Directional bias of initial visual exploration
A symptom of neglect in Parkinson’s disease

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Summary
In the present study, side preferences in spontaneous visual exploration were assessed systematically in 27 patients with idiopathic Parkinson’s disease (IPD) and 17 age-matched controls. Assessment of initial visual exploration asymmetry (IVE) was based on the exploration of texture arrays requiring attentive oculomotor scanning. As shown in a previous study, most healthy subjects exhibit a marked asymmetry of IVE with a strong left-sided bias when assessed by this paradigm, while most neglect patients initiate exploration in the right half of the arrays. Standard assessments for symptoms of neglect (line bisection, line cancellation and double simultaneous stimulation) were performed as reference tests. In the IVE task 65% of normal controls and 69% of patients with predominantly right-sided IPD started exploration in the left half of the arrays. By contrast only 14% of patients with predominantly left-sided disease showed a leftward IVE. The majority showed an ambiguous (21%) or rightward (64%) directional bias for initial exploration and thus a behaviour that corresponds to the IVE abnormalities found in neglect patients. No abnormalities were found in the standard neglect tests in any of the groups. The atypical IVE in patients with predominantly left-sided Parkinson’s disease should be interpreted in the context of recent concepts of attention postulating that a bias in early spontaneous orientation directed to the ipsilesional hemifield reflects a mild and residual manifestation of hemineglect. Since this subtle orientational bias is less subject to compensation than more conspicuous clinical signs of neglect, sensitivity is higher in IVE testing than in conventional neglect assessments in chronic disorders with subclinical neglect. The present findings contribute a new aspect to the complex picture of cognitive and visuospatial abnormalities in Parkinson’s disease. Furthermore our results extend previous knowledge on the mechanisms of neglect and the role of dopamine in the mediation of attention.

Keywords: neglect; attention; dopamine; Parkinson’s disease

Abbreviations: IPD = idiopathic Parkinson’s disease; IVE = initial visual exploration; LEI = left exploration index; LPD = (predominantly) left-sided Parkinson’s disease; RPD = (predominantly) right-sided Parkinson’s disease; UPDRS = Unified Parkinson’s Disease Rating Scale

Introduction
Neglect has been defined as a failure to report, respond or orient to novel or meaningful stimuli presented to the side opposite a brain lesion not explained by primary sensory or motor deficits (Heilman, 1979). Animal models of neglect suggest a possible significance of dopaminergic nigral input to striatal, mesolimbic and mesofrontal regions for the mediation of directional attention. Side preferences of turning behaviour in rats and reduced responsiveness to contralesional sensory stimulation and directional hypokinesia in primates have been induced by means of unilateral manipulations of nigrostriatal dopamine pathways (for review, see Heilman et al., 1993). Asymmetric degeneration of dopaminergic nigrostriatal pathways is the major pathogenetic mechanism underlying the motor symptoms of IPD. However, signs of directional neglect have only rarely been reported in patients with IPD (Starkstein et al., 1987; Ventre et al., 1992). On the contrary, Wright et al. (1990) found a facilitation of disengagement in covert orientation in patients with IPD, a behaviour diametrically opposed to that seen in patients with neglect due to parietal lesions. A possible reason for the apparent discrepancy between findings in experimental animals and patients with IPD is the susceptibility of most
Table 1 Patient data

<table>
<thead>
<tr>
<th></th>
<th>LPD</th>
<th>RPD</th>
<th>Control</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>(n = 14)</td>
<td>(n = 13)</td>
<td>(n = 17)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>59.3 (10.3)</td>
<td>63.5 (6.3)</td>
<td>61.4 (9.00)</td>
</tr>
<tr>
<td>Female:male ratio</td>
<td>3:11</td>
<td>3:0</td>
<td>3:14</td>
</tr>
<tr>
<td>Education (years)</td>
<td>13.1 (2.8)</td>
<td>12.0 (1.9)</td>
<td>12.6 (2.6)</td>
</tr>
<tr>
<td>Duration of illness (months)</td>
<td>35.1 (29.5)</td>
<td>50.8 (32.9)</td>
<td>—</td>
</tr>
<tr>
<td>UPDRS score</td>
<td>16.1 (5.6)</td>
<td>13.5 (7.3)</td>
<td>—</td>
</tr>
<tr>
<td>UPDRS-left</td>
<td>9.9 (3.2)</td>
<td>2.2 (2.2)</td>
<td>—</td>
</tr>
<tr>
<td>UPDRS-right</td>
<td>1.6 (1.5)</td>
<td>7.4 (4.2)</td>
<td>—</td>
</tr>
</tbody>
</table>

