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Visual and spatial symptoms in Parkinson's disease

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Abstract

The interaction of visual/visuospatial and motor symptoms in Parkinson's disease (PD) was investigated by means of a 31-item self-report questionnaire. The majority of 81 non-demented patients reported problems on non-motor tasks that depended on visual or visuospatial abilities. Over a third reported visual hallucinations, double vision and difficulty estimating spatial relations. Freezing of gait was associated with visual hallucinations, double vision and contrast sensitivity deficits. Visual strategies frequently were employed to overcome freezing. The results underscore the importance of investigating visual and visuospatial impairments in PD and their relation to motor symptoms, in order to help patients develop successful compensatory strategies.

Keywords: Parkinson's disease; Vision; Spatial; Hallucinations; Freezing of gait

1. Visual and spatial symptoms in Parkinson's disease

Parkinson's disease (PD) is a progressive neurodegenerative disorder that is characterized by the death of dopaminergic neurons in the substantia nigra pars compacta and resulting functional changes that involve all components of the fronto-thalamo-striatal circuit. Traditionally, PD has primarily been conceptualized as a motor system disorder. However, in recent years, it has become recognized that besides affecting motor functioning, PD has an impact on sensation and perception (Amick, Cronin-Golomb, & Gilmore, 2003; Bodis-Wollner et al., 1987), cognition (reviewed in Cronin-Golomb & Amick, 2001; Waterfall & Crowe, 1995) sleep (Garcia-Borreguero, Larrosa, & Bravo, 2003) and emotional functioning (Oertel et al., 2001). Because the several symptoms of PD have the same fundamental etiology related to the basal ganglia, it may be expected that there exist reciprocal associations between symptom components. It is of interest to examine how visual and spatial deficits impinge upon daily activities in PD and to investigate the relations between visual and spatial problems and motor symptoms in PD.

1.1. Visual and spatial impairment in PD

Self-report measures of visual and spatial deficits in PD support laboratory measurements, as patients report difficulties related to perception of space in questionnaire surveys (Lee & Harris, 1999; McDowell & Harris, 1997b). PD patients report problems such as bumping into doorways and difficulties with navigation around their environment in everyday life (Lee & Harris, 1999). Visuospatial problems in PD are likely caused by compromised functional basal ganglia loops that include the posterior parietal cortex (Middleton & Strick, 2000), given the role of this area in spatial abilities (e.g. Cronin-Golomb & Amick, 2001). Basal ganglia impairment may directly influence spatial cognition (Fimm et al., 2001; Karnath, Himmelbach, & Rorden, 2002) and dopaminergic depletion in peripheral visual

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structures in PD (Harnois & Di Paolo, 1990; Nguyen-Legros, Harnois, Di Paolo, & Simon, 1993) may influence performance on tasks that rely on visual abilities. Basic visual processes that are affected in PD include spatial contrast sensitivity (Amick et al., 2003; Bodis-Wollner et al., 1987; Bulens, Meerwaldt, & van der Wildt, 1988; Bulens, Meerwaldt, van der Wildt, & Keemink, 1986; Pieri, Diederich, Raman, & Goetz, 2000; Regan & Maxner, 1987; Trick, Kaskie, & Steinman, 1994), color discrimination (Diederich et al., 1998; Haug, Trenkwalder, Arden, Oertel, & Paulus, 1994; Pieri et al., 2000) and oculomotor control (Crevits & De Ridder, 1997; Shibasaki, Tsuji, & Kuroiwa, 1979; White, Saint-Cyr, Tomlinson, & Sharpe, 1983).

Investigation of higher-order cognitive abilities in PD has demonstrated impaired performance on tasks that depend on visuospatial processing (see review by Cronin-Golomb & Amick, 2001). PD adversely affects the perception of space (Harris, Atkinson, Lee, Nithi, & Fowler, 2003; Lee, Harris, Atkinson, & Fowler, 2001), ability to mentally rotate in three dimensions (Amick, Schendan, Ganis, & Cronin-Golomb, submitted for publication; Lee, Harris, & Calvert, 1998; Lee et al., 1998), visuospatial problem solving (Cronin-Golomb & Braun, 1997) and spatial working memory (Owen et al., 1993). In addition, PD patients frequently report visual hallucinations in the absence of dementia or impaired insight (Fenelon, Mahieux, Huon, & Ziegler, 2000). Impaired performance on visuospatial tasks in PD (Maeshima, Itakura, Nakagawa, Nakai, & Komai, 1997) and deficits in color discrimination (Diederich, Raman, Leurgans, & Goetz, 2002) are associated with level of motor functioning and difficulties performing activities of daily living.

