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Color Vision: A Study of Essential Tremor Cases vs. Normal Controls

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Abstract

Background—Patients with essential tremor (ET) and Parkinson's disease (PD) may exhibit overlapping clinical features. Also, a growing number of non-motor features are being documented in ET. Color vision abnormalities, though well known to occur in PD, have not been studied extensively in ET. We assessed color vision in ET cases and controls. We furthermore assessed subgroups of ET cases with clinical features that might link them to PD (i.e., ET cases with a family history of PD, and ET cases with rest tremor) to determine whether these cases had greater color vision abnormalities than ET cases without those features.

Methods—Participants were enrolled in a case-control study at Columbia University Medical Center. Color discrimination testing was performed using the Farnsworth–Munsell 100 Hue test. The total error score (TES) for the hue test was determined.

Results—The TES was similar in 55 ET cases and 55 controls (144.6 ± 91.8 vs. 145.6 ± 96.6 , $p = 0.96$). ET cases with rest tremor ($n = 8$) were similar to ET cases without rest tremor ($n = 47$) with respect to the TES (117.0 ± 73.4 vs. 149.3 ± 94.4 , $p = 0.36$), as were ET cases with a family history of PD ($n = 9$) vs. without ($n = 46$) (144.4 ± 57.0 vs. 144.6 ± 97.6 , $p = 0.996$).

Conclusions—Although a number of links exist between ET and PD, and non-motor features have been described in both, a color vision abnormality does not seem to be a feature of ET.

Keywords

essential tremor; non-motor; color vision; Farnsworth-Munsell 100 Hue Test

Introduction

In recent years, a number of non-motor (esp. cognitive) features have been described in patients with essential tremor (ET) [1]. Many of these features are similar to those that are seen in patients with Parkinson's disease (PD), although to a lesser degree [1]. Patients with

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ET and PD may also exhibit overlapping motor phenomenology, with rest tremors occurring in patients with ET and action tremors in PD [2]. Furthermore, brainstem Lewy bodies have been detected in ET cases in some postmortem series [3], and epidemiological studies suggest an association between the two diseases [4]. Studying the similarities and/or links between these two diseases is an emerging focus of ET research.

A non-motor feature that has been well documented in patients with PD is an abnormality of color vision [5, 6], which may reflect decreased dopamine levels in amacrine and retinal cells [6]. In contrast to PD, there are nearly no data on color vision in ET. One recently published study examined color discrimination in 36 ET cases vs. 34 controls, detecting no difference [6], yet we are unaware of other published data. There is some neuroimaging evidence of a mild abnormality of the dopaminergic system in ET cases [7], providing additional justification to explore the issue of color vision in ET.

In the current study, we assessed color vision in 55 ET cases and 55 normal controls in order to determine whether ET cases have color vision abnormalities compared with normal controls. We furthermore assessed subgroups of ET cases with clinical features that might link them to PD (i.e., ET cases with a family history of PD, and ET cases with rest tremor) to determine whether they had greater color vision abnormalities than ET cases without those clinical features. Documenting such an abnormality would provide additional clinical evidence of a link between ET and PD.

Methods

Study Sample

All participants were enrolled in an epidemiological research study of tremor at Columbia University Medical Center (CUMC) [8]. The majority of ET cases were patients at the Center for Parkinson's Disease and Other Movement Disorders (CPD) at the Neurological Institute of New York (CUMC). They were selected randomly from a list of patients seen over the past five years, using the Neurological Institute's computerized billing database. Each had been diagnosed with ET by a CPD neurologist specializing in movement disorders. The initial diagnosis of ET was based on the presence of moderate or greater amplitude action tremor in the arms or head tremor in the absence of another known cause (e.g., medications, PD, or dystonia); as described below, this diagnosis was reconfirmed in each case using published diagnostic criteria [9]. Normal controls were selected from the same source population as ET cases (i.e., the same set of zip codes). They were recruited using random-digit telephone dialing and frequency-matched by age, gender, and race to ET cases. The majority also received their health care at the same medical center (CUMC) as the cases in various outpatient departments (e.g., medicine, surgery).

Study Procedure

Upon enrollment, all participants signed informed written consent approved by the CUMC Institutional Review Board. Participants were evaluated in person by a trained tester who administered structured clinical questionnaires that elicited demographic and clinical information, including family history information (e.g., presence of a first- or second-degree relative with PD).

Along with the questionnaires, color discrimination testing was performed in all participants as part of the standard research assessment. Testing was performed in a binocular fashion using the Farnsworth–Munsell 100 Hue test (FMT)[10], which has been widely used for the examination of color discrimination [6]. Participants arranged a series of colored discs in sequence between pairs of reference discs. The order of discs was then plotted and analyzed on a circular diagram, which illustrated the degree of error. All participants were examined

under the same conditions in a silent, darkened room, with the discs illuminated by a single light source. No time limit was set for the completion of the test. The total error score (TES) for the hue test was determined, with a higher TES indicative of more errors. Participants with a history of achromatopsia were excluded.

The Folstein Mini-Mental State Exam (MMSE)[11] was administered as a brief test of cognition. Each ET case also underwent a videotaped neurological examination, with an assessment of postural tremor and five tests of kinetic tremor. A senior movement disorders neurologist (E.D.L.) reviewed all videotaped examinations, and the severity of postural and kinetic tremors were rated (0 - 3), resulting in a total tremor score (range = 0 - 36 [maximum]), a measure of the severity of action tremor. Based on the videotaped examination and treating neurologist's clinical records, the senior movement disorders neurologist confirmed diagnoses of ET using published diagnostic criteria (moderate or greater amplitude kinetic tremor on 3 tests or head tremor, in the absence of PD or dystonia) [9]. ET cases were videotaped while seated, standing and walking, and the presence of rest tremor in the arms was noted if it was present.

Statistical Analyses and Sample Size Calculation

Statistical analyses were carried out using SPSS (version 19; Chicago, Illinois). Demographic and clinical characteristics were compared using chi-square tests (X^2) and Student's t-tests. The TES was normally distributed (Kolmogorov-Smirnov $z = 1.19$, $p = 0.12$); therefore, parametric tests (Student's t test, Pearson's rho) were used when assessing this variable.

Using published data (log TES in controls = 4.27 ± 0.51) [6], our sample size (55 ET and 55 controls) had 99.2% power to detect as little as a 10% increase in the TES in ET cases vs. controls (assuming $\alpha = 0.05$). For our analyses of subgroups, the study was adequately powered (89.0% power for rest tremor, and 92.0% power for family history of PD) to detect as low as a 15% increase in the TES in ET cases vs. controls (assuming $\alpha = 0.05$).

Results

ET cases and controls were similar in age, gender, race, education, and MMSE score (Table 1). The TES was similar in ET cases and controls (144.6 ± 91.8 vs. 145.6 ± 96.6 , $t = 0.06$, $p = 0.96$) (Table 1). In a series of three separate sensitivity analyses, the lack of a case-control difference remained: (1) after excluding two ET cases and two controls with MMSE scores <24 (TES = 146.4 ± 93.0 in 53 ET cases vs. 146.5 ± 97.8 in 53 controls, $t = 0.002$, $p = 0.998$), (2) after excluding 18 ET cases and 4 controls currently taking medications that could affect color vision (e.g., anticonvulsants and digitalis) (TES = 147.7 ± 96.6 in 37 ET cases vs. 143.1 ± 92.4 in 51 controls, $t = 0.23$, $p = 0.82$), and (3) after excluding 15 ET cases and 17 controls with a history of any eye diseases (e.g., glaucoma, cataracts, and macular degeneration) (TES = 126.2 ± 79.8 in 40 ET cases vs. 138.0 ± 91.4 in 38 controls, $t = 0.61$, $p = 0.55$), thereby indicating that the lack of a case-control difference persisted irrespective of these issues.

Eight (14.5%) of 55 ET cases had rest tremor on examination. ET cases with vs. without rest tremor were similar with respect to age, gender, education, MMSE score and tremor duration (Table 2, all $p > 0.05$). ET cases with rest tremor made fewer errors (lower TES), but not to any significant degree (117.0 ± 73.4 vs. 149.3 ± 94.4 , $t = 0.92$, $p = 0.36$, Table 2).

Nine (16.4%) of 55 ET cases had a family history of PD in a first- or second-degree relative. ET cases with a family history of PD vs. ET cases without a family history of PD were similar with respect to age, gender, education, MMSE score and disease duration (Table 2,

all $p > 0.05$). They were nearly identical in term of the TES (144.4 ± 57.0 vs. 144.6 ± 97.6 , $t = 0.005$, $p = 0.996$, Table 2).

In controls, the TES was moderately correlated with age in years ($r = 0.39$, $p = 0.003$) and moderately and inversely correlated with years of education ($r = -0.32$, $p = 0.02$), but not with MMSE score ($r = -0.09$, $p = 0.51$) or gender ($t = 0.51$, $p = 0.61$). The TES was not correlated with tremor duration ($r = 0.16$, $p = 0.24$) or total tremor score ($r = -0.17$, $p = 0.25$) in ET cases.

Discussion

Patients with ET and PD may have overlapping clinical features [2]. A growing number of non-motor features are also being documented in ET [1]. Yet color vision abnormalities, though well known to occur in PD [5], have not been studied extensively in ET. Studying the similarities and/or links between these two diseases is an emerging focus of ET research, and documenting another similarity (i.e., a color vision abnormality) would provide additional clinical evidence of a link between ET and PD.

In the current study, we assessed color vision in 55 ET cases and 55 normal controls using the FMT. We did not detect a color vision abnormality in ET. Furthermore, when we stratified ET cases into those with rest tremor and those with a family history of PD (i.e., clinical features that could link them to PD), we again did not detect a color vision abnormality.

One recently published study examined color discrimination in 36 ET cases vs. 34 controls, and detected no difference [6]. Hence, their results were similar to ours. That study; however, did not further stratify ET cases into subgroups based on clinical features such as rest tremor or family history of PD. Also, the characteristics of the two samples differs considerably with respect to demographic and clinic features, with the prior sample being younger, largely female, and having a shorter disease duration (mean = 4.1 years) [6], hence the current study broadens to spectrum of ET cases to have been sampled.

Our ET cases with rest tremor did not demonstrate evidence of a color vision abnormality. This finding serves to further support the notion that ET patients with rest tremor do not necessarily have early PD. Indeed, a recent postmortem study indicated that Lewy bodies were not detectable in the substantia nigra of ET patients with isolated rest tremor [12]. ET patients with rest tremor may be distinguished from PD patients in a number of important respects. The former generally have longstanding and severe ET [2]. Furthermore, the rest tremor occurs in isolation of other cardinal signs of parkinsonism.

This study had several limitations. The TES for the hue test was determined but we did not determine the partial error score (PES) for the red–green axis and blue–yellow axis. The prior study of ET cases did not find such red–green axis or blue–yellow axis differences compared with controls [6]. Our study also had strengths. To our knowledge, this is only the second study to have looked at color vision abnormalities in ET, and the sample size was more than 50% larger than the previous study. We furthermore assessed subgroups of ET cases with clinical features that might link them to PD (i.e., ET cases with a family history of PD, and ET cases with rest tremor) to determine whether they had greater color vision abnormalities than ET cases without those clinical features. Although the number of ET cases with rest tremor or a family history of PD was low, the study was adequately powered (>80% power to detect as low as a 15% difference) to assess this issue. Nonetheless, additional studies would serve to confirm and strengthen our observations.

In summary, although a number of links exist between ET and PD, and non-motor features have been described in both ET and PD, a color vision abnormality does not seem to be a feature of ET.

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Table 1

Demographic and clinical characteristics of ET cases and controls

	ET (n = 55)	Controls (n = 55)	Significance
Age (years)	72.0 ± 11.6	71.1 ± 11.7	$t = 0.43, p = 0.67$
Women	30 (54.5%)	33 (60.0%)	$\chi^2 = 0.33, p = 0.56$
Race			$\chi^2 = 1.68, p = 0.64$
Non-Hispanic White	52 (94.5%)	51 (92.7%)	
Non-Hispanic Black	1 (1.8%)	2 (3.6%)	
Hispanic	1 (1.8%)	2 (3.6%)	
Other	1 (1.8%)	0 (0.0%)	
Education (years)	15.9 ± 2.6	16.2 ± 2.5	$t = 0.49, p = 0.62$
MMSE score	28.7 ± 1.5	28.9 ± 1.6	$t = 0.64, p = 0.53$
Tremor duration (years)	33.0 ± 17.7	Not applicable	Not applicable
Total tremor score	20.5 ± 6.0	Not applicable	Not applicable
TES	144.6 ± 91.8	145.6 ± 96.6	$t = 0.06, p = 0.96$

Values represent means ± standard deviations or numbers (percentages).

MMSE = Folstein Mini-Mental State Exam. TES = total error score on the Farnsworth–Munsell 100 Hue test.

Table 2

Demographic and clinical characteristics of ET subgroups

	ET + rest tremor (n = 8)	ET – rest tremor (n = 47)	ET + family history of PD (n = 9)	ET - family history of PD (n = 46)
Age (years)	74.5 ± 13.8	71.6 ± 11.3	69.4 ± 12.2	72.5 ± 11.6
Women	5 (62.5%)	25 (53.2%)	5 (62.5%)	25 (53.2%)
Education (years)	16.1 ± 2.9	15.9 ± 2.6	14.8 ± 2.8	16.1 ± 2.6
MMSE score	28.3 ± 2.4	28.8 ± 1.3	28.8 ± 1.2	28.7 ± 1.6
Tremor duration (years)	34.0 ± 22.0	32.8 ± 17.3	31.8 ± 13.6	33.2 ± 18.5
TES	117.0 ± 73.4	149.3 ± 94.4	144.4 ± 57.0	144.6 ± 97.6

Values represent means ± standard deviations [medians] or numbers (percentages).

MMSE = Folstein Mini-Mental State Exam. TES = total error score on the Farnsworth–Munsell 100 Hue test.