Values are means (SD). Mean UPDRS scores reflecting lateralized motor symptoms are differentiated for right and left side.

Clinical signs of neglect to compensation. Recent studies suggest that while obvious clinical signs of neglect tend to disappear in chronic post-lesional stages, a subtle directional bias in visual exploration persists even years after apparent clinical recovery. The paradigms employed to demonstrate this bias comprise overlapping pictures (Gainotti et al., 1991), chimeric faces (Mattingley et al., 1994), the Wundt–Jastrow illusion (Pizzamiglio et al., 1992) and texture arrays (Hättig, 1992). Since striatal dopamine depletion in idiopathic Parkinson’s disease is a slowly progressive process, possible attentional impairments might well be subject to compensation and these latter types of assessments might be required to detect more subtle lateralized attentional deficits.

In this study, IVE was assessed in patients with IPD and controls by means of a newly developed paradigm of visual exploration (Hättig, 1992). The test is based on arrays of textures derived from texture research (Julesz, 1981) and highly standardized with respect to information content and attentional demand. Attentive oculomotor scanning is required to differentiate distinct textures and directional bias in the initiation of visual exploration can be reliably detected.

In validation experiments in healthy controls a physiological asymmetry of IVE to the left was found for right-handed individuals. At the same time, right-hemispheric lesions were associated with a reversal of the IVE, regardless of whether additional signs of neglect were present or not (Hättig, 1992). The present study was designed to test whether a predominantly right-sided degeneration of nigral dopamine-producing cells in asymmetrical IPD would have similar effects on IVE as structural right-hemispheric lesions.

Methods

Subjects
Twenty-seven patients with a diagnosis of IPD according to established clinical criteria (Gibb and Lees, 1988) and 17 age-matched controls recruited from a volunteer panel were studied (see Table 1 for subject characteristics). All subjects were right-handed as assessed by a modified version of the Edinburgh Handedness Inventory (Oldfield, 1971). All patients were clinically examined by a neurologist (G.E.) and IPD disability was scored using the motor part of the Unified Parkinson’s Disease Rating Scale (UPDRS). All patients had clear asymmetric disease and were assigned to one of two groups according to the side of predominant involvement: right (RPD) or left (LPD) IPD group. To quantify the degree of symptom asymmetry in the patient groups, mean left and right sum scores of those UPDRS items (20–26) assessing lateralized symptoms are depicted in Table 1. Ten patients had been newly diagnosed and were assessed before treatment had been initialized. The other patients were tested on their ongoing medication (see Table 2) and in the case of the seven patients with motor fluctuations during an ‘on’ phase with their individually best possible control of motor deficits. None of the fluctuating patients had disabling degrees of on-period dyskinesias or dyskinesias involving the neck and face. Dementia and depression were excluded in all subjects by means of the Mini-Mental Scale and the Geriatric Depression Scale (Sheik and Yesavage, 1986), respectively. The study was approved by the local ethical committee and all subjects gave informed consent to participate.