1.2. Disturbances of posture and movement in PD

The classic cardinal symptoms of PD are resting tremor, bradykinesia, rigidity and disturbances of posture and gait. To some extent, these symptoms may have separate neurological substrates, even comprising areas beyond the frontostriatal circuit (Bartels et al., 2003; reviewed in Hallett, 2003). Vision affects postural mechanisms (Paulus, Straube, & Brandt, 1984) and visual impairment is a risk factor for a propensity for falling in the general population (Ivers, Cumming, Mitchell, & Attebo, 1998). Schaafsma et al. (2003) found that postural control and abnormal gait in PD contribute to the risk of falling, whereas the extent of tremor, rigidity and bradykinesia do not. Wood, Bilclough, Bowron, and Walker (2002) reported that 82% of 109 fallers with PD had reduced visual acuity, compared with 66% of non-fallers.

Postural problems in PD include instability and abnormal lateral and anterior–posterior body sway (Bloem, Beckley, & van Dijk, 1999) as well as difficulty turning (Lakke, 1985). Besides being influenced by vision, posture is under vestibular and somatosensory control (Day, Steiger, Thompson, & Marsden, 1993; Isableu, Ohlmann, Cremieux, & Amblard, 1997; Paulus et al., 1984). It has been suggested that PD involves a generalized dysfunction of sensorimotor integration and proprioception, a result of impaired basal ganglia functions that relate to processing and integrating sensory input to organize and guide movement and posture (Schneider, Diamond, & Markham, 1987). Indeed, PD patients are known to have difficulty integrating proprioceptive and visual information on postural challenges (Bronstein, Hood, Gresty, & Panagi, 1990) and when performing pointing tasks (Adamovich, Berkinblit, Hening, Sage, & Poizner, 2001).

The basal ganglia are important for kinesthesia, the perception of motion and direction of movements (Maschke, Gomez, Tuite, & Konczak, 2003). Not surprisingly given their basal ganglia dysfunction, PD patients experience reduced kinesthetic feedback (Demirci, Grill, McShane, & Hallett, 1997; Jobst, Melnick, Byl, Dowling, & Aminoff, 1997; Maschke et al., 2003). PD patients' increased reliance on visual guidance or feedback is well documented (Azulay, Mesure, Amblard, & Pouget, 2002; Bronstein et al., 1990; Connor & Abbs, 1991; Cooke, Brown, & Brooks, 1978; Maurer et al., 2003). The extent of such visual dependence becomes magnified in complex tasks in which visual control is used to manipulate posture (Azulay et al., 2002). Bronstein et al. (1990) and Azulay et al. (1999) have suggested that increased visual dependence in PD may serve as a compensatory mechanism for reduced kinesthetic feedback. In healthy individuals, increased reliance on vision may be sufficient to compensate for impaired proprioception. However, it is likely that individuals whose visual functioning is unreliable will present with even more exaggerated disturbances of posture and gait.

Among common gait disorders in PD are episodes of transient motor blocks (freezing) and reduced stride length, which is accompanied by festinating gait (Giladi, 2001). Visual sensory input may trigger the onset of freezing episodes in PD as well as often being of help in overcoming them. Visual input that commonly initiates freezing episodes includes approaching an obstacle in the path or entering narrow spaces such as doorways (Fahn, 1995). Martin (1967) described the effectiveness of various visual aids in compensating for gait difficulties in parkinsonism. It is now evident that conditions that trigger the onset of freezing (Nieuwboer et al., 2001) as well as the usefulness of visual tricks (Kompoliti, Goetz, Leurgans, Morrissey, & Siegel, 2000; Stern, Lander, & Lees, 1980) and extrinsic visual cues in overcoming freezing episodes in PD (Azulay et al., 1999) are highly idiosyncratic. Giladi et al. (1992), Isableu et al. (1997) and Azulay et al. (1999) have

attributed inconsistencies in the effectiveness of visual cues to compensate for gait and postural abnormalities to individual differences at the perceptual rather than at the motor level. Individual characteristics that contribute to episodes of freezing and affect the effectiveness of compensatory strategies have not been investigated in PD. Mestre, Blin, and Serratrice (1992) reported increased spatial contrast sensitivity in a nonparkinsonian patient with primary progressive freezing of gait. However, PD is usually associated with decreased spatial contrast sensitivity (Amick et al., 2003; Bodis-Wollner et al., 1987).

It is of interest to investigate PD patients' subjective evaluation of their visual and spatial problems and to determine how these problems may interact with motor symptoms. Impaired basic-level visual functioning may affect one's ability to make full use of the visual information that is needed to interact with the dynamic environment and to successfully engage in everyday activities. In light of the relations between visual mechanisms and posture and gait, multiple interactions would be expected between visuospatial and motor disturbances in PD. The present study aimed to describe self-perceived visual and visuospatial problems in PD and their relation to several aspects of motor performance.

