

## Impairment of High-Contrast Visual Acuity in Parkinson's Disease

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**Summary:** Several studies have shown that the visual system is affected in Parkinson's disease (PD) with reduced contrast sensitivity, low-contrast acuity, and flicker sensitivity, as well as altered electroretinograms (ERGs) and pattern visual evoked potentials (VEPs). Apparently, however, no study has yet specifically determined whether visual acuity to high-contrast stimuli is impaired in PD. Visual acuity was measured in a group of 16 patients with PD, both on and off drugs (for 24 h), and 16 age- and sex-matched normal control subjects. Acuity was impaired in the PD group both on standard Snellen chart and on a screen in a computerized test of visual resolution. The degree of impairment was 24 and 25%, respectively, in the two tests. The PD patients had marginally better acuity on both tests while receiving drugs, but the differences were not significant. The difference between the two groups was consistent with impaired resolution and could not be accounted for by any perceptual dysfunction that may also have been present in the PD group. Conversely, however, impaired acuity may be implicated in studies that have reported mild deficits of visuospatial/visuoperceptual function in PD. Reduced acuity appears to be a subtle sequela of dopaminergic deficiency in the visual system. **Key Words:** Visual acuity—Parkinson's disease.

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Substantial evidence shows that visual dysfunction exists in Parkinson's disease (PD). Spatial resolution deficits have been demonstrated on low-contrast sensitivity tests using sinusoidal gratings, particularly for midrange spatial frequencies (1-5), and on low-contrast letter charts (4,6). Deficits have also been shown to be dependent on the temporal frequency of stimulation on tests of contrast sensitivity and flicker sensitivity (3,4). Electrophysiologic evidence of visual dysfunction in PD includes prolonged latency of pattern visual evoked potentials (VEPs) (7-9), although only for smaller checkerboard elements (7,10) and reduced amplitude of

the flash electroretinogram (ERG) (8,11) and pattern ERG (8,12,13).

The abnormalities appear to be related to a dopaminergic deficiency at several sites. Alteration of the ERG in PD provides strong evidence for abnormality at the retinal level (8,11-13). Fredrick et al. (14) demonstrated the presence of dopaminergic neurons in the interamacrine and interplexiform cells of the human retina. The interplexiform cells may carry feedback signals related to spatial contrast processing to retinal horizontal cells (3). Perhaps the best demonstration of a direct link between retinal dopamine and visual dysfunction is in monkeys displaying Parkinsonian-like symptoms after administration of 1-methyl,4-phenyl-1-2-3-6 tetrahydropyridine (MPTP) in which specific changes in the pattern-VEP and pattern-ERG occur with a drop in retinal dopamine (15). One possible mech-

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anism whereby reduced retinal dopamine could affect vision both subjectively and electrophysiologically is by decreasing retinal sensitivity, an effect similar to that of reduced mean luminance. The contrast sensitivity data of Bodis-Wollner et al. (3) do not preclude this possibility because curves for PD patients show attenuated peak sensitivity and leftward shift consistent with reduced luminance curves in normal subjects. Prechiasmatic involvement, possibly retinal, is also consistent with reports of unilateral contrast sensitivity loss (2,3,16) and VEP asymmetry (7).

Evidence also shows that impaired VEPs in PD may be of retinal origin. Dyer et al. (17) showed that administration of a dopamine-blocker ( $\alpha$ -methyl-*para*-tyrosine) to rats resulted in significantly increased latencies of early peaks in the flash VEP; recordings at both the optic tract and geniculate nucleus showed changes similar to those observed at the cortex. Direct stimulation of the optic nerve, which failed to reveal drug-induced changes, provided further support for the retinal origin of VEP delays. Dyer et al. (17) suggest that impairment of amacrine cell function, as would be expected by dopamine depletion, would lead to a desynchronizing influence on ganglion cell responsiveness and thus to prolonged VEP latencies.

