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Impairment in preattentive visual processing in patients with Parkinson's disease

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Summary

We explored the possibility of whether preattentive visual processing is impaired in Parkinson's disease. With this aim, visual discrimination thresholds for orientation texture stimuli were determined in two separate measurement sessions in 16 patients with idiopathic Parkinson's disease. The results were compared with those of 16 control subjects age-matched and 16 young healthy volunteers. Discrimination thresholds were measured in a four-alternative spatial forced-choice paradigm, in which subjects judged the location of a target embedded in a background of distractors. Four different stimulus configurations were employed: (i) a group of vertical targets among horizontal distractors ('vertical line targets'); (ii) targets with varying levels of orientation difference on a background of spatially filtered vertically oriented noise ('Gaussian filtered noise'); (iii) one 'L' among 43 '+' signs ('texton'), all of which assess preattentive visual processing; and (iv) control condition, of one 'L' among 43 'T' distractors ('non-texton' search target), which reflects attentive visual processing. In two of the preattentive tasks (filtered noise and texton), patients with Parkinson's disease required significantly greater orientation differences and longer stimulus durations, respectively. In contrast, their performance in the vertical line target and non-texton search target was comparable to that of the matched control subjects. These differences were more pronounced in the first compared with the second session. Duration of illness and age within the patient group correlated significantly with test performance. In all conditions tested, the young control subjects performed significantly better than the more elderly control group, further indicating an effect of age on this form of visual processing. The results suggest that, in addition to the well documented impairment in retinal processing, idiopathic Parkinson's disease is associated with a deficit in preattentive cortical visual processing.

Keywords: Parkinson's disease; visual search; preattentive processing; stimulus orientation

Introduction

It is now well established that along with the primary motor signs of rigidity, tremor and akinesia, Parkinson's disease is associated with impaired visual function. This impairment is reflected by a loss of contrast sensitivity to visual stimuli defined by luminance (Bodis-Wollner *et al*., 1987; Bodis-Wollner, 1990; Mestre *et al*., 1990*a*, *b*; Masson *et al*., 1993; Tebartz Van Elst *et al*., 1997) and colour-contrast (Haug *et al*., 1995). Electrophysiological evidence of visual pathology has been related to delays in visually evoked potentials (Bodis-Wollner and Yahr, 1978; Delwaide *et al*., 1980; Gawel *et al*., 1981; Marx *et al*., 1986) and a reduced amplitude in the pattern-electroretinogram (Ghilardi *et al*., 1989; Ikeda *et al*., 1994; Langheinrich *et al*., 1998). Mechanisms selective to stimuli with medium-to-high spatial frequencies and medium temporal frequencies appear to be most affected (Marx *et al*., 1986; Bodis-Wollner *et al*., 1987). The stimulus-specific loss in contrast sensitivity is often taken as a sign of selective impairment in visual neurons with correspondingly sized receptive fields (Ikeda *et al*., 1994).

Dopamine is an important neurotransmitter in the visual pathway (Bodis-Wollner *et al*., 1987). The presence of dopamine in the mammalian retina has been well documented (Haggendal and Malmfors, 1963; Dowling and Ehinger, 1975; Massey and Redburn, 1987; Skrandies and Wässle, 1988), including the human retina (Frederick *et al*., 1982). In addition to the loss of dopaminergic neurons in the pars compacta of the substantia nigra, Parkinson's disease has been associated with a reduction in the level of dopamine in the retina (Harnois and Di Paolo, 1990). There is some evidence that dopamine might also act at synapses in the lateral geniculate nucleus (Papadopoulos and Parnavelas, 1990) and the visual cortex (Reader and Quesney, 1986; Parkinson, 1989). Such dopaminergic activity could be diminished in Parkinson's disease.

Although most studies have concentrated on visual function in the retina of Parkinson's disease patients, there have been scattered reports that higher visual function might also be impaired. An orientation-selective loss in contrast sensitivity has been demonstrated in patients with Parkinson's disease (Regan and Maxner, 1987; Bulens *et al*., 1988). Orientation selectivity is an attribute thought to arise first in the striate visual cortex, where receptive fields are tuned to a specific range of orientations (Hubel and Wiesel, 1962; Hubel and Wiesel, 1968; Hubel *et al*., 1977). Orientation-specific visual illusions and after-effects are assumed to be related to the processing of stimulus orientation and orientation differences in primary visual cortex (Blakemore and Campbell, 1969; Blakemore and Nachmias, 1971; Magnussen and Kurtenbach, 1980; Greenlee and Magnussen, 1988). Drugs that inhibit the uptake of dopamine at receptor sites can affect the magnitude of orientation illusions (Gelbtuch *et al*., 1986; Harris *et al*., 1986). In addition to sensitivity loss, patients with Parkinson's disease have also been shown to require more time to detect a vertically oriented bar among horizontal distractors (Troscianko and Calvert, 1993), an effect which could be related to cortical pathology in mechanisms involved in the coding of stimulus orientation.

Visual search for targets among distractors can be performed in parallel, implying that the time required to detect the presence of a target is independent of the number of distractors in the display (Treisman, 1982; Wolfe *et al*., 1990). This extraordinary performance of the visual system has been called preattentive 'pop-out', since the target is immediately salient, despite the fact that it is embedded in distractors. The role of attention in visual search tasks has been investigated earlier (for a review, see Palmer *et al*., 1993). These authors define preattentive vision as stimulus-driven, automatic processing, whereas attentive vision is conjointly affected by stimulus and voluntary processing factors. Preattentive vision is thought to have a large capacity, whereas attentive vision is limited in capacity. Palmer *et al*. (1993) formulate a signal-detection model of set size effects (i.e. effect of number of distractors on threshold). They conclude that set-size effects can be accounted for by changes occurring in the decision process.