2. Method

2.1. Participants

2.1.1. Demographics and motor disability

There were 81 PD patients who volunteered to participate in the study. Sixty-nine percent of participants were men ($n = 56$), which reflects the higher rate of PD for men than women (Van Den Eeden et al., 2003). Participants' mean age was 63.8 years (SD 10.3; range 37–84). Mean disease duration was 7.2 years (SD 4.8; range 0.5–22) and the median Hoehn and Yahr (H&Y) stage of motor disability was 2 (range 1–3) (Hoehn & Yahr, 1967). One patient was stage 1, seven participants were stage 1.5, 40 were stage 2 and 33 were stage 3. In the case of participants who were referred from neurology clinics, their most current H&Y score was obtained from their neurologist ($n = 25$). For other participants ($n = 56$), a H&Y score estimate was based on responding to key questions on the motor section of the questionnaire.

2.1.2. Medications

Participants were asked to provide information on their use of medications. The majority of participants used dopamine agonists or levodopa (62.5% and 67.5%, respectively). Thirty percent used monoamine oxidase inhibitors and 25% reported using catechol-O-methyltransferase inhibitors. Twenty percent of participants used antidepressants and 15% sleep medications.

2.1.3. Side of motor symptom onset

Participants were asked to indicate on which side of the body their motor symptoms started. Equal numbers of participants (35) indicated that the motor symptoms started on their left side and on their right. Three respondents indicated bilateral onset of symptoms and side of symptom onset was unknown for 8 individuals. Side of motor symptom onset was considered a potentially important variable in the study because it has been found to affect perception of space in PD patients (Harris et al., 2003; Lee et al., 2001), and unilateral basal ganglia lesions cause contralateral postural deficits (Labadie, Awerbuch, Hamilton, & Rapesak, 1989; Ungerstedt & Arbuthnott, 1970).

2.1.4. Dementia and depression assessment

A Mini-Mental State Examination score (MMSE) (Folstein, Folstein, & McHugh, 1975) was available from 34 participants who recently had engaged in other research projects within the laboratory. The mean MMSE score was 28.7 (SD 1.1; range 26–30), indicating absence of dementia. Age, duration of PD and degree of motor impairment were similar for these participants and those whose MMSE scores were not available. Information on mood functioning (Beck Depression Inventory [BDI]; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) was available for 30 of the participants. The mean BDI score was 9.8 (SD 5.9; range 0–28). There were 23 participants with minimal level of depression (BDI range 0–14), 3 with mild depression (BDI range 14–19) and 4 with moderate depression (BDI range 20–28). Age, duration of PD and degree of motor symptom severity (H&Y) were similar for individuals with minimal depression and those with mild or moderate symptoms of depression.

2.1.5. Neuro-ophthalmological examination

Thirty-six of the 81 participants (44%) had recently undergone a detailed neuro-ophthalmological examination as a part of another research project within the laboratory and were determined not to have any ocular disease or other abnormalities. These individuals were similar to those who had not undergone such an eye exam in terms of disease duration, age and performance on all sections of the vision questionnaire. Accordingly, these two groups were collapsed into one group for data analysis.

2.1.6. Spatial contrast sensitivity and acuity

Recent measurements of spatial contrast sensitivity levels were available for 18 participants. These measurements

were performed with the Vistech Contrast Sensitivity Chart (Vistech Consultants, Dayton OH). A spatial contrast sensitivity level was determined for the spatial frequencies 1.5, 3, 6, 12 and 18 cycles per degree (cpd) with log sensitivity values of 1.77, 1.96, 1.83, 1.61 and 1.11, respectively. A Snellen eye chart was used to measure binocular visual acuity of these participants. All of them had corrected binocular visual acuity that was 20/32 (0.20 LogMAR) or better. Visual acuity of participants ranged from 20/16–20/32 (−0.10 to 0.20 LogMAR). The median acuity score was 20/20 (0.00 LogMAR).

2.2. Materials

The 31-item self-report questionnaire developed by Lee and Harris (1999) demonstrated presence of visual and spatial deficits in PD, along with inquiring about motor symptoms, and was therefore deemed an appropriate measurement tool for the goal of the present study. The questionnaire included four sections, developed in order to assess the nature and severity of motor, visual and spatial symptoms that PD patients experience. Questions were either structured or open-ended. In the process of the study, nine questions were added to the questionnaire to further estimate the extent of visuospatial problems. The first section of the questionnaire regarded background variables, including age, sex, prescription of medications and diagnoses of long-term illnesses. A second section on motor symptoms asked participants to respond to questions that concerned the kind and degree of motor symptoms they experienced and the extent to which medications alleviated those symptoms. The third section regarded visual and spatial perception. Participants were asked to indicate visual and spatial problems, including whether they had difficulties with estimating spatial relations or perceiving movement or if they had experienced visual hallucinations. In the case of endorsement of hallucinatory experiences, details were elicited, including frequency of visual hallucinations, form, duration and time of the day when they appeared. The additional nine items were structured questions concerning judging relations of objects, distances between objects, color perception and double vision. The fourth section consisted of open-ended questions in regard to how participants' daily activities were affected and which strategies they used to counteract difficulties.