The abnormal shape of some contrast sensitivity curves, however, raises the possibility that other sites may be involved. Spatiotemporal investigations by Bodis-Wollner et al. (3) suggest changes in spatiotemporal tuning linked to dopamine deficiency in the brain. This alternative locus of visual system dopamine deficiency is supported by the findings of Regan and Maxner (4). They measured contrast sensitivity in 10 patients with PD using a 2 cycle/degree sinewave grating; in 6 patients with loss of contrast sensitivity, the loss was maximal for horizontal orientation of the grating. This dependence of contrast sensitivity losses on orientation was confirmed in a study by Bulens et al. (5), although they noted that the greater loss was as common for the vertical as the horizontal orientation. Both Regan and Maxner (4) and Bulens et al. (5) concluded that because orientation-sensitive neurons are not found peripheral to the primary cortex, orientation selectivity implicates abnormality in the striate cortex. In addition, the presence of notch loss in PD, as evidenced by striking dips in the contrast sensitivity function at intermediate spatial frequencies (2,3,5), is attributed to cortical neurons

and not to those in retina or geniculate body (2,5,18). These results are consistent with decreased dopamine concentrations in the visual cortex of PD patients as demonstrated by positron emission topography (19).

Despite the evidence for substantially impaired acuity for low- to medium-contrast stimuli—both sinusoidal gratings and optotypes—there has been no report of impairment of high-contrast acuity, such as on the standard Snellen chart. Indeed, several studies state or imply that visual defect in PD occurs with sparing of visual acuity (2–4,6). As part of a more extensive study of sensory-motor function in PD, we measured high-contrast visual acuity by Snellen chart optotypes and by a computerized task of visual resolution and found it to be significantly impaired on both tests.

## METHODS

### Subjects

The experimental group comprised 16 patients with PD made up of 9 men and 7 women. Ages ranged from 38 to 72 years (mean 57 years 2 months). All were within grades I–III on the Hoehn-Yahr scale (20) (2 on I, 5 on II, 9 on III), were not suffering from “on-off,” and had no dyskinesia. Duration of illness ranged from 0.4 to 12 years (mean 5.5 years). All subjects were being treated with either L-DOPA plus a decarboxylase inhibitor (6 subjects) or an anticholinergic (7 subjects) or both (3 subjects), supplemented in some patients by either bromocriptine (1 subject) or amantadine (4 subjects). Mean doses were: L-DOPA 300 mg/day, benzotropine mesylate 4 mg/day, orphenadrine hydrochloride 170 mg/day, procyclidine hydrochloride 6 mg/day, amantadine 300 mg/day, and bromocriptine 20 mg/day. No patient received more than one type of anticholinergic drug, and bromocriptine and L-DOPA were not used together.

The control group comprised 16 subjects who had no neurologic symptoms or history. They were matched against the PD group (using a paired experimental design) for both age (range 38–74 years, mean 57.7 years, NS) and sex. Subjects in both groups were included only if they had a corrected visual acuity of 6/9 or better in one eye, and no visual field defect. All patients had normal ophthalmoscopic findings and appeared mentally normal on routine clinical assessment. Indeed, no subjects

were rejected from study because they did not meet the visual screening criteria.

#### Apparatus and Tests

Visual acuity was measured by two quite different tests. The first used a standard back-projected Snellen chart at 6 m, with refractive errors being corrected. The contrast between letters and white background was 97%, with the white background having an average luminance of 346 cd/m<sup>2</sup> (2). The acuity of each eye was measured separately as the line of smallest characters at which half or more of the letters were correctly identified.

The second test was a computerized test of visual resolution. Test stimuli were generated by a PDP-11/34 computer and displayed on a VT11 oscilloscopic (i.e., non-raster) graphics screen (279 × 228 mm; green phosphor). Each stimulus comprised a "dot" (diameter 0.9 mm, 173 cd/m<sup>2</sup>, 97% contrast relative to screen) presented at various positions on and to either side of a vertical line (width 0.5 mm, 17.6 cd/m<sup>2</sup>, 70% contrast relative to screen). Contrast between the dot and line was 69%. Dot displacements were in multiples of 0.273 mm (i.e., horizontal screen pixels) which, for an eye-screen distance of 132 cm, gave an angular resolution of 0.71 min of arc (equivalent to a Snellen acuity of 6/4.3). The test consisted of 20 trials comprising two with a dot-line separation of 10 pixels and three at each separation from 5 to 0 pixels (a displacement of 1 pixel resulted in a dot being on but *bulging* to one side of line). Dot displacements were randomly divided between right and left of the line. For each trial, subjects were asked whether the dot was exactly on the center of the line or to either side. Visual resolution was defined as the minimum separation at and beyond which a subject always correctly identified the dot as being off the center of the line.

#### Experimental Procedure

All subjects were assessed twice, 1 week apart. The patients were receiving their normal drug regimen for one session but not their anti-Parkinsonian medication for 24 h for the other session. The sequence of the on- and off-drug sessions was evenly but randomly allocated between patients to allow determination of the effect of medication on acuity

\* All contrasts defined as the Weber fraction  $(L_{\max} - L_{\min})/L_{\max}$ , where  $L_{\max}$  and  $L_{\min}$  are the maximum and minimum luminances, respectively.

while balancing out any confounding order effects between sessions. Although the Snellen acuity for both the right and the left eyes was recorded, only that of the best eye was used in this study. This is considered essentially the same as that of binocular visual acuity (21) which was used in the visual resolution test. The nonparametric Wilcoxon matched-pairs statistic was used for between-group comparisons because of its greater robustness over its parametric paired t-test equivalent with only minimal loss of power.

#### RESULTS

No difference was noted in acuity between on-drug and off-drug sessions in the PD group on either the Snellen chart (6/6.37 vs. 6/6.78, 6.4%, NS) or the visual resolution test (2.03 vs. 2.12 min of arc, 4.4%, NS). Consequently, the following results represent averaged data from the on-drug and off-drug sessions for all subjects.

Comparison of the experimental and control groups showed that acuity was impaired in the PD subjects as measured on both the Snellen chart (6/6.58 vs. 6/5.25, 25%,  $p < 0.01$ ) and the visual resolution test (2.08 vs. 1.68 min of arc, 24%,  $p < 0.01$ ). Converted into angles subtended at the eye, the Snellen resolutions became 1.10 and 0.88 min of arc for the PD and control groups, respectively. These were smaller than the resolutions determined by the visual resolution test by 0.89 min of arc for the PD group and 0.91 min of arc for the control group.

Visual resolution curves, the average accuracy of subjects' responses at each of the dot-line separations in the visual resolution test, are shown in Fig. 1 for both groups. The visual resolution curve of the PD group was very similar to that of the control group, except for a shift to a larger dot-line separation, equivalent to 0.20 min of arc at the 50% accuracy level. This shift supports an overall reduction in acuity in the PD subjects but is only half the 0.40 min of arc difference in visual resolution scores between the two groups. This can probably be attributed to the difference in definitions of mean visual resolution scores (i.e., 100% accuracy at and beyond that separation for a particular subject) and mean 50% accuracy separations.

#### DISCUSSION

The differences in resolutions estimated by the two tests deserves comment. The differences oc-

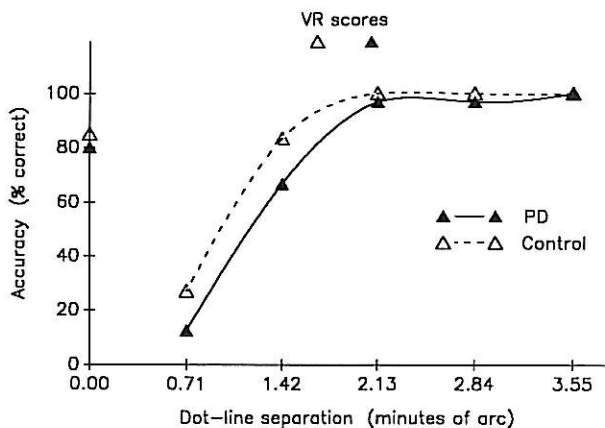


FIG. 1. Visual resolution (VR) curves (accuracy at different dot-line separations on visual resolution test) for parkinsonian (PD) and control groups. VR scores (top) represent the mean dot-line separations at and beyond which subjects correctly identified the dot as being off the line. Except for a shift to the right, the PD curve is essentially the same as the control curve. This lack of distortion is supported by differences in resolution between the two groups being significant only at dot-line separations of 0.71 ( $p < 0.01$ ) and 1.42 ( $p < 0.05$ ) min of arc (i.e., 1- and 2-pixel separation, respectively).

curred largely because resolution measured by the visual resolution test specifies the distance between the *centers* of two finite-size objects (i.e., dot and vertical line) in contrast to the *gap* between two objects, as is essentially the case with the Snellen chart. Thus, the resolutions measured on the visual resolution test are of *displacement* and, because the gap between the dot and line is less by 1.82 min of arc, subjects are able to detect a smaller gap on this than on the Snellen chart. Indeed, small displacements with zero gaps can be detected on the visual resolution test because subjects are able to perceive the dot "bulging" to one side of the line. This ability is enhanced by the different intensities of the dot and line. The issue is further complicated by the abrupt dark-light transitions on the Snellen chart (i.e., high spatial bandwidth) as compared with the less sharp intensity dropoff on either side of the dot and line on the oscilloscopic display. Resolutions measured by the Snellen chart are also likely to be advantageously biased owing to concomitant perceptual information in its alphabet characters (cf., illiterate E, Landolt's C, and visual resolution tests).

Our study apparently is the first to report impairment of high-contrast visual acuity in PD. This raises several questions. Could our finding be artifactual? Why have previous studies in which Snellen acuities were measured not reported similar deficits? What is the mechanism of reduced visual

acuity in PD? What is the significance of reduced visual acuity in PD?

The evidence that the difference in acuity between the PD and control groups is real is strong. The horizontal shift in visual resolution accuracy curves between PD and control subjects without concomitant distortion (Fig. 1) supports the view that the visual resolution test measures acuity and is not contaminated by any higher order visuospatial or perceptual dysfunction that may be present (22-24). The reduction in acuity as measured by the two quite independent and different tests was remarkably similar at 24 and 25%, and it is unlikely that some confounding factor would have biased both tests to such a similar degree. The matched-pairs experimental design and tight matching of age between the PD and control groups exclude the possibility that an age-related decrease in acuity (25) explains the difference. Similarly, the remote possibility that gender is involved was eliminated by matching.

Several studies showing deficits of low-contrast vision in PD have not demonstrated loss of high-contrast acuity using standard Snellen charts. There are several possible reasons. First, reduction in high-contrast acuity in PD is relatively subtle as compared with that in low-contrast acuity and sensitivity. Despite detection of substantial contrast sensitivity losses in several studies, evaluation of high-contrast acuity has been relatively crude. Visual acuity in PD has been regarded as normal if 6/9 or better (3), 7/10 or better (2), or within 2.5 SD from the control mean (4,6). Similarly, all subjects in our study had "normal" acuity of 6/9 or better when receiving medication (the acuity of one PD subject decreased to 6/12 when the subject was not receiving medication). Second, in other studies data have been considered case by case, rather than by grouping of subjects, using normal mean minus 2 SD (2,3,5) or SD (4,6) as the lower limit for normality. Although this is appropriate for detection of deficits in single patients, it is much less sensitive than statistical comparison of groups; e.g., enough of the raw Snellen chart data were presented in the study of Regan and Maxner (4) to allow us to gain a reasonable estimate of the difference in high-contrast (84% contrast) letter chart results between their age-matched PD group ( $n = 10$ ) and controls ( $n = 15$ ). A difference of 5.6% ( $t = 1.32$ ,  $df = 23$ ,  $p < 0.1$ ) was noted between the two groups on average acuity for right and left eyes. Even though loss of visual acuity was of borderline significance