Visual search appears to be altered in Parkinson's disease. Contrary to that found in age-matched controls (Treisman, 1982; Sagi and Julesz, 1985; Scinto *et al*., 1986), visual search time increases with increasing number of distractors in patients with Parkinson's disease (Troscianko and Calvert, 1993). This finding suggests that the preattentive processing of line orientation and 'orientation contrast' is disturbed in parkinsonian vision. The latter authors measured reaction times and found an overall increase in reaction time in patients with Parkinson's disease, in agreement with earlier work (Evarts *et al*., 1981; Brown and Marsden, 1991). Using reaction times as a dependent variable, however, has the disadvantage that impairments in visual processing could be confounded by several factors including motor symptomatology. We, therefore, designed a stimulus-response paradigm that allowed subjects to respond within a virtually unlimited time window. To establish the generalizability of the findings of Troscianko and Calvert (1993), we studied preattentive visual processing in Parkinson's disease with three different stimulus configurations ('vertical line target', 'filtered noise' and 'texton'; Fig. 1A–C) and introduced a control condition requiring attentive visual processing ('non-texton' search target; Fig. 1D). We compared test performance of the patients with that of 16 well-matched control patients. To establish the test–retest reliability of our results, a subgroup of patients with Parkinson's disease and control patients were re-examined after several days. To examine further the effect of ageing, we measured test performance in an additional control group of young healthy subjects. The results indicate that patients with Parkinson's disease are significantly impaired in preattentive visual processing, whereas attentive processing appears to remain intact. Furthermore, duration of illness and age within the patient group have a significant effect on test performance.

Material and methods

Stimuli and procedures

The visual stimuli were created on a PowerMac 7600 and displayed on a high-resolution colour monitor (17 inch; Eizo, Japan) at a frame rate of 75 Hz. Luminance was measured with a spot photometer (Minolta luminance meter) with an aperture of 1° and was 59 cd/m^2 for the line segments and 3.6 cd/m^2 for the background, resulting in a contrast of 88.5%. The filtered noise stimuli had a mean luminance of 47 cd/m^2 . Stimuli were presented at a distance of 114 cm, subtending 12° of visual angle. The visual angle of the target patch was 1.25°, presented 2° eccentric of fixation. The ambient light in the otherwise darkened room had an illuminance of ~10 lux.

The patients and control subjects viewed the stimulus display binocularly. They were comfortably seated in an examination chair and rested their head and arms on appropriately positioned rests. They were instructed to direct their gaze to the centre of the display, where the fixation cross was displayed during each trial. A four-alternative forced-choice paradigm was used, where the patients reported whether the target (Fig. 1A–D) appeared left, right, above or below the centre of the display. The subjects indicated their response by pressing the appropriate button on a response box. To assess the discrimination of line orientation, three stimulus configurations were presented in separate experiments. Each configuration consisted of a display containing a single target presented among distractors. These targets could be processed preattentively, i.e. without use of focal attention. The first target consisted of a patch of 4×4 vertical line segments on a background of horizontal line segments (Fig. 1A; vertical line target). The second target consisted of differentially oriented line segments on a background of vertically oriented line segments (Fig. 1B;