2.3. Procedure

The participants were referred to the study by local neurology clinics or were recruited at local PD support group meetings. The participants completed the questionnaire in the laboratory, at support group meetings or at their home. All 81 individuals completed the 31-item questionnaire and 56 of them completed the additional nine items.

3. Results

3.1. Visual and visuospatial problems

The majority of PD patients indicated problems in visual and visuospatial functioning. The results revealed that 78% of participants endorsed at least one problem related to vision or visuospatial functioning. When problems that may to some extent have arisen from motor symptoms (bumping into objects and freezing in narrow spaces) were removed from the analysis, the proportion of participants who endorsed visual and spatial problems still reached 57%. Having endorsed at least one visual or visuospatial problem (first subgroup) vs. endorsing no such symptoms (second subgroup) was related neither to severity of motor impairment as estimated with H&Y score (Kolmogorov–Smirnov $Z = 0.96$, $p = .32$) nor to disease duration ($t = .93$, df[77], $p = .36$). The percentage of participants who endorsed specific visual and spatial problems is provided in Fig. 1. Forty-four percent of participants reported having consulted with a medical doctor about a visual problem (see Fig. 1). Having sought medical advice about vision problems was not associated with participants' age, H&Y score, duration of PD or age at PD onset.

Thirty-seven percent of participants reported visual hallucinations, generally consisting of images of animals or people. The images tended to last for several minutes and appeared in the afternoon or night. Seventy-six percent of participants who experienced visual hallucinations reported experiencing such phenomena five times a week or less and approximately a quarter reported fear upon seeing the images. Hallucinatory experiences (present vs. absent) were not associated with motor impairment as estimated by H&Y score (Kolmogorov–Smirnov $Z = 1.1$, $p = .18$) but there was a trend for association between having had such experiences and increased duration of PD ($t = 1.8$, df[77], $p = .077$).

There was no association between hallucinations and use of dopaminergic medications (levodopa, dopamine agonists). Those who experienced visual hallucinations were more likely to take sleep medications than those who did not hallucinate ($\chi^2 = 3.99$, df[1], $p < .05$), implying an association between hallucinations and sleep disturbances. Of motor symptoms, freezing was the only symptom that was significantly associated with experiencing of hallucinations ($\chi^2 = 5.27$, df[1], $p < .05$). Furthermore, hallucinatory experiences were associated with difficulty estimating spatial relations ($\chi^2 = 4.37$, df[1], $p < .05$), self-report account of frequently bumping into doorways ($\chi^2 = 5.51$, df[1], $p < .05$), and experiencing of double vision ($\chi^2 = 4.16$, df[1], $p < .05$). Those who experienced visual hallucinations were also more likely to have consulted a doctor about visual problems

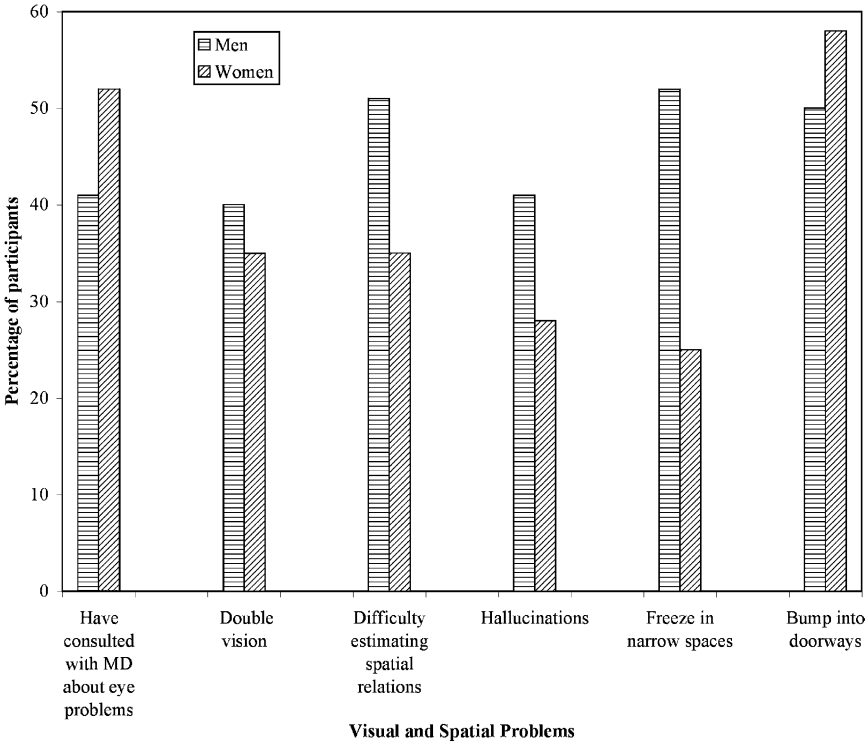

Fig. 1. Percentage of men and women with PD who endorsed visual or visuospatial problems. $N = 81$ (56 men, 25 women) except for two items (difficulty estimating spatial relations and double vision) where $N = 55$ (35 men, 20 women).

than those who had not experienced hallucinations ($\chi^2 = 6.89$, df[1], $p < .01$).

