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L-Dopa improves colour vision in Parkinson's disease

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Summary. In recent studies disorders of colour vision in Parkinsonian patients have been demonstrated. Up to now, the influence of dopaminergic treatment on those phenomena remains unclear. We therefore performed a colour vision test (Farnsworth-Munsell 100 Hue Test) in 19 patients with Parkinson's disease before and after the oral application of the morning dose of L-Dopa. The colour discrimination was significantly improved after the ingestion of L-Dopa. There was no different effect of L-Dopa on the blue-yellow or red-green axis of colour vision. The morphological structures responsible for these colour vision disturbances are unknown, but it can be concluded that the dopamine deficiency in Parkinson's disease is not restricted to the basal ganglia but may involve the visual system as well.

Keywords: Parkinson's disease, colour vision, colour discrimination, Farnsworth – Munsell 100 Hue Test, L-Dopa.

Introduction

Simple colour vison tests were not sufficient enough to demonstrate the existence of a colour perception disorder in Parkinson's disease (PD) (Kupersmith et al., 1982). Recently dysfunctions of colour vision in PD could be demonstrated using the Farnsworth-Munsell 100 Hue Test and a computer-based determination of colour contour perception (Büttner et al., 1992, 1993; Price et al., 1992). However, it remains unclear whether the colour perception disorder is due to medical treatment or to dopamine deficiency because both studies comprise patients of various clinical stages and on different treatment.

We therefore studied the colour discrimination assessed by the Farnsworth-Munsell 100 Hue Test in Parkinsonian patients before and after the application of the morning dose of L-Dopa to determine the effect of L-Dopa treatment on colour vision.

Patients and methods

A colour vision test was performed in 19 patients before and after the oral application of the morning L-Dopa dose (100 mg L-Dopa in 14, 75 mg L-Dopa in 2 and 50 mg L-Dopa in 3 patients, in combination with benserazide or carbidopa respectively). Dopaminergic drugs were withheld for at least 12 hours prior to the test. The further comedication had been taken in each case at least one hour before the first colour vision examination was performed. The second run of the test was started 30 minutes after the application of the individual L-Dopa medication. Between 15 and 30 minutes were necessary to fulfill the exercise. Accordingly, the second run was finished in all cases at least within 60 minutes after the L-Dopa application. The patients were not allowed to take their breakfast before finishing the second test in order to avoid a delay of L-Dopa resorption (Montgomery, 1992).

The study comprises 13 male and 6 female patients with a mean age of 62.1 ± 10.7 years (range 38–75 years). Idiopathic parkinsonism has been diagnosed in all cases. Exclusion criteria were dementia as defined by the DSM-III R (American Psychiatric Association, 1987), clinical, electrophysiological or neuroradiological evidence of additional CNS pathology exceeding PD, medication with digitalis, sedativa or antiepileptic drugs and visual disorders, especially distorted visual acuity, glaucoma, retinopathy or colour misperceptions. All patients underwent a complete ophthalmologic examination, including split-lamp examination and determination of visual acuity. The visual acuity was better than 0.6 in all patients. Depression was recorded in all patients using a standardized inventary (Beck et al., 1961).

The severity of Parkinsonism was assessed immediately before each colour vision test by the Hoehn-Yahr staging and the Unified Parkinson's Disease Rating scale (UPDRS)/part motor examination (scoring method: motor features point 18–31). The clinical data of the patients and their medication are presented in Table 1.

As a reference 19 age- and sex-matched healthy controls with a mean age of 62.8 years (40–79 years) were examined. Additionally, 9 subjects (healthy controls (3), multiple sclerosis (3), PD (1), diabetic retinopathy (1), digitalis medication (1)) were tested twice according to the same protocol to evaluate exercise effects.

The colour vision was measured in a binocular fashion using the Farnsworth-Munsell 100 Hue Test (Farnsworth, 1943). The examinations were performed in a noise-isolated darkened room. The coloured plates of the test were illuminated by a daylight lamp (Biolux, Osram, 6,500 K). As recommended for patients with neurological disorders no time limit was applied to the completion of the test.