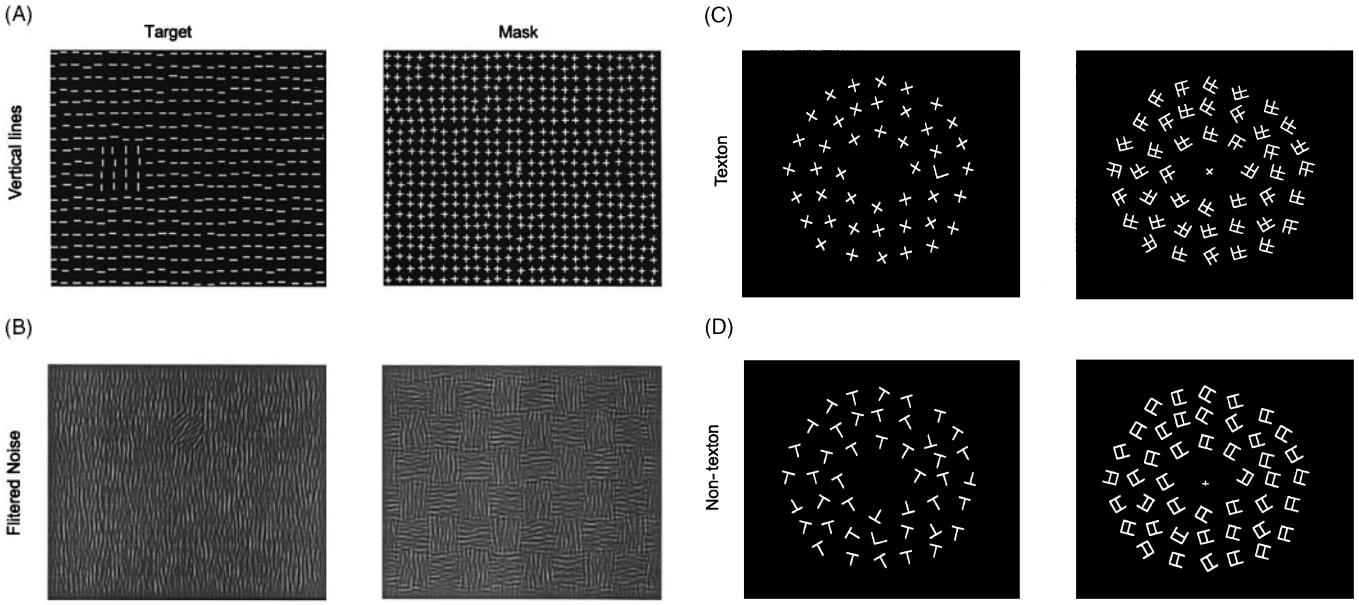

Fig. 1 Examples of the target and mask stimuli used in the present study: (**A**) vertical line target; (**B**) filtered noise; (**C**) 'L' among '+'s; (**D**) 'L' among 'T's. The appropriate mask is displayed for each type of stimulus.

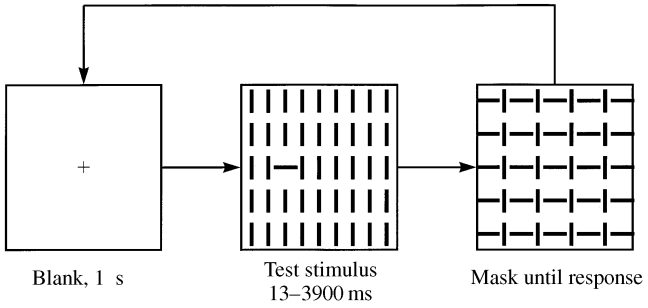

Fig. 2 Schematic illustration of a typical trial. Each trial began with the presentation of a fixation cross. The fixation cross was extinguished after 1 s and was followed by the presentation of the test stimulus. The stimulus duration was either fixed (for the filtered noise condition) or it was varied according to the Best-PEST predicted threshold estimate. Each test stimulus was followed by a mask, which was displayed until the subject made a response (button press).

filtered noise). The third target was a 'L' in a group of 43 '+' distractors (Fig. 1C; texton target). As a control experiment, subjects had to search for a 'L' in a group of 43 'T' distractors (Fig. 1D; non-texton target). This latter target is not processed in parallel, but has to be searched for by use of focal attention.

The time sequence of stimulus presentation is presented schematically in Fig. 2. Each trial started with a fixation interval of 1 s duration. Subsequently, the target stimulus appeared for a variable time interval (13–3900 ms, presentation time varied in integer frame durations, where 1 frame lasted 13 ms), which was followed by a mask. The mask was presented to suppress any after-image and to terminate visual processing of the stimulus display (Fig. 1). Stimulus duration for the filtered noise condition was held constant at 208 ms. Subjects responded by pressing one of the four response buttons. The response period was not limited in time, but we encouraged subjects to respond quickly. After the subject's response, the next fixation interval and target presentation followed immediately. The rate of trial presentation could thus be determined by each subject individually. Performance was quantified either as the threshold presentation time (targets given in Fig. 1A, C and D) or the threshold orientation difference required to locate the target correctly (Fig. 1B; cf. Nothdurft, 1992). As a quantitative psychometric procedure, we applied the Best-PEST algorithm (Parameter Estimation by Sequential Testing; Lieberman and Pentland, 1982) to estimate the thresholds. This procedure assumes that performance is a monotonically increasing function of stimulus intensity (or, in the present study, the stimulus duration or line orientation difference). The function describing the relationship between performance and stimulus intensity is called the psychometric function. For our task, stimulus duration (or orientation difference) was plotted on a logarithmic time (linear angle) scale, and the best fitting curve is a sigmoid logistic function (Fig. 3). It is a useful convention to define the threshold as the steepest point in the slope of the psychometric function, which is at its half height. With four alternatives, the guessing rate is 25%, and the threshold is set at 62.5% correct. The Best-PEST procedure uses a maximum likelihood criterion for determining the stimulus intensity of the next trial. The results of all preceding trials are accumulated to calculate the presentation time (orientation difference) that is the most likely estimate of the putative threshold. Presentation of stimulus durations or intensities at or near this current threshold estimate will maximally increase the information regarding the 'true' threshold position. Based on pilot experiments, 32 trials for each target were presented while the Best-PEST 'homed in' on the threshold (see Fig. 3). To motivate the subjects, every fourth presentation was a 'bonus

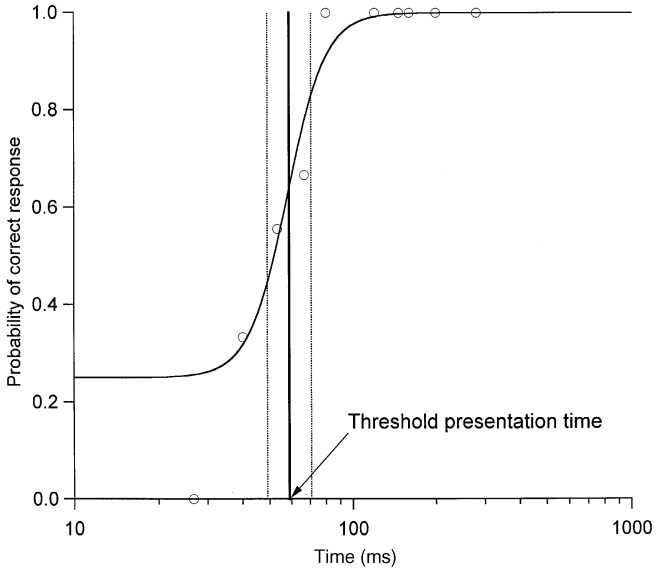

Fig. 3 Example of the psychometric function fit to the probability of a correct response as a function of the stimulus duration (on log scale). The S-shaped function is the cumulative normal logistic function and the solid vertical line intersects this function at its steepest point. This point corresponds to the Best-PEST estimate of the threshold. The dotted lines show ±1 SE of this estimate.