Twenty-five participants in the study had recently undergone a neuro-ophthalmological exam as a part of another research study in the center. All of them had normal visual acuity and no association was found between acuity levels and experiencing of visual hallucinations. The number of participants who both had experienced visual hallucinations and had had visual testing in the laboratory ($N = 4$) was not large enough to permit a thorough analysis of the relation between hallucinations and spatial contrast sensitivity. However, those with visual hallucinations appeared to have lower contrast sensitivity at the highest spatial frequency tested (18 cpd; mean log sensitivity = 0.95; SD = 0.25) than did those without hallucinations (mean log sensitivity = 1.16; SD = 0.25). Contrast sensitivity at this frequency was not related to motor severity.

It is of note that "bumping into objects" was the most prevalent visuospatial problem, with approximately half of participants endorsing this item (Fig. 1). While this symptom may certainly to some extent be affected by motor functioning, in the present sample there was no correlation between bumping into objects and participants' subjective estimation of the severity of their motor symptoms or their H&Y score. Instead, endorsement of this item was related to visual variables such as visual hallucinations, as noted above. Furthermore, a quarter of the participants who reported bumping into objects attributed this problem to an inability to distinguish objects from a background of similar color. Bumping into objects was also associated with having consulted a medical doctor for an eye problem ($\chi^2 = 5.99$, df[1], $p = .05$). Of note is that participants with onset of motor symptoms on the left side of the body reported more often bumping into the left side of doorways than into the right side, whereas participants with right side onset of motor symptoms reported no such differences.

Ten percent of men and one woman reported color perception deficits. Thirty-eight percent of participants reported double vision and 45% reported difficulty estimating spatial relations (Fig. 1). No association was found between duration or severity of PD and these symptoms.

3.2. Everyday activities

Participants were asked about their ability to perform everyday activities in a set of open-ended questions. Forty-two percent stated that they were not able to read as well as they used to and a substantial number attributed their reading difficulties to problems with vision and concentration. Seventy-five percent reported difficulty writing. Those who had difficulty reading usually also had difficulty writing ($\chi^2 = 15.35$, df[1], $p < .001$). Endorsing problems with reading or writing was not related to demographic variables, age at onset or duration

of PD. Problems with reading were related to bumping into doorways ($\chi^2 = 7.85$, df[1], $p < .01$) and there was a trend for reading difficulties to be related to experiencing of visual hallucinations ($\chi^2 = 2.98$, df[1], $p < .09$).

Several participants spontaneously offered reports of difficulties with activities such as driving a car due to poor vision, especially at night. In addition, participants frequently described difficulties with reading maps, using navigational devices, giving directions and navigating when driving. Problems with eating, walking and maintaining balance also were often reported.

3.3. Motor symptoms

Of motor symptoms, participants most frequently endorsed problems with posture and gait (85%), tremor (85%) and rigidity (69%). Motor symptoms related to freezing and abnormalities of posture and gait were of specific interest. Problems with posture and gait were related neither to demographic variables nor to endorsement of visuospatial symptoms. Forty-four percent of participants reported episodes of motor freezing, which was associated with increased duration of PD (freeze vs. non-freeze groups, $t = 2.86$; df[76], $p < .01$) and higher H&Y score (Kolmogorov–Smirnov $Z = 1.47$, $p < .05$). Of individuals who reported freezing, 60% related freezing episodes when moving through narrow spaces, such as doorways.

Motoric freezing was associated with lower contrast sensitivity at the spatial frequency of 1.5 cpd (Spearman's rho = $-.69$, $p < .01$). A regression analysis was conducted to examine the relative contributions of spatial contrast sensitivity at 1.5 cpd, motor impairment (H&Y), and PD duration to freezing severity. Contrast sensitivity and H&Y stage were significant predictors for severity of freezing ($F(3,14) = 13.3$, $p < .001$). An examination of standardized regression coefficients revealed a larger contribution of contrast sensitivity at 1.5 cpd than general motor impairment as measured with H&Y to the severity of freezing (standardized beta coefficients of .45 and .42, respectively). An analysis of covariance revealed that the level of spatial contrast sensitivity at 1.5 cpd (high/low, divided at the mean sensitivity level) continued to significantly contribute to the severity of motor freezing when the effects of motor impairment were accounted for ($F = 17.56$, df[2], $p < .001$).

