection of appropriate muscles for injecting botulinum toxin is one of the main factors determining the effectiveness of therapy as the ideal therapy would be to inject in only the dystonic muscles sparing the non-affected muscles.

2. Techniques of choice

Clinical and video graphic examination: The patient is examined at rest and during writing a long paragraph, drawing a straight line or spirals. The test is done with the patient seated comfortably and writing on a table and the appearance of dystonia is noted. However, the complexity of such movements often makes it difficult to determine which movements are dystonic and which are part of the[18] normal pattern for that activity. The analysis of dystonic patterns may be further complicated by the presence of compensatory movements that may not be voluntary or even conscious. To improve the selection of muscles, it has been suggested that patients should be examined for abnormal postures at rest and while carrying out the affected task in question as well as other tasks (such as using a cup or a comb).[19] Simple techniques such as the localization of subjective pain and fatigue accompanied by palpation of the area of discomfort have also been used.[20] This can probably explain the difference in treatment efficacy with botulinum injection in wrist flexor and extensor dystonia. Previous studies have shown that treatment is more effective in wrist extensor compared to wrist flexor dystonia,.[21-22]

Results

In our study, Frequency of larger mean difference: >3.7 in all muscles, the $\chi^2 \cong 2.7$ (~ 2.7429) for 1 df, which is not significant at 5%., p = 0.0976. On comparing the corresponding channels on writing with the right versus left hand, versus left, larger mean differences (> 3) in muscle pairs were seen in 2 out of 4 patients in the D group and in 6 out of 8 patients in the C group (see the Table 1). Even in analysing only the first 4 channels alone, larger differences (of muscle pairs) were seen in 2 out of 4 and 6 out of 8 patients in the D, and C groups respectively – larger differences (>3.7) were seen in more than 1 channel in 1 out of 4 and 6 out of 8 of D and C groups respectively (see the Table 2).

Table 1: The Frequency of large mean difference: >3 in all muscles[23]

Group	Y	N	
D	2	2	4
C	6	2	8
	8	4	12

$\chi^2 \cong 0.7500$ for 1 df, which is not significant at 5% with p = 0.3864.

Table 2: The Frequency of larger mean difference: >3.7 in all muscles[24]

Group	Y	N	
D	1	3	4
C	6	2	8
	7	5	12

$\chi^2 \cong 2.7$ (~ 2.7429) for 1 df, which is not significant at 5%., p = 0.0976.

Overall larger differences in means in C group between the right and left handwriting would suggest that the dystonic force, which is more marked while writing with the right hand, is not opposed by a compensatory force. This opposition would possibly explain the reduced mean difference seen in the D group activity. At the same time this increased activity could explain the increased variances in the D group.

This was consistent with the means differences seen in fifth muscle, larger mean differences (> 3), being seen in only 1 out of 4 of the D group and 4 out of 8 of the C group. (Table 3)

Table 3: The Frequency of large mean difference: >3 in fifth muscle[25]

Group	Y	N	
D	1	3	4
C	4	4	8
	5	7	12

$\chi^2 \cong 0.6857$ for 1 df, which is not significant at 5% with p = 0.4076.

Overall, the left-hand means tended to be larger than the right-hand means. Three out of first 4 channels showed a negative value for the difference, in 1 out of 4 and 3 out of 8 patients of the D and C group respectively (Table 4)

Table 4: The Left handwriting > Right handwriting (L>R) 1st 4 muscles[26]

Group	Y	N	
D	1	3	4
C	3	5	8
	4	8	12

$\chi^2 \cong 0.1876$ for 1 df, which is not significant at 5% with p = 0.810.

The 5th channel was negative in all 4 of the D group and 6 out of 8 C patients. This would suggest that the dystonic muscle force unopposed by a compensatory movement (as they were

selected by looking at mirror movements while writing with the left hand) was (definitely) larger than while writing with the right hand. And this was seen in the C group as an increased mean difference, both in the first four channels (i.e., ECR, ECU, FCR and FCU) plus in the 5th muscle. (Table 5)

Table 5: The fifth muscle: frequency of L>R and R>L[27-30]

Group	L>R	R>L	
D	4	0	4
C	6	2	8
	10	2	12

$\chi^2 \cong 1.2$ (~ 1.200) for 1 df, which is not significant at 5% with p = 0.2732.

Conclusion

Twelve patients with writer's cramp (8 with concordant and 4 with discordant) were assessed in this study. On comparison of the measures of dispersion, the D-group had statistically significant difference between left handwriting and right handwriting (variance, standard deviation, and F ratio) with a larger variance in left, as compared to C group where variances and standard deviations were equal or smaller in the right compared to left. Mean amplitudes for right handwriting and left handwriting for the same muscles, though differ significantly in statistical terms, showed a consistent pattern only in the fifth muscle with a larger mean amplitude on left side in all patients and were not of value in differentiating between concordant © and discordant (D) groups of patients.

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Conflict of Interest

None.

References

1. Marsden 1976, Sheehy M.P, Marsden C.D.Writer's cramp–a focal dystonia. Brain 1982;105.(2):461–80
2. Fahn S, Marsden C. D, Calne D. B. Classification and investigation of dystonia. In: Marsden CD, Fahn S, eds. Movement disorders 2. London: Butterworths, 1987:332-58.
3. Bressman S. B. Dystonia genotypes, phenotypes, and classification. Adv Neurol 2004;94:101-7,
4. Fahn S, Bressman S. B, Marsden C. D. Classification of dystonia. Adv Neurol 1998;78.(3):1-10.
5. De C.A.P.M, Ozelius L. J. Classification and genetics of dystonia. Lancet Neurol 2002;1.(5):316-25.
6. Nemeth A.H The genetics of primary dystonias and related disorders. Brain 2002;125:695-721.3-7
7. Nutt J.G., Muenter M.D., Aronson A, et al. Epidemiology of focal and generalized dystonias in Rochester, Minnesota. Mov Dis 1988; 3: 188-94.
8. The ESDE (Epidemiological Study of Dystonia in Europe) Collaborative Group. A prevalence study of primary dystonia in eight European countries. J Neurol 2000; 247: 787-92.
9. Castelon K.E, Trender-Gerhard I, Kamm C, et al. Service-based survey of dystonia in Munich. Neuroepidemiology 2002; 21. (4): 202-6.
10. Muller J., Kiechl S., Wenning G.K, et al. The prevalence of primary dystonia in the general community. Neurology 2003; 61: 1294-6.
11. DeFazio G., Berardeli A., Abbruzzese G., et al. Risk factors for the spread of primary adult onset blepharospasm: a multicenter investigation of the Italian movement disorders study group. J Neurol Neurosurg Psychiatry 1999; 67. (5): 613-9.
12. Khanh D.L, Nilsen B., Dietrichs E. Prevalence of primary and segmental dystonia in Oslo. Neurology 2003; 61. (9): 1294-6.
13. Gimenez R.S, Delgado G., Martin M., Villanueva J.A, Mateo D. Hereditary torsion dystonia in Gypsies. Adv Neurol 1988; 50: 73-81.
14. Duffey P.O.P, Butler A.G, Hawthorne M.R, Barnes M.P. The epidemiology of primary dystonias in the north of England. Adv Neurol 1998; 78: 121-5.
15. Pekmezovic T., Ivanovic N., Svetel M., et al. Prevalence of primary late-onset focal dystonia in the Belgrade population. Mov Dis 2003; 18. (11): 1389-92.
16. Korczyn A.D., Kahana I., Zilber N., Streitler M., Carasso R., Alter M. Torsion dystonia in Israel. Ann Neurol 1980; 8. (4): 387-91.
17. Li S, Schoenberg B., Wang C.C., et al. A prevalence survey of Parkinson disease and other movement disorders in the People's Republic of China. Arch Neurol 1985; 42.(7):655-7.
18. Nakashima K., Kusumi M., Inoue Y., Takahashi K. Prevalence of focal dystonias in the western area of Tottori prefecture in Japan. Mov Dis 1995; 10. (4): 440-3.
19. Matsumoto S., Nishimura M., Shibasaki H, Kaji R. Epidemiology of primary dystonias in Japan - comparison with western countries. Mov Dis 2003; 18. (10): 1196-8.
20. Kandil M., Tohagamy S.A., Farrha M.A., et al. Prevalence of chorea, dystonia and athetosis in Assiut, Egypt: a clinical and epidemiological study. Neuroepidemiology 1994; 13. (5): 202-10.
21. Das S.K., Banerjee T.K. et al Community survey of primary dystonoia in the city of Kolkatta, India, Mov Disord 2007;22. (14):2031-6
22. Fletcher N.A., Harding AE, Marsden CD. The relationship between trauma and idiopathic torsion dystonia. J Neurol Neurosurg Psychiatry 1991;54. (8):713–7.
23. Jedynak P.C.,Tranchant C, Zegers de Beyl D. Prospective clinical study of writer's cramp. Mov Disord 2001;16. (3):494–9.
24. Cohen L.G., Hallett M. Hand cramps: clinical features and electromyographic patterns in a focal dystonia. Neurology 1988; 38: 1005–12.
25. Cohen L.G, Hallett M., Geller B.D., Hochberg F. Treatment of focal dystonias of the hand with botulinum toxin injections. J Neurol Neurosurg Psychiatry 1989; 52: 355–63.
26. Hallett M. Dystonia: Abnormal movements result from loss of inhibition, Advances in Neurology 94 (2004), 1–9.
27. Nakashima K, Rothwell J.C, Day B.L , Thompson P.D, Shannon.K, Marsden C.D, Reciprocal inhibition in writer's and other occupational cramps and hemiparesis due to stroke, Brain 112.(3) (1989), 681–97.
28. Panizza, M., Lelli, S., Nilsson, J., & Hallett, M. H-reflex recovery curve and reciprocal inhibition of H reflex in different kinds of dystonia. *Neurology*, 40.(5) 824–8.
29. Berardelli, A., Rothwell, J. C., Day, B. L., & Marsden, C. D. Pathophysiology of blepharospasm and oromandibular dystonia, Brain 108.(3) (1985),593–608.
30. Ziemann, U., Rothwell, J. C., & Ridding, M. C. Interaction between intracortical inhibition and facilitation in human motor cortex, Journal of Physiology (London) 496 (1996) (Pt 3), 873–81