trial', where the presentation time (orientation difference) was three times the current threshold estimate. Performance on these trials did not enter into the Best-PEST estimate procedure. Thresholds were determined for each of the targets in an interleaved block-design and the test sequence was randomized across subjects. Rest periods of 1 min in duration were given between each experimental block.

Subjects

All subjects were recruited consecutively from the in-patient clinic of the Neurology Department at the University of Freiburg, Germany. They were first informed about the general aims of the investigation. Participation was strictly on a voluntary basis and only occurred after informed consent was given. Approval to study patients with psychophysical experiments was obtained from the local ethical board of the University of Freiburg. Any additional CNS or eye disease or the diagnosis of a possible (or probable) multiple system atrophy led to exclusion from the study. The ward consultants, who were uninformed as to the specific aims of the study, made the clinical diagnoses.

A total of 16 patients with idiopathic Parkinson's disease and 16 age-matched control patients with other neurological disorders not affecting the CNS participated. Of the control patients, five suffered from a disc prolapse; two from a pain syndrome of the hand or foot; three from peripheral polyneuropathy; one from a spinal form of multiple sclerosis; one from post-surgical peripheral nerve lesion; one from an asymptomatic stenosis of carotid artery and three with diffuse complaints. As a further control group, 16 young subjects without any neurological or psychiatric disorders were investigated. As shown in Table 1, patients with Parkinson's disease and the control patients were carefully matched for age, education, handedness, visual acuity [Landolt C discrimination, as determined by the Freiburg Visual Acuity Test (Bach, 1996); range 0.8–1.6 in both groups]. Contrast sensitivity was determined using a low contrast version of the Freiburg Visual Acuity Test (Table 1). Significant differences were found between the Parkinson's disease patients and the young control subjects (*post hoc* Bonferroni/Dunn, $P < 0.01$), as well as between the age-matched controls and the young controls ($P < 0.02$). The difference in contrast sensitivity between the Parkinson's disease patients and the age-matched controls was not significant. Eleven male and five female patients with Parkinson's disease were tested. Mean time since first diagnosis of Parkinson's disease was 7.8 (SD = 7.0) years (range 1–24 years). Thirteen of the Parkinson's disease patients and 10 of the control patients were retested after 14.5 (SD = 10.0) days or 4.3 (SD = 2.2) days, respectively. The severity of the disease was calculated by the ward consultant prior to the investigation by using the motor scale of the Unified Parkinson's Disease Rating Scale. Parkinson's disease patients and control patients did not differ in performance on Digit Span (taken from the Wechsler Memory Scale, Wechsler, 1987) at the first and second investigation (Table 1). Six Parkinson's disease patients were untreated at the time of the first investigation and were retested after introduction of L-dopa therapy.

Autobiographical and screening test data are shown in Table 1: age, gender, education (as calculated by the sum of years of education), handedness (as determined by the Edinburgh Handedness Inventory (Bryden, 1982), visual acuity and contrast sensitivity, digit span performance and test–retest interval. Clinical data for the patients are summarized in Table 2, which consisted of illness duration, severity of motor symptoms (as determined by the Unified Parkinson's Disease Rating Scale) and medication (nominal scale).

Data analyses

Data were analysed using ANOVA (analysis of variance) for repeated measures either on the raw values (stimulus duration, orientation difference) or on the standard score (*Z*-score) normalized thresholds. The main effects and interactions were determined for the following factors: group (Parkinson's disease patients, matched control patients, young control subjects), type of target (three line orientation targets, one non-texton target), and time of investigation (first and second investigation). Significant findings were further analysed with the *post hoc* Bonferroni/Dunn test. Age, gender, education, duration and severity of disease, medication, visual contrast sensitivity and acuity were correlated with the dependent variables by regression analysis.

Table 1 *Autobiographical and screening test data for all subjects*

	Parkinson's disease patients	Controls	Young controls
Number	16	16	16
Age (years ± SD)	64.5 ±5.7	64.4 ± 7.2	23.1 ± 3.3
Gender (male/female)	11/5	7/9	6/10
Education (years ± SD)	11.3 ± 3.5	11.3 ± 3.6	15.9 ± 3.1
Handedness (right/left)	16/0	16/0	16/0
Visual acuity ± SD	1.1 ± 0.2	1.1 ± 0.2	1.4 ± 0.3
Contrast sensitivity ± SD	70.4 ± 46.3	99.1 ± 52.6	154.4 ± 61.7
Digit span (1./2. Version)			
Test	5.5 ± 1.3/4.3 ± 1.3	5.4 ± 1.0/4.4 ± 1.2	6.4 ± 0.7/5.7 ± 0.6
Retest	5.8 ± 1.1/4.8 ± 1.1	6.1 ± 1.3/4.8 ± 1.4	
Test–retest interval (days ± SD)	14.5 ± 10.0	4.3 ± 2.2	