Eighty-one percent of individuals who reported freezing episodes used various strategies to reinstate movement. These individuals commonly indicated visual strategies, with a number of them reporting methods such as focusing on a specific target, looking straight ahead or closing the eyes. Non-visual strategies that were frequently mentioned included humming a song, taking a step backwards, counting with cadence, lifting a foot and stretching.

3.4. Gender differences

Forty-seven percent of participants considered their symptoms to be disabling. More men than women perceived themselves as disabled by their illness ($\chi^2 = 5.96$, df[1], $p < .05$), reflected in a higher H&Y staging for men in the study (Kolmogorov–Smirnov $Z = 1.49$, $p < .05$) despite no gender differences in extent of duration of illness or differences in demographic variables. Men tended to express more subjective difficulty, on a scale of 1–5, than women in starting to move (Kolmogorov–Smirnov $Z = 1.49$, $p < .05$).

A total of 78% of men and 76% of women reported at least one problem related to visual or visuospatial functioning. Fifty-one percent of men and 35% of women reported problems with non-motor estimation of spatial relations, including tasks such as estimating one's position relative to objects in the environment and estimating distances (Fig. 1). Informal examination of the data indicated that side of motor symptom onset has moderating effects on the association between gender and complaints of visuospatial problems. The number of participants (women) in this study did not allow enough statistical power to reliably conduct a multi-level chi-square analysis of the data, as cell sizes did not fulfill criteria for expected frequencies. Fig. 2 provides information in regard to the trends of association between gender, side of motor symptom onset and endorsement of difficulty estimating spatial relations. Whereas men and women with right motor symptom onset did not differ in their complaints of difficulty estimating spatial relations, men with motor symptom onset on the left

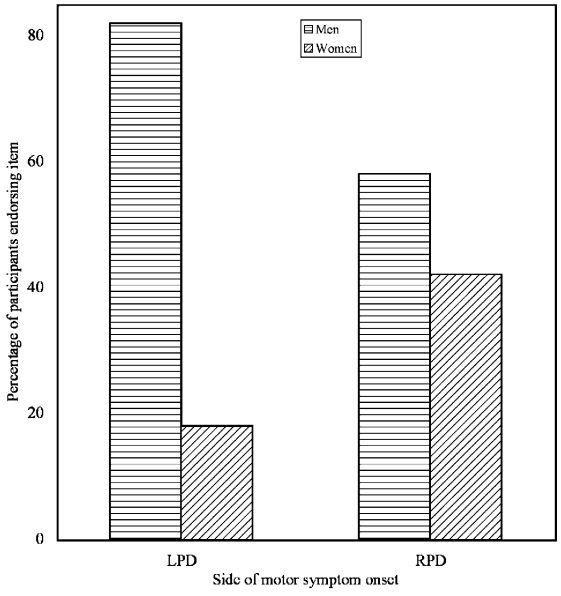

Fig. 2. Interaction of side of motor-symptom onset and gender: percentage of men and women with PD who endorsed having difficulty estimating spatial relations. $N = 55$ (35 men, 20 women).

side of the body tended to more often complain of such problems than women with left motor onset.

4. Discussion

This study documents that visual and visuospatial symptoms regularly occur in PD. A considerable percentage of the PD patients who participated in this study reported difficulty estimating spatial relations, experiencing of visual hallucinations, double vision, freezing in narrow spaces and bumping into components of the environment, such as doorways.

4.1. Visual hallucinations

The proportion of PD patients who reported visual hallucinations in this study (37%) is comparable to that reported in other recent studies (Fenelon et al., 2000; Inzelberg, Kipervasser, & Korczyn, 1998; Pappert, Goetz, Niederman, Raman, & Leurgans, 1999). Although participants in this study primarily reported hallucinations that consisted of images of humans or animals, diverse visual hallucinations in PD have been described (Barnes & David, 2001; Fenelon et al., 2000). These range from simple photopic phenomena to more complex visual images.

Theories regarding causal mechanisms of visual hallucinations in PD include sleep disorders, effects of dopaminergic medications and a complex interplay between impaired visual abilities and compensatory top-down processes. Given the broad range of characteristics of hallucinatory experiences in PD (Barnes & David, 2001), a variety of explanations for these phenomena should be evaluated accordingly. Although dopaminergic medications are often cited as a cause of visual hallucinations in PD (see review of Barnes & David, 2001; Manford & Andermann, 1998), in the present study, no evidence was found to support this notion.

Whereas sleep disturbances were not directly examined in this study, the use of sleep medications was associated with visual hallucinatory experiences, suggesting a link between sleep disorders and visual hallucinations. Research indicates that PD patients who hallucinate are prone to daytime somnolence (Arnulf et al., 2000; Fenelon et al., 2000), experience altered dream phenomena (Pappert et al., 1999) and frequently present with REM-sleep behavior disorder (Nomura et al., 2003). It has been suggested that hallucinations in PD are a result of dream imagery, due to REM-sleep intrusions during wakefulness (Arnulf et al., 2000; Manni et al., 2002). In a review of mechanisms that may underlie complex visual hallucinations, Manford and Andermann (1998) attributed complex visual hallucinations in PD to potential abnormalities in the brainstem and the reticular activating system.