Paradigm
The IVE assessment is based on the exploration of a series of arrays containing different target and distractor textures. All textures are texture identical, i.e. do not provide information allowing for pre-attentive differentiation, and foveal fixation of each texture is required to distinguish between targets and distractors (Fig. 1A). Since peripheral vision only allows for prediction of the location, but not of the category of the textures, the search for a target requires successive saccades

Table 2 Treatment of patients

<table>
<thead>
<tr>
<th></th>
<th>LPD</th>
<th>RPD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 14)</td>
<td>(n = 13)</td>
</tr>
<tr>
<td>De novo</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Treated</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>l-Dopa</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Agonists</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Deprenyl</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Amantadine</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
Neglect in Parkinson's disease

Fig. 1 (A) Textures used in the IVE experiment. Target textures are '10' and '01'. Distractors are depicted in the lower row. (B) Array used for catch trials: both halves contain the same type of target texture. The dotted line (not visible during the experiment) depicts the area where target textures are located. The position of the area and the location of target textures is symmetrical between right and left. (C) Array used for test trials: left and right halves contain different target textures.

In the arrays with identical targets '10' and '01' targets were each presented eight times. In the arrays with different targets '10' and '01' were each presented 18 times on the left half and 18 times on the right half, respectively.

Balance of relative stimulus strength between right and left visual field is a critical determinant of orientative behaviour (Mark et al., 1988). Exploratory bias predominates in situations of uncertainty (Karnath, 1988; Gainotti et al., 1991) and optimal assessment sensitivity requires non-lateralized information content as (in contrast to other procedures) warranted by the present IVE approach.

Procedure

The arrays were presented on a PC screen (white textures on black background) with a search field starting from the central fixation point of -13° visual angle to each side and 10° in upward and downward direction, respectively. The visual angle between two textures was -2° and horizontal and vertical extension of each texture comprised -0.8°. During the assessment, patients were not aware of the presence of arrays with different targets on both halves ('test trials', e.g. Fig. 1C). Instead, they were falsely informed that the procedure was performed to assess the speed of target detection. Each trial was initiated by a white asterisk located in the centre of the blank screen that disappeared after 1000 ms and was immediately followed by a texture array. To warrant the search being directed from the centre to the periphery of the search field, each array contained a central reference target that was visible for 1000 ms and was then replaced by a distractor. Subjects were required to find a target among the surrounding distractors and to determine whether this target was identical or distinct from the initially presented reference target. The examiner registered the responses ('distinct' or 'identical') operating a keyboard that was connected to the PC (IBM-486). Simultaneous to response registration the keystroke also removed the array and started the next trial. If subjects failed to find a target within 6000 ms, the array was automatically removed and the respective trial was repeated after a random interval during the session. Arrays with identical targets on both sides ('catch trials', e.g. Fig. 1B) served to ensure that the responses were not based on guessing but on unequivocal identification of the targets. A maximum of four faulty responses (corresponding to a 3.8% probability for guessing) was accepted during catch trials. The results of patients committing more than four faults were excluded from further IVE analysis.

Asymmetrical spontaneous exploration was assessed according to the responses obtained during presentation of test trials. Since the target distribution in these trials is dichotomic between right and left halves the type of target identified ('10' or '01') allows deduction of which side of the array was explored initially.

Standard tests of neglect were performed as reference assessments. They included line bisection (Schenkenberg...
et al., 1980), line cancellation (Albert, 1973) and visual double simultaneous stimulation. Double simultaneous stimulation was performed during confrontation testing to assess extinction phenomena with the examiner presenting brief finger twitches in the periphery of the visual fields. Forty trials were performed for each subject with 20 bilateral, 12 left-sided and eight right-sided stimuli in random order. Subjects were required to report verbally the type of stimulus ('both', 'left' or 'right') after each trial.

**Analysis**

We first calculated the percentage of leftward explorations during test trials for each subject [left exploration index (LEI)]. Following a theoretical binomial distribution \( n = 100 \) and \( p = q = 0.5 \) subjects were assigned to one of three groups according to exploration preference. Since for the LEI, the confidence interval of \( 2\sigma \) for chance directional bias lies between 39% and 61% a definite (92.7% confidence) preference for leftward exploration was defined as a LEI of \( \geq 61\% \) and corresponding subjects were defined as leftward explorers. Analogous definite rightward preference was assumed when the LEI was 39% or smaller (rightward explorers). When the LEI was between 40% and 60%, subjects were defined as ambiguous explorers.