Table 2 *Clinical data for the 16 Parkinson's disease patients*

	Test	Retest
Mean illness duration (years ± SD)	7.8 ± 7.0	6.7 ± 8.0
Mean UPDRS* score (motor part)	37.5 ± 17.2	29.8 ± 14.1
Medication (no. of patients)		
0: neither LD† nor DA‡	6	0
1: <375 mg LD or DA only	0	3
2: 375–500 mg LD or <375 mg LD and DA	5	5
3: 500–750 mg LD or <500 mg LD and DA	2	4
4: >750 mg LD or <750 mg LD and DA	3	4
Medication (code ± SD)	1.8 ± 1.5	2.5 ± 1.2

*UPDRS = Unified Parkinson's Disease Rating Scale, a scale to assess disease severity; †LD = L-dopa; ‡DA = dopaminergic agonist.

Results

Test performance during the first session

ANOVA using normalized threshold values (standard scores) was performed to assess the effects of patient group and the (repeated measure) target type. The mean threshold values are presented in Fig. 4A–D. The main effect for group was significant [$F(2,47) = 34.1$, $P < 0.0001$]. *Post hoc* pairwise comparisons (Bonferroni/Dunn) showed that the thresholds of the Parkinson's disease patients were significantly higher than those of the age-matched and young control patients, and thresholds of the young control subjects were significantly lower than those of the older control patients. The main effect of target type was highly significant for the non-standardized raw threshold times [$F(2,4) = 187.2$, $P < 0.0001$]: threshold presentation time in the non-texton condition was 2.5 times higher than that found for the texton condition, while the threshold time for the Line Target task was 4.5 times lower than that found for the texton condition. There was a significant interaction term between the main effects of group and target type [$F(6,141) = 2.9$, $P < 0.01$], where the Parkinson's disease patients showed a significant effect for the filtered noise and texton conditions (Fig. 4B and C) but no significant effect for the vertical Line and non-texton conditions (Fig. 4A and D). *Post hoc* Bonferroni/Dunn analyses revealed that not only the different performance in detection of texton targets, but also in detection of targets in the filtered noise condition accounted for this main interaction. Given the fact that the filtered noise target and vertical line target are not directly comparable to the non-texton search targets, we also calculated main effects and the interaction term for texton versus non-texton targets separately, which were statistically significant: main effect for patient group, [$F(2,47) = 28.9$, $P < 0.0001$]; main effect for Target Type [$F(1,2) = 122.9$, $P < 0.0001$]; interaction term Group × Target Type [$F(2,47) = 7.5$, $P < 0.002$]. *Post hoc* paired comparisons revealed highly significant differences between the young and old control subjects ($P < 0.001$) as well as between the patients with Parkinson's disease and the age-matched control subjects ($P < 0.02$).

Test–retest: stability and reliability

We analysed performance of Parkinson's disease and control patients on two different days to investigate whether the effects are stable across time, vary with clinical improvement or change due to learning effects. Thirteen of the Parkinson's disease patients and 10 of the control patients were investigated twice within a period of 14.5 (SD = 10.0) days and 4.3 (SD = 2.2) days, respectively. ANOVA of performance at the second investigation with patient group

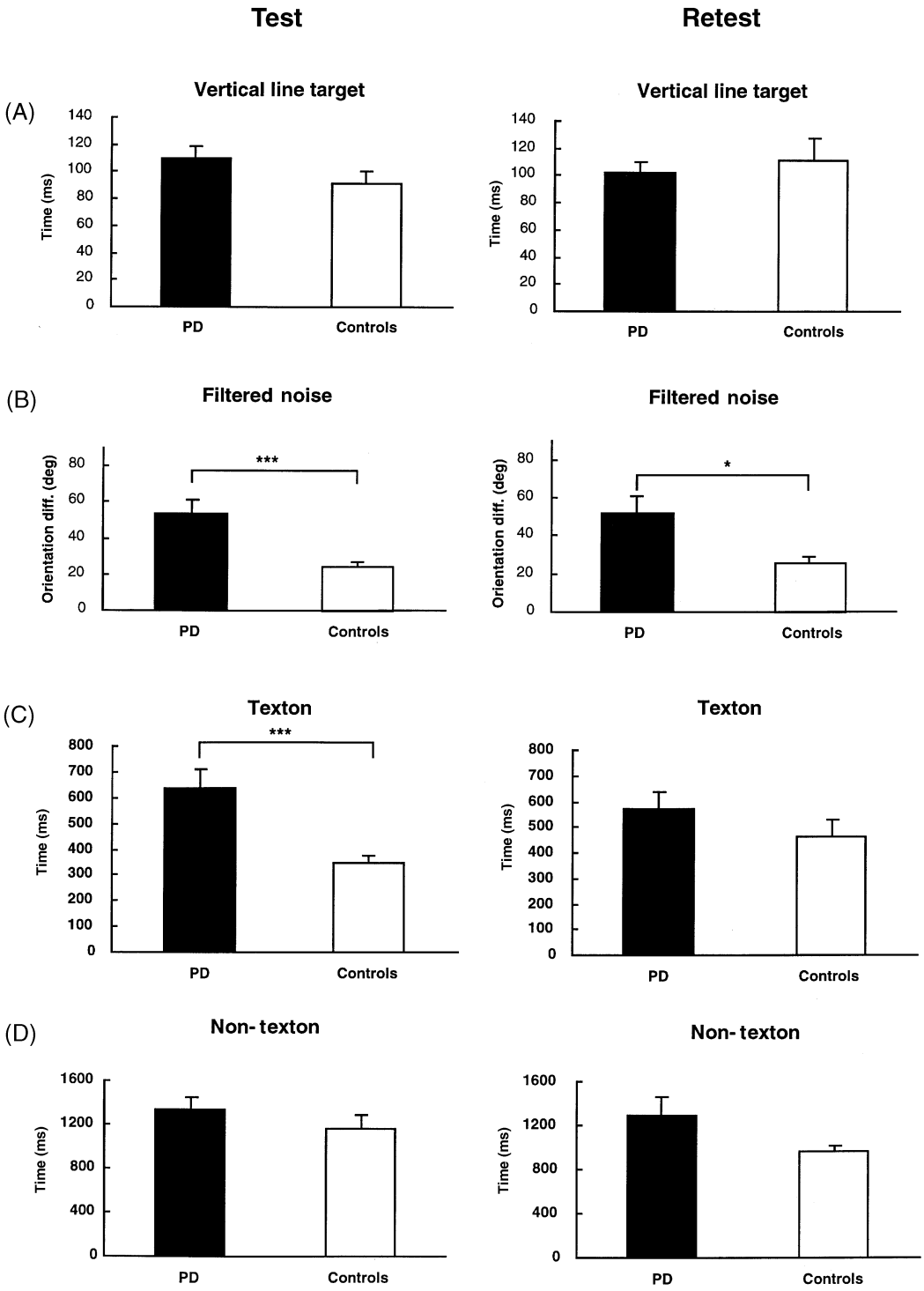

Fig. 4 Mean threshold presentation times or threshold orientation difference for patients with Parkinson's disease (PD) or the age-matched control subjects (Controls). The values for the first test session are shown in the panels on the left and those for the retest are shown in the panels on the right. Results are shown for the condition with (**A**) the vertical line target, (**B**) filtered noise, (**C**) texton and (**D**) non-texton target stimuli. Error bars show +1 SE of the mean and the significance level is denoted by asterisks (*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$).

and target type as independent variables revealed again significant main effects for patient group [$F(1,23) = 7.5$, $P < 0.01$] and target type [$F(3,69) = 4.0$, $P < 0.01$]. There was also a significant interaction term between the main effects of patient group and target type [$F(3,69) = 2.9$, $P < 0.05$]. *Post hoc* analyses for the second investigation revealed that the performance in the detection of targets in the filtered noise condition accounted for this interaction,

with Parkinson's disease patients showing significantly higher thresholds for the detection of such targets than control patients ($P < 0.05$). In contrast to the first investigation, performance in the detection of texton targets was no longer statistically significant between Parkinson's disease and control patients.

We analysed the data further to check whether the test performance of Parkinson's disease patients or control patients improved in the second investigation compared with the first, e.g. due to learning effects. ANOVA with time of investigation and target type as variables did not show any statistically significant differences between the first and second investigation for both patients with Parkinson's disease and the control patients. Although threshold values for the detection of all targets decreased in the Parkinson's disease patients (though not statistically significant), test performance of control patients became worse (however, again not statistically significant) in all tests with the exception of detection of non-texton targets. Performance in the texton target detection task was no longer significantly different at retest. This lack of difference is probably related to the decline in performance of the control patients at retest.

A further important aspect of the results is related to their test–retest reliability. Since there was considerable variability in the results of the patients with Parkinson's disease, we could correlate the results for the first and second measurement session to assess the amount of common variance. This analysis was performed on the mean results for each patient separately (*Z*-scores averaged over conditions). The resulting correlation coefficient was $r = 0.884$, so that 78.1% of the variance is common in the two measurements.

Correlation with clinical course and effect of medication

The patients varied with respect to the duration and severity of their illness and also with respect to medication. We sought to explore a possible relationship between these inter-individual differences among the Parkinson's disease group. Table 2 presents the mean and standard deviations of the duration of illness and the scores on the Unified Parkinson's Disease Rating Scale, as well as a description of the medication taken at the time of study (nominally scaled from 0–4 according to the criteria listed in the table). Although there was a tendency for the performance to decline with increasing medication score, this trend was not significant [$F(4,20) = 1.92$; ns].

We used the Unified Parkinson's Disease Rating Scale to describe the extent of disability caused by the disease. The motor part of this rating scale was administered during the first and second session prior to the experiments. During the time period between measurement sessions, the clinical status of Parkinson's disease patients improved to some extent, but this improvement was not significant. The mean score was 37.5 (SD = 17.2) at the first and 29.8 (SD = 14.1) at the second investigation. The results of either measurement did not correlate with test performance. There was, however, a significant correlation between test performance and the amount of time elapsing since the initial diagnosis, as well as between test performance and the patient's age (Fig. 5A–D): thresholds in the filtered noise condition and threshold presentation times for vertical line targets positively correlated with the time elapsing since first diagnosis (Fig. 5C and D) while thresholds for filtered noise and non-texton targets correlated with age (Fig. 5A and B). These results indicate that a significant amount of the within-group variance can be accounted for by person-related variables such as age and illness duration. Significant negative correlations were also found between time thresholds in the texton task and visual acuity (Fig. 5E), as well as between thresholds in the vertical line target task and contrast sensitivity (Fig. 5F).

Performance of young control subjects

We also investigated the test performance of a group of young physically and psychologically healthy subjects. As shown in Table 1, compared with the older control subjects, these subjects had a higher visual acuity [$F(1,30) = 9.4$; $P < 0.005$] and higher contrast sensitivity [$F(1,30 = 7.2$; $P < 0.012$]. They also had higher educational levels. The young control subjects exhibited significantly lower time thresholds and required less orientation difference in the red noise condition compared with the more elderly control group. The main effect of control group (young versus older controls) was highly significant [$F(1,30) = 5.7$, $P < 0.0001$], as was the interaction term between control group and target type [$F(7,159) = 14.3$; $P < 0.0001$].

Discussion

The present results indicate that the processing of orientation differences is significantly impaired in Parkinson's disease. Significant differences were found between patients with Parkinson's disease and age-matched control patients (without CNS disorders) on tasks requiring the preattentive processing of orientation differences. Single-unit recordings in cats (Nothdurft and Li, 1985), in monkeys trained to make perceptual discriminations (Knierim and Van Essen, 1992; Lamme, 1995; Lamme *et al*., 1998), and electrophysiological recordings in human subjects (Bach and Meigen, 1992) indicate that this processing could be occurring in primary visual cortex. However, higher visual areas are certainly also involved, especially those contributing to the processing of object characteristics such as shape, texture and colour. In macaques, area V4 has been shown to be important in the processing of figure-ground segmentation (Schiller and Lee, 1991; Merigan, 1996). In humans, lesions in the fusiform and lingual cortex lead to a disturbance in colour perception (Zeki, 1990), but also appear to disturb pattern discrimination and second-order spatial perception (Cowey and Heywood,