Visual hallucinatory phenomena range in their site of pathology, from more peripheral visual structures to the cerebral cortex (Adamczyk, 1996). Manford and Andermann (1998) suggested that visual pathway lesions may cause visual hallucinations, either as a result of defective visual processing or cortical release phenomena. Visual hallucinations in psychologically healthy individuals with poor vision (Charles-Bonnet syndrome) have become increasingly recognized and have been related to sensory deprivation (Teunisse, Cruysberg, Hoefnagels, Verbeek, & Zitman, 1996), including reduced visual acuity (Holroyd et al., 1992; Scott, Schein, Feuer, & Folstein, 2001). When vision is corrected, hallucinations often resolve (Siatkowski, Zimmer, & Rosenberg, 1990).

In this study, visual hallucinations in PD were associated with difficulty perceiving spatial relations, double vision and having sought medical advice due to vision problems, indirectly indicating impaired visual input. The number of individuals who both underwent formal contrast sensitivity testing and experienced visual hallucinations was not large enough to allow a reliable statistical analysis of relations between visual hallucinatory phenomena and contrast sensitivity. However, individuals who had experienced visual hallucinations had a tendency to have reduced contrast sensitivity at high spatial frequencies. Whereas the impact of impaired visual perception in PD in regard to visual hallucinations has on occasion been minimized (Fenelon et al., 2000; Klein, Kompf, Pulkowski, Moser, & Vieregge, 1997; Manford & Andermann, 1998), visual hallucinations in PD have been associated with deficits in color vision and spatial contrast discrimination (Diederich et al., 1998), decreased acuity (Holroyd, Currie, & Wooten, 2001) and object perception deficits (Barnes, Boubert, Harris, Lee, & David, 2003). Defective visual input may indeed increase the brain's efforts to fill in missing or unclear details, increasing the emphasis on top-down cognitive processing. Also, release phenomena or spontaneous compensatory activity in deafferentated cortical areas has been cited as a possible causal factor for hallucinations in PD (Diederich, Pieri, & Goetz, 2000). The possibility that spontaneous compensatory neural firing in visual pathways contributes to visual hallucinations is supported by studies that indicate functional abnormalities in the visual cortical areas in PD (Abe et al., 2003; Bulens et al., 1988; Regan & Maxner, 1987; Trick et al., 1994).

Ffytche et al. (1998) used functional magnetic resonance imaging (fMRI) to demonstrate relations between the content of specific visual hallucinations reported in Charles-Bonnet syndrome and increased cerebral activity in certain areas of the ventral extrastriate visual cortex. These associations reflected known functional organization of hemispheric regions. Santhouse, Howard, and Ffytche (2000) used factor analysis to create clusters of hallucinatory experiences in Charles-Bonnet syndrome.

They argued that the characteristics of diverse clusters could be used to establish their associations with different areas of the visual system, given the known functional organization of the visual cortex. The hypothesized origin of their hallucinatory clusters included projections towards the ventral and dorsal streams and towards the intermediately placed superior temporal sulcus (Santhouse et al., 2000). Middleton and Strick (1996) proposed that dysfunctional connections between the inferotemporal lobe and the basal ganglia may cause visual hallucinations. By complement, the relation found in the present study between visual hallucinations and difficulty estimating spatial relations in PD may reflect a common dorsal stream origin of pathology.

Hallucinations in PD are transient, rendering imaging studies an unfeasible option. Therefore, further insight into hallucinatory phenomena in PD may best be achieved by a closer investigation of symptom characteristics of hallucinators with PD and the association of particular hallucinatory experiences with distinct visual problems.

4.2. Visual changes and freezing of gait

Consistent with Giladi, Kao, and Fahn (1997), almost half of the participants in the present study reported freezing of gait, which was correlated with duration of PD. Freezing was the only motor symptom in PD that was associated with disturbances in vision, more specifically visual hallucinations and impaired contrast sensitivity at lower spatial frequencies. Potential etiological associations between freezing episodes, experiencing of visual hallucinations and spatial contrast sensitivity levels in PD have not been considered prior to this study, although it is recognized that visual hallucinations and freezing episodes may co-occur in advanced PD (e.g. Klein et al., 1997). While an association between freezing, hallucinations and spatial contrast sensitivity may be explained by an advanced progression of PD and more pronounced symptomatology, it may also reflect a common visual-stream neuropathology. The current results indicated that impaired contrast sensitivity at low spatial frequency contributes specifically to motor freezing, independent of PD duration or of the severity of motor impairment as measured by the Hoehn and Yahr scale.

The results of this study showed that decreased sensitivity at low spatial frequencies is associated with increased propensity for freezing in PD. The association between motoric freezing and spatial contrast sensitivity was robust enough to be significant from testing only the subgroup who had received contrast sensitivity assessment. Such visual information may be especially important to maintain or initiate motor behavior in PD, a disorder in which patients rely to a great extent on visual information for sensorimotor integration (Azulay et al., 2002). The effectiveness of visual cues for improving gait in PD, which partly depends on the cues' physical characteristics such as the width and orientation of floor lines (Martin, 1967), may be a function of patients' basic visual abilities. Enhancing the visual signals in the environment may aid cortical processing, in turn activating neurological circuits that reinstate movement by use of external cues. It appears paradoxical that the freezing episodes of Mestre's et al. (1992) patient with nonparkinsonian primary progressive freezing of gait benefited from the presentation of visual cues. If the patient had been hypersensitive to visual stimulation, as Mestre et al. (1992) hypothesized, presentation of visual cues should have increased the probability of freezing episodes. Whereas evidence for increased visual dependence and visual grasping in PD has been reported (Azulay et al., 2002; Crevits & De Ridder, 1997; McDowell & Harris, 1997a), such characteristics have not been empirically associated with motoric freezing.

While the association between visual and visuospatial problems and freezing is extensive enough to be revealed by self-report questionnaires, more sensitive instruments are needed to fully understand the relation between those symptoms. In particular, because visual interventions have proven successful to some extent in treating gait disorders (Azulay et al., 1999; Martin, 1967), a more detailed analysis of the participants' characteristics that contribute to freezing is needed in order to develop more effective compensatory strategies.

It is as yet unclear through which mechanisms strategies to overcome gait disturbances achieve their benefits. Cunnington, Iansek, Bradshaw, and Phillips (1995) suggested that movement facilitation by external cues in PD occurs through a circumvention of the compromised basal ganglia-supplementary motor area axis, which is involved in internally determined movement. Whereas the role of basal ganglia circuits in internally guided movement remains controversial (e.g., Jahanshahi et al., 1995), the role of cerebellum in externally guided movements or discontinuous movements has become better established (Mano, Ito, & Shibutani, 1996; Spencer, Zelaznik, Diedrichsen, & Ivry, 2003). Cerebellar loops overlap to some extent with areas to which the basal ganglia project, including the posterior parietal cortex (Clower, West, Lynch, & Strick, 2001; Dum & Strick, 2003), prefrontal cortex (Dum & Strick, 2003; Middleton & Strick, 2001) and primary motor cortex (Hoover & Strick, 1999). The cerebellum and its projections may indeed serve as the alternative circuit that compensates for impaired basal ganglia functioning in motor behavior.

4.3. Relation of gender and side of motor symptom onset to visual, visuospatial, and motor variables

Whereas equal proportions of men and women in this study endorsed problems related to visual and visuospatial functioning, there was evidence that the dominant

side of hemispheric neurodegeneration differentially affects visuospatial abilities for men and women with PD. Other studies have suggested that gender is not only a factor in prevalence rates for PD (Van Den Eeden et al., 2003) but also impacts upon the performance of cognitive tests (Cronin-Golomb & Amick, 2001). Also, there is evidence that men and women may apply different strategies when performing visuospatial tasks, such as women relying to a greater extent on verbal strategies than men (Meurling, Tonning-Olsson, & Levander, 2000). Although caution is recommended when interpreting the relation of gender and PD symptomatology in this study because of the possibility of gender-specific response biases, findings of other researchers lend support to the impression that gender effects may reflect a differential impact of PD on cognitive ability in men and women (Carey, Deskin, Josephson, & Wichmann, 2002). The gender differences that were revealed underscore the importance of including both men and women in research on perception and cognition in PD.

Our findings indicated that side of motor symptom onset differentially impacts PD patients' ability to navigate through their environment. Whereas patients with right-side onset reported bumping equally into left and right side of doorways, patients with motor symptom onset on the left side of the body primarily reported bumping into the left side of doorways. This may indicate a mild neglect for the left hemispace in the left-onset group, which is consistent with the findings of Lee et al. (2001). The absence of further evidence in regard to interactions of visuospatial symptoms and side of motor symptom onset was unexpected, considering the empirical evidence for the impact of the side of onset on the perception of space (Harris et al., 2003; Lee et al., 2001). It is likely that instruments that are more sensitive than a self-report questionnaire are needed to detect finer characteristics of visuospatial impairment in PD.

The results of this questionnaire study demonstrated that there are interactions between visual, visuospatial and motor symptoms in PD. This finding provides a rationale to further investigate the association between these symptoms in PD, as increased understanding of these mechanisms may promote improvement of currently used compensatory strategies, as well as the development of new strategies. Specifically, the association of contrast sensitivity deficits with everyday gait disturbances may have implications for the development of compensatory strategies. Other important conclusions of this study regard gender differences in endorsement of visual and visuospatial symptoms.

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