To assess the relationship between directional preference and diagnosis, statistical analysis was performed with \( \chi^2 \) tests and non-parametric standard procedures (SPSS-PC 4.0).

**Results**

**Initial visual exploration assessment**

The percentual distribution of subjects between the three groups is depicted in Fig. 2. Patients with LPD showed marked rightward shift of their initial visual exploration, while controls and patients with RPD showed a preference for leftward exploration. The finding that 65% of normal subjects showed a leftward bias in initial spontaneous exploration is in agreement with previous studies (Hättig, 1992). A Kruskal–Wallis analysis of variance was performed showing significant between-groups difference \( (P = 0.012) \). After Bonferroni adjustment the Mann–Whitney rank sum tests showed significant differences between controls and LPD and between RPD and LPD at a level of significance for the whole test of 0.05. No difference in exploration behaviour was detected between patients with RPD and healthy controls (Fig. 3). Rightward shift of IVE was present in all untreated LPD patients tested, while in treated cases this shift was less absolute (see Table 3). Comparison of the LEIs with a Mann–Whitney \( U \) test showed a tendency for a difference between \textit{de novo} and treated LPD patients \( (P = 0.07) \). This finding can be interpreted as a trend for dopaminergic therapy to reverse partly the pathological IVE shift in LPD. No trends for treatment effects were seen in RPD cases. No significant difference between groups was found for the frequency of faulty responses in catch trials (Table 4).

**Reference assessments**

Deviations from the midline in the assessment of line bisection did not differ in extent or direction between groups. Concerning line cancellation no omissions were observed in either of the groups and execution was performed with a left
to right approach by all subjects. No extinctions were noticed during double simultaneous stimulation.

Discussion

Asymmetries of spontaneous exploration in healthy individuals

The results of this study confirm a physiological leftward bias in IVE behaviour in normals and correspond to the results reported by Hättig (1992) in a younger age group with the same paradigm and also to the asymmetries found in the assessment of overlapping pictures (Gainotti et al., 1991). The neurophysiological basis for initial visual orientation to the left is most likely related to lateralized hemispheric specialization for visuospatial functions. Hättig (1992) reported significantly reduced leftward bias in left-handers, a finding which is evidence against reading habits being the reason for this phenomenon. Dominance of the right hemisphere for motor (Meador et al., 1989) and sensory (Heilman and Van Den Abell, 1980; Yamaguchi et al., 1994) aspects of visuospatial control has been confirmed by various authors. This lateralization must be regarded as the critical factor for the major susceptibility to neglect and other visuospatial deficits of patients with right-hemispheric lesions (De Renzi et al., 1970; Gainotti et al., 1972; Heilman et al., 1993) and possibly accounts for the left-sided preference in visuospatial tasks reported in healthy subjects (De Renzi et al., 1970; Chèdru et al., 1973; Gainotti et al., 1991; Hättig, 1992). Furthermore, results of clinical (Heilman et al., 1985), electrophysiological (Heilman et al., 1978) and PET studies (Fiorelli et al., 1991) suggest that the right hemisphere is also dominant for the mediation of arousal and intention. Thus all major functions possibly involved in directing initial visual exploration seem to be controlled predominantly by the right hemisphere.

It has been shown that the right-hemispheric lateralization of visuospatial control is specific for the human species (Heilman et al., 1993) and related to speech dominance of the left hemisphere (Meador et al., 1989). The proportion of up to 20% of right-handers showing a right-hemispheric or bilateral distribution of speech dominance (McManus, 1984) might thus account, in part, for ambiguous or atypical right-sided IVE observed in 35% of our normal subjects.

Asymmetry of spontaneous exploration in IPD

In contrast to healthy controls, patients with LPD showed an IVE directed to the right and thus a behaviour which corresponds to that found in patients with neglect due to structural right-hemispheric lesions (Gainotti et al., 1991; Hättig, 1992; Pizzamiglio et al., 1992; Mattingley et al., 1994). Since, in patients with LPD, loss of dopