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Assessment of Non-Motor Symptoms in Essential Tremor

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Abstract

In the clinical picture of essential tremor (ET), in addition to tremulous hyperkinesis, the importance of non-motor manifestations has recently been discussed. Despite their high occurrence, in most cases these manifestations remain unverified. The purpose of this study was to assess the incidence of non-motor symptoms (NMS) in patients with ET. The study included 3 groups comparable by sex and age. Group 1 (the main group) consisted of 53 patients with ET; Group 2 consisted of 57 patients with Parkinson's disease (PD); Group 3 consisted of 111 individuals without ET or PD, and without burdened heredity for extrapyramidal diseases. In study Groups the distribution by ethnicity was as follows: 22(41.5%) ethnic Yakuts and 31(58.5%) ethnic Russians in Group 1, 29(50.9%) ethnic Yakuts and 28(49.1%) ethnic Russians in Group 2, and 67(60.4%) ethnic Yakuts and 44(39.6%) ethnic Russians in Group 3. All subjects filled out the NMSQuest scale, which contains 30 questions for various groups of NMS. The analysis of NMS using the NMSQues scale in the three study groups showed a similarity between ET plus and PD in non-motor manifestations. The spectrum of NMS in patients with ET plus of both ethnic groups is heterogeneous and prevails in patients of the Russian ethnic group. Thus, Yakut patients with ET plus and PD showed a similarity in the frequency of hyposmia to Russian representatives with ET plus and PD in hyposmia, dysphagia, pain, sadness and restless legs syndrome. Excessive sweating was found in more than 64% of patients with ET plus of both ethnic groups. The results indicate a similarity in manifestations of ET plus and PD, which is possibly due to both the genetic and phenotypic affinity of these nosologies, and suggests that ET plus can be a transitional form of PD. (**International Journal of Biomedicine. 2019;9(4):308-312.**)

Key Words: essential tremor • Parkinson's disease • non-motor symptoms • NMSQuest

Introduction

ET is considered the most common disease of the extrapyramidal system, with a slowly progressing and disabling course.[1] A classic manifestation of the disease is a progressive kinetic-postural hand tremor, most often in combination with a tremor in a different location. ET is now considered to be a "syndrome" that can be associated with other symptoms. Based on a new classification of tremor,[2] ET can be classified as Essential Tremor and Essential Tremor plus. ET plus is a tremor with similar characteristics but may have additional neurological signs, such as impaired tandem gait or memory, dystonia or other mild neurological signs of unknown significance.[2] In the clinical picture of the disease, in addition to tremulous hyperkinesis, the importance of non-motor symptoms (NMS) has recently been discussed.[3] The spectrum of NMS in ET includes cognitive, psychiatric, sensory and other disorders (sleep disturbances, decreased body mass index, decreased quality of life).[3-11] NMS in ET, along with obligate symptoms, make up a common, rather complex phenotype of the disease.[12]

A number of authors do not exclude the probability of a manifestation of the disease with NMS.[9,10] Patients with ET are diagnosed with a variety of cognitive impairments: from mild/moderate impairment to dementia.[4] Psychiatric symptoms of ET include depression, increased anxiety, apathy, and changes in personality traits.[3] In general, studies show that patients with ET are observed with a high frequency of depression, apathy, situational anxiety, and social phobia,[13,15,16] often

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diagnosed with sensory impairment in the form of hearing loss and olfactory dysfunction.[17,18] The spectrum of NMS in ET is supplemented by sleep disturbances in this category of patients.[19]

Materials and Methods

The study included 3 groups comparable by sex and age. Group 1 (the main group) consisted of 53 patients (average age of 62.62±2.3 years) with ET: 19(35.8%) men and 34(64.2%) women. In Group 1, the distribution by ethnicity was as follows: 22(41.5%) ethnic Yakuts and 31(58.5%) ethnic Russians. Group 2 consisted of 57 patients (average age of 67.1±1.02 years) with Parkinson's disease (PD), including 23(40.4%) men and 34(59.7%) women. In Group 2, the distribution by ethnicity was as follows: 29(50.9%) ethnic Yakuts and 28(49.1%) ethnic Russians. Group 3 (the control group) consisted of 111 individuals (average age of 63.4±0.93 years) without ET or PD, and without burdened heredity for extrapyramidal diseases. In Group 3, the distribution by ethnicity was as follows: 67(60.4%) ethnic Yakuts and 44(39.6%) ethnic Russians.

All subjects filled out the NMSQuest scale, which contains 30 questions for various groups of NMS.[20] Each positive answer was scored as 1 point.

Statistical analysis was performed using statistical software package SPSS version 17.0 (SPSS Inc, Chicago, IL). Categorical variables were analyzed using the Chi-square test with the Yates' correction. The critical level of statistical significance for the three groups was determined at $P \leq 0.05/3=0.017$ (P_{1-2}, P_{2-3}, P_{1-3}).

The study was carried out in compliance with Ethical Principles for Medical Research Involving Human Subjects, Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the 52nd WMA General Assembly, Edinburgh, Scotland, October 2000. The study was approved by our regional ethics committee**.** All patients gave their written informed consent.

Results and Discussion

According to the results of the survey, in Group 1 the most frequent NMSs were nightly urination (64.2%), excessive sweating (62.3%), insomnia (41.5%), dizziness (feeling light-headed) (41.5 %), sadness (39.6%), constipation (39.6%), subjective feeling of memory loss (35.8%), anxiety (34.0%), hyposmia (30.2%), false urge to urinate (26.4%), and incomplete defecation (26.4%). The analysis revealed statistically significant differences in symptoms, such as hypersalivation, constipation, sexual dysfunction, falls and daytime sleepiness due to their frequent occurrence in patients of Group 2 ($P<0.017$). In Group 1, falls were due to tremor of the lower extremities in one person and vertigo in two people. At the same time, statistically significant differences in dysphagia, hyposmia and apathy were found due to their rare frequency in the healthy individuals of Group 3. Patients of Group 1 were characterized by a high frequency of excessive sweating and insomnia, unlike patients of Group 2.

Table 1.
Distribution of NMS of in the study group

NMS	Group 1	Group 2	Group 3	*P*-value
Hypersalivation	5(9.4%)	19(38%)	1(2.6%)	P=0.000 P_{1-2}=0.001 P_{1-3}=0.234 P_{2-3}= 0.000
Hyposmia	16(30.2%)	24(48%)	3(7.7%)	P=0.000 P_{1-2}=0.064 P_{1-3}=0.008 P_{2-3}= 0.000
Dysphagia	14(26.4%)	12(24%)	2(5.1%)	P= 0.026 P_{1-2}=0.777 P_{1-3}=0.008 P_{2-3}=0.015
Nausea. vomiting	6(11.3%)	6(12%)	1(2.6%)	P=0.444
Constipation	21(39.6%)	40(80%)	15(38.5%)	P=0.000 P_{1-2}=0.000 P_{1-3}=0.909 P_{2-3}=0.000
Enuresis	1(1.9%)	2(4%)	0	P=0.798
Incomplete defecation	14(26.4%)	0	6(15.4%)	P=0.001 P_{1-2}=0.000 P_{1-3}= 0.205 P_{2-3}=0.014
False urge to urinate	14(26.4%)	7(14%)	2(5.1%)	P=0.020 P_{1-2}=0.118 P_{1-3}=0.008 P_{2-3}=0.306
Nocturia	34(64.2%)	22(44%)	18(46.2%)	P=0.084
Unexplained pain	13(24.5%)	15 30%)	6 (15.4%)	P=0.27
Weight fluctuations	2(3.8%)	7(14%)	2(5.1%)	P= 0.11
Memory loss	19(35.8%)	31(62%)	19(48.7%)	P=0.03 P_{1-2}=0.008 P_{1-3}=0.215 P_{2-3}=0.210
Apathy	14(26.4%)	13(26%)	3(7.7%)	P=0.054
Hallucinations	3(5.7%)	3(6%)	0	P=0.3
Difficulty concentrating	10(18.9%)	14(28%)	7(17.9%)	P=0.42
Sadness	21(39.6%)	22(44%)	6(15.4%)	P=0.000 P_{1-2}=0.652 P_{1-3}=0.012 P_{2-3}=0.004
Anxiety	18(34.0%)	19(38%)	13(33.3%)	P=0.88
Hypoactive sexual desire disorder	4(7.5%)	32(64%)	(20.5%)	P=0.000 P_{1-2}=0.000 P_{1-3}=0.068 P_{2-3}=0.000
Sexual dysfunction without sexual desire disorder	2(3.8%)	14(28%)	0	P=0.000 P_{1-2}=0.001 P_{1-3}=0.615 P_{2-3}=0.000

Table 1.

Distribution of NMS of in the study group (Continued)

NMS	Group 1	Group 2	Group 3	*P*-value
Feeling light-headed	22(41.5%)	28(56%)	15(38.5%)	P=0.189
Falls	3(5.7%)	11(22%	2(5.1%)	P=0.012 P_{1-2}=0.016 P^{1-3}=0.724 P_{2-3}=0.025
Excessive daytime sleepiness	11(20.8%)	26(52%)	9(23.1%)	P=0.001 P_{1-2}=0.001 P^{1-3}=0.790 P_{2-3}=0.006
Imsomnia	22(41.5%)	10(20%)	16(41%)	P=0.037 P_{1-2}=0.018 P^{1-3}=0.964 P_{2-3}=0.030
Vivid dreaming	11(20.8%)	10(20%)	9(23.1%)	P=0.936
Sleep-talking	10(18.9%)	14(28%)	4(10.2%)	P=0.111
Restless legs syndrome	9(17.0%)	10(20%)	8(20.5%)	P=0.891
Swelling (edema)	12(22.6%)	6(12%)	5(12.8%)	P=0.273
Excessive sweating	33(62.3%)	8(16%)	4(10.2%)	P=0.000 P_{1-2}=0.000 P^{1-3}=0.000 P_{2-3}=0.431
Double vision	4 (7.5%)	1 (2%)	1 (2.6%)	P=0.313
Illusions	2 (3.8%)	0	0	P=0.658

Symptoms such as hyposmia, apathy, and dysphagia were equally common in Groups 1 and 2 (Table 1).

Considering the presence of other extrapyramidal phenomena in the clinical aspect of ET, we also evaluated NMS in patients with ET plus in the ethnic aspect. Patients with ET plus of the Yakut and Russian ethnic groups comprised 17/45(37.8%) and 28/45(62.2%) patients, respectively. Group 2 included 29/57(50.9%) ethnic Yakuts and 28/57(49.1%) ethnic Russians. Group 3 consisted of 35/57(61.4%) ethnic Yakuts and 22/57(38.6%) ethnic Russians.

Statistically significant differences were shown between the 3 study groups for such NMS as hypersalivation, hyposmia, constipation, sexual dysfunction, and daytime sleepiness, due to their frequent occurrence in ethnic Yakuts of Group 2 (Figure 1). We found no statistically significant difference in the incidence of hyposmia in patients with ET plus and patients with PD of the Yakut ethnic group.

In patients with ET plus of the Russian ethnic group, sweating was diagnosed statistically significantly more often compared to Groups 2 and 3 (P<0.017) (Table 2). Statistical differences were identified for apathy (35.7% in Group 1 and 39.3% in Group 2) compared to Group 3 (0%).

At the same time, constipation, difficulty concentrating, and sexual dysfunction were statistically significantly more common in patients of Group 2 compared to Group 1. Patients with ET and PD were similar in such NMS as hypersalivation, hyposmia, dysphagia, pain, sadness, and restless legs syndrome (P>0.017).

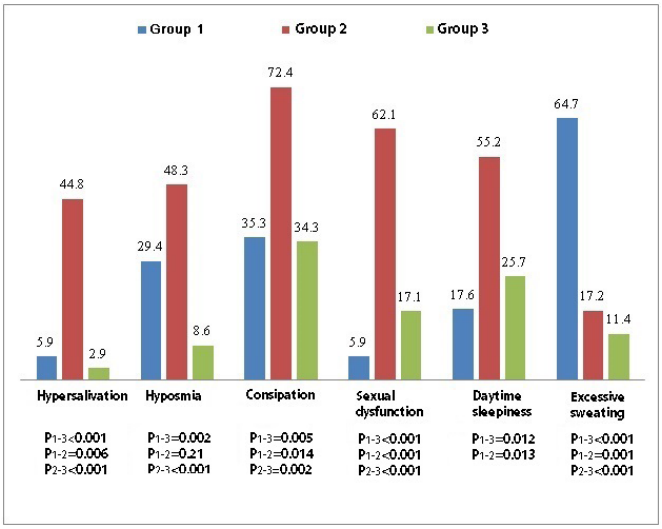

Fig. 1. *The spectrum of NMS in the Yakut representatives of the study groups*

Table 2.

The spectrum of NMS in the Russian representatives of the study groups

NMS	Group 1 (n=28)	Group 2 (n=28)	Group 3 (n=22)	*P*-value
Hypersalivation	2(7.1)	9(32.1)	1(4.5)	P=0.031 P_{1-2}=0.019 P^{1-3}=0.813 P_{2-3}=0.039
Hyposmia	9(32.1)	14(50)	2(9.1)	P=0.009 P_{1-2}=0.174 P^{1-3}=0.108 P_{2-3}=0.002
Dysphagia	10(35.7)	13(46.4)	2(9.1)	P=0.017 P_{1-2}=0.415 P^{1-3}=0.029 P_{2-3}=0.004
Nausea. vomiting	2(7.1)	8(28.6)	0	P=0.024 P_{1-2}=0.036 P^{1-3}=0.581 P_{2-3}=0.019
Constipation	13(46.4)	23(82.1)	7(31.8)	P=0.001 P_{1-2}=0.005 P^{1-3}=0.295 P_{2-3}=0.000
False urges to urinate	8(28.6)	3(10.7)	0	P=0.042 P_{1-2}=0.093 P^{1-3}=0.019 P_{2-3}=0.325

Table 2.

The spectrum of NMS in the Russian representatives of the study groups (Continued)

NMS	Group 1 (n=28)	Group 2 (n=28)	Group 3 (n=22)	*P*-value
Unexplained pain	7(25.0)	13(46.4)	2(9.1)	P=0.013 P_{1-2}=0.094 P^{1-3}=0.279 P^{2-3}=0.011
Apathy	10(35.7)	11(39.3)	0	P=0.005 P_{1-2}=0.783 P^{1-3}=0.008 P^{2-3}=0.004
Difficulty concentrating	5(17.8)	15(53.6)	2(9.1)	P=0.001 P_{1-2}=0.005 P^{1-3}=0.634 P^{2-3}=0.001
Sadness	14(50.0)	17(60.7)	4(18.2)	P=0.009 P_{1-2}=0.420 P^{1-3}=0.020 P^{2-3}=0.002
Sexual dysfunction without sexual desire disorder	2(7.1)	14(50.0)	8(36.4)	P=0.002 P_{1-2}=0.000 P^{1-3}=0.027 P^{2-3}=0.335
Falls	3(10.7)	8(28.6)	0	P=0.042 P_{1-2}=0.093 P^{1-3}=0.325 P^{2-3}=0.019
Restless legs syndrome	5(17.8)	11(39.3)	1(4.5)	P=0.01 P_{1-2}=0.076 P^{1-3}=0.318 P^{2-3}=0.004
Excessive sweating	18(64.3)	8(28.6)	2(9.1)	P=0.000 P_{1-2}=0.007 P^{1-3}=0.000 P^{2-3}=0.176

Conclusion

Thus, analysis of non-motor symptoms using the NMSQues scale in the three study groups showed a similarity between ET plus and Parkinson's disease in non-motor manifestations. The spectrum of non-motor symptoms in patients with ET plus of both ethnic groups is heterogeneous and prevails in patients of the Russian ethnic group. Thus, Yakut patients with ET plus and Parkinson's disease showed a similarity in the frequency of hyposmia to Russian representatives with ET plus and Parkinson's diseasein hyposmia, dysphagia, pain, sadness and restless legs syndrome. Excessive sweating was found in more than 64% of patients with ET plus of both ethnic groups. The results indicate a similarity in manifestations of ET plus and Parkinson's disease, which is possibly due to both the genetic and phenotypic affinity of these nosologies, and suggests that ET plus can be a transitional form of Parkinson's disease.

Competing Interests

The authors declare that they have no competing interests.

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