The total error score was determined by a method previously proposed. (Verriest et al., 1982). To determine the existence of an axis the error score was separated into blue-yellow and red-green partial scores (Smith et al., 1985). For further analysis the square roots of the scores were used in order to obtain a normal distribution and to yield homogenous variances (Kinnear, 1970; Verriest et al., 1982). For statistical comparisons the Wilcoxon matched pairs signed ranks test, the paired samples t-test and the Pearson's correlation test were carried out.

Results

The mean total error score (MTES) of the Parkinsonian patients before L-Dopa treatment was 16.47 (SD 1.86; range 13.8–20.0) as compared to 13.6 (SD 0.6; range 13.27–16.0) in the reference group ($p < 0.001$).

Higher values were observed in advanced PD (Table 2). No significant correlation between severity of depression and MTES could be demonstrated ($r = -0.09$, $p = 0.7$).

Table 1. Clinical data and medication of the patients with PD

Male: 13	Female: 6
Mean age: 62.1 ± 10.7	(range: 38–75 years)
Medication:	
L-Dopa* (monotherapy)	3
L-Dopa* + Dopamine agonist**	7
L-Dopa* + Dopamine agonist** + Deprenyl	9
Hoehn/Yahr staging:	
II	10
III	5
IV	4
Duration of Parkinson's Disease: 8.7 ± 5.2 years (range: 3–19 years)	

*, + Benserazide or Carbidopa; ** Lisuride, Bromocriptine. Dose ranges of medications: L-Dopa 250–750 mg/d; Lisuride 1–2 mg/d; Bromocriptine 7.5–30 mg/d; Deprenyl 5–10 mg/d

Table 2. Total error scores in the Farnsworth-Munsell 100 Hue Test depending on the stage of PD

Hoehn/Yahr	Error score	n
II	15.51 (SD 1.61)	10
III	17.15 (SD 2.20)	5
IV	17.76 (SD 1.21)	4

In the second run of the test 30 to 60 minutes after oral application of L-Dopa the MTES was 15.41 (SD 1.01, range 13.3–18.2). The difference between the MTES before and after treatment with the L-Dopa morning dose was statistically significant ($p < 0.01$) (Fig. 1, Table 3). All patients showed a significant improvement of the Parkinsonian symptoms after the ingestion of L-Dopa ($p < 0.001$). Six of them developed L-Dopa induced dyskinesia during the second run of the colour vision examination. Furthermore a significant positive correlation between the improvement of the UPDRS partial scores and the MTES was demonstrated ($r = 0.57$, $p < 0.05$).

In those 9 control subjects tested twice no significant improvement during the second run of the colour vision examination could be established (MTES 1st run 13.93, SD 0.56; MTES 2nd run 13.99, SD 0.71; t-test: $t = -0.39$, $p = 0.7$).

The analysis of partial scores showed that the improvement of colour vision after L-Dopa treatment does occur in both axis of the test (Table 3).

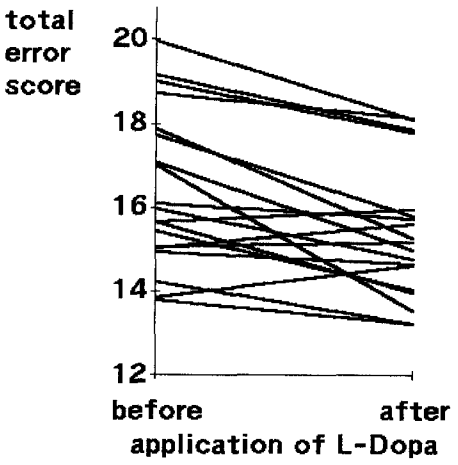

Fig. 1. Total error scores in the Farnsworth-Munsell 100 Hue Test of 19 patients with Parkinson's disease before and after the oral application of L-Dopa. The second examination is started 30 minutes after the ingestion of L-Dopa. The total error scores of nearly all patients are improved in the second examination ($p < 0.01$)

Table 3. Means of total and partial error scores in the Farnsworth-Munsell 100 Hue Test in Parkinsonian patients before and after application of the morning L-Dopa dose

	before L-Dopa application	after L-Dopa application	
Total error score	16.47 (SD 1.86)	15.41 (SD 1.61)	$p < 0.01$
Partial error score (blue-yellow)	11.21 (SD 1.15)	10.47 (SD 0.99)	$p < 0.05$
Partial error score (red-green)	12.05 (SD 1.62)	11.30 (SD 1.33)	$p < 0.01$

Discussion

Dysfunctions of the visual system in PD have been demonstrated by visual evoked potential (VEP) and electroretinogram (ERG) recordings and the psychophysical determination of contrast sensitivity (Bodis-Wollner and Yahr, 1978; Bodis-Wollner et al., 1987; Gawel et al., 1981; Hutton et al., 1991; Mestre et al., 1990; Regan and Maxner, 1987). These alterations could be partially restored by a dopaminergic medication (Bodis-Wollner and Tagliati, 1993; Sollazzo, 1985; Terziivanov et al., 1982). Additionally circadian fluctuations of contrast sensitivity and the dependance on "on"- and "off"-phases in patients with motoric fluctuations support the hypothesis of visual disorders in PD due to dopamine-deficiency (Bodis-Wollner and Tagliati, 1993; Struck et al., 1990). Therefore one may conclude that disturbances of achromatic vision seem to be related to dopamine deficiency in PD (Bodis-Woller and Tagliati, 1993).

Recently the affection of chromatic vision in PD could be demonstrated by a computer aided determination of the colour contour perception and by the measurement of the colour discrimination with the Farnsworth-Munsell Test respectively (Büttner et al., 1992, 1993; Price et al., 1992). However. in contrast to achromatic vision the underlying pathophysiology of the colour perception disorder in PD is still unknown. The aim of our study was to evaluate the influence of dopaminergic treatment on the colour discrimination in PD.

In our prospective study we could show that the colour discrimination, measured by the Farnsworth-Munsell 100 Hue Test, is significant improved after the application of L-Dopa. We tested the colour discrimination before the morning dose of L-Dopa was given after a drug-free interval of at least 12 hours. The colour test was repeated 30 minutes and completed within at least 60 minutes after the oral ingestion of the morning L-Dopa dose. This time interval guarantees a maximum L-Dopa plasma level during the second run of the test in the majority of the patients (Contin et al., 1993; Montgomery, 1991). The improvement of motor symptoms at this time interval in all patients confirms this assumption. As the dopaminergic comedication was applicated after the completion of the second run of the test a significant influence of dopamine agonists on the detected improvement of colour vision can be excluded.

In a control group tested according to the same protocol as the patient group no significant exercise effect could be demonstrated. The improvement of colour discrimination was independent of the severity of depression. We conclude that the improvement of colour discrimination is directly due to an effect of L-Dopa because all the other conditions were not changed during the examinations. The correlation between the motor and visual improvement suggests that the colour vision deficit in PD is related to dopamine deficiency.

The colour discrimination disorder depends on the severity of PD as reported in a previous study (Price et al., 1992). To determine the influence of L-Dopa on a specific axis of colour vision, the scores were separately evaluated for the blue-yellow and the red-green partial scores, but a different effect of L-Dopa could not been proven (Smith et al., 1985).

Dopamine is present in the amacrine and interplexiform cells of the retina of all mammalians examined (Bodis-Wollner and Tagliati, 1993). There is a considerable evidence indicating that dopamine is a major retinal neurotransmitter (Kramer, 1971). In Parkinsonian retinas reduced dopamine content could be shown as compared to age-matched controls (Harnois and Di Paolo, 1990). The amplitude of the B-wave in the ERG of Parkinsonian patients decreased after L-Dopa ingestion (Terziivanov et al., 1982). The B-wave originates in the bipolar cell layer of the retina were maximum dopaminergic activity is present. It seems to be possible that a retinal dopamine deficiency is responsible for the colour vision dysfunction in PD. Resubstitution of retinal dopamine would result in improvement of colour discrimination. However, an additional disturbance of the central dopaminergic pathways is imaginable. A specialized neuronal system processing

chromatic vision exists in the Corpus geniculatum laterale and the visual cortex, which may be involved in the pathology of PD (Livingstone and Hubel, 1984). Some phenomena regarding achromatic vision in PD could not be explained by retinal defects alone (Bulens et al., 1988; Regan and Maxner, 1987).

Although the anatomical structures responsible for visual disorders, especially distorted colour vision, in PD are unknown, the studies of visual functions result in the conclusion that PD is not exclusively to be regarded as a motor disease but a perceptual disease as well. The underlying pathophysiology could be a dopamine deficiency affecting both the basal ganglia and the visual system.

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