only, this finding supports our view that subtle diminution of contrast acuity has existed in previous studies. Third, in several studies, PD subjects have had a substantially higher mean age than controls (3,6,16). Although contrast sensitivity has been shown to be largely independent of age (2,3,26), the same is not true of high-contrast acuity, which decreases appreciably with age, especially after 55 years (25). Thus, it is difficult to draw definitive conclusions from small differences in acuity in such studies. Fourth, although the relationship between visual acuity and contrast sensitivity is complex, in part because the stimuli in previous studies were luminance-modulated by rectangular and sinusoidal functions, respectively, acuity from the contrast sensitivity curve can be estimated by using spatial frequencies of the order  $\geq 30$  cycles/degree (cpd) (27). Most of the studies have, however, used upper spatial frequencies which were considerably less than this [e.g., 19.2 cpd (3), 12 cpd (2), and 2 cpd (4)] making detection of reduced acuity via the contrast sensitivity approach impossible.

From this study alone, it is not possible to suggest which part of the visual system is responsible for reduction in acuity in PD. Nevertheless, the reduction is likely to be part of the generalized loss of contrast sensitivity noted in PD that may reflect dopamine depletion in the retina (1-3,16). This is distinct from the notch loss observed superimposed on some contrast sensitivity curves, indicating selectively greater impairment in certain spatial frequency channels, which is presumed to reflect a cortical component in visual loss (2). Although the presence of oculomotor dysfunction is well established in PD, the most common abnormalities of hypometric saccades and impaired smooth pursuit (28-30) probably do not affect the ability to fixate as required in acuity tasks. Nystagmus is not a feature of this disorder, but there is evidence of involuntary "square wave jerks" (31), which are sporadic horizontal conjugate saccades away from the point of fixation. Because the occurrence of such saccades in PD is relatively low (31), our results probably cannot be attributed to impaired ocular fixation. Anticholinergic or other therapy probably was not the cause of diminished visual acuity in the present study because the tests did not require close fixation and there was no difference in the vision of those subjects receiving anticholinergics as compared with those not receiving anticholinergics. In addition, drug withdrawal did not alter the results significantly. We cannot be certain that the effect of

anticholinergics and amantadine had completely worn off after 24 h, but deterioration in the patients' parkinsonian state precluded longer drug withdrawal.

The presence of dopamine-containing neurons in both the retina (14,15,17,32,33) and visual cortex (19) has been well established by histobiochemical and other means. Likewise, considerable evidence exists for dopamine's active transmitter role in the visual pathways, as demonstrated by reduced visual function after administration of MPTP (15) and dopamine-receptor blockers (34). In addition, improvement in visual function has been reported after L-DOPA treatment (7,9,11,16). Therefore, it is of interest to question why no change in visual acuity was noted in the Parkinsonian subjects of the current study after discontinuation of their medication. This may have been because their neuronal reserves of dopamine were not depleted 24 h after last administration of L-DOPA. Alternatively, their dopamine receptors may have been less intact than in other studies in which patients were starting L-DOPA therapy for the first time (7,9,16).

The extent of the reduction in acuity in PD is relatively small. Although the mean acuity of the PD group was 25% less than that of the controls, at 6/6.58 it was only marginally worse than the often-quoted "6/6" average of the "normal population." Indeed, no subject was excluded from the study because corrected acuity was worse than 6/9 (for best eye and while receiving drugs); this is commonly considered an upper limit of normal acuity (2,3). Therefore, from the patients' view point, this slight loss of sharpness in their vision will usually be of minor consequence, especially when considered relative to coexisting motor and cognitive deficits. Even mild impairment of visual acuity could, however, have a significant effect on the results of studies in which clear vision is important, including studies of PD that have used a variety of tasks to assess visuoperceptual (22-24,35-39) and visuomotor functions (40-53). Many of these studies have produced conflicting results and, with the exception of those of one group of investigators (50,51), none have mentioned visual acuity. The integrity of the visual system cannot be taken for granted in PD, and future studies that depend on vision must take this into account.

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