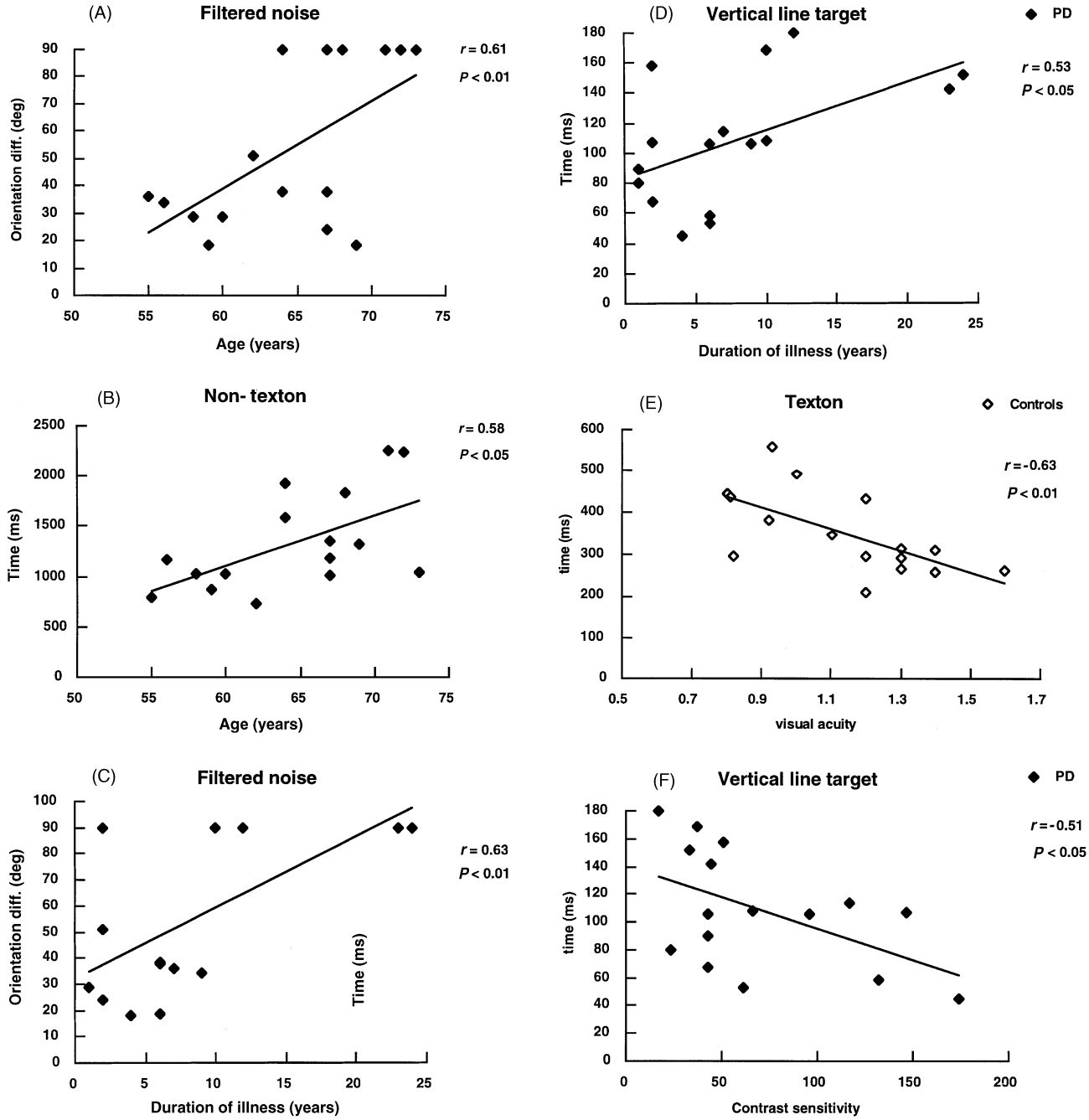

Fig. 5 Scatterplots depicting the correlation between test scores and important person-related data for Parkinson's disease patients (filled diamonds) and controls (open diamonds): (**A**) correlation between the threshold orientation difference in the filtered noise condition and the patients' age; (**B**) correlation between threshold presentation time and age for the non-texton condition in patients; (**C**) correlation between threshold orientation difference in the filtered noise condition and the illness duration; (**D**) correlation between the threshold presentation time and illness duration for the vertical line target; (**E**) correlation between the threshold presentation time and visual acuity in the age-matched control subjects for the texton condition; (**F**) correlation between threshold presentation time and contrast sensitivity in the patients with Parkinson's disease for the vertical line target.

1995; Merigan *et al*., 1997). Although caution should be taken when comparing the results of lesion studies in macaques and human subjects (Merigan, 1993), ventral extrastriate regions in the human brain do appear to be involved, among other functions, in the processing of orientation texture. Our results suggest that the preattentive processing of second-order spatial information, such as that derived from orientation differences in texture configurations, might be disturbed in patients with Parkinson's disease.

There are, however, several possible confounding factors that need to be considered before any conclusions can be drawn from such results. The effects of the ocular media could affect performance to an unknown extent. In a recent study, we have demonstrated how lens opacification can

mimic the effects of neurodegenerative diseases on the pattern-ERG (Langheinrich *et al*., 1998). The present group of parkinsonian patients represents a careful selection, so that the patients and controls were matched not only on age, but also on visual acuity and contrast detection thresholds (Table 1). Indeed, the negative correlations between thresholds and visual acuity and contrast sensitivity (Fig. 5E and F) point to the importance of early visual factors on performance. The stimuli used in the present study were also designed so that all subjects could easily see the patterns, given a sufficiently long stimulus duration. It is important to note that the patients were not impaired on all of our tests. Results of the vertical line target and the non-texton conditions did not significantly differ between the patients and age-matched controls (Fig. 4A and D). Contrast attenuation resulting from dense ocular media would impair subsequent processing in all of the conditions tested. Visual search based on the patchwise analysis of orientation texture was significantly impaired in the patients studied here (Fig. 4B and C), suggesting a site beyond the retina and lateral geniculate nucleus. To discriminate an oriented patch of visual noise from an otherwise homogeneously textured background, the patients with Parkinson's disease required orientation differences in the order of 50°, compared to a mean threshold of 25° for the controls. Such an impairment in low level visual function will most certainly have consequences for vision in everyday circumstances. The pattern of results therefore suggests a neural impairment rather than a defect related to the optics of the eye.

Another obvious problem involved in the testing of higher visual function in Parkinson's patients is related to task difficulty. We think it is crucial that the experiments are designed in such a way that the patients have a fair chance at scoring well on the test in question. With this goal in mind, we used a four-alternative forced-choice paradigm guided by the Best-PEST search algorithm (Lieberman and Pentland, 1982) to assess threshold presentation times. The Best-PEST efficiently samples performance, as it adapts to the individual performance of each subject, thereby avoiding ceiling or floor effects and minimizing total measurement time. Furthermore, the Best-PEST technique can provide confidence limits for the threshold estimate. This leads to a more robust and rapid estimate compared with the method of constant stimuli that requires the experimenter to make assumptions about where thresholds lie. The high test–retest reliability ($r = 0.884$) further suggests that the results acquired with this method are highly reliable.

A further hazard involved in the testing of higher visual function in Parkinson's disease patients is related to age. It is well established that normal ageing affects the visual system at several levels beginning with the optics of the eye and ending with cortical processing (Owsley *et al*., 1983; Werner *et al*., 1990). To assess the overall effect of age, we tested an additional group of young healthy volunteers. The results of these tests indicate that the young control subjects required by far the lowest presentation duration or threshold difference in orientation. This finding suggests that age alone affects our ability to discriminate preattentively between patterns of different orientation. Such an age effect should be kept in mind when evaluating the effects of pathology on higher visual processing. The significant correlation between illness duration and test performance suggests that, in addition to the age of the patient, the illness duration and course can further affect performance in visual discrimination tasks.

The present results extend those of Troscianko and collaborators (Troscianko and Calvert, 1993; Weinstein *et al*., 1997) who found an impairment in the parallel processing of 'pop-out' stimuli in Parkinson's patients, but no differences for tasks requiring serial search. Contrary to that earlier work, we did not find a significant performance difference on the vertical line target task, for which Troscianko and Calvert (1993) did find a difference. Although we have no simple explanation for these differences, it should be pointed out that the stimuli used in the two studies differed along a number of dimensions.

In conclusion, the present results suggest that preattentive visual processing of stimulus orientation and orientation texture is impaired in patients with Parkinson's disease. The findings thus suggest that not only the retina but also striate and extrastriate visual cortex are affected by this neurodegenerative disease. As such, the results provide an important extension to earlier findings on the visual pathology associated with Parkinson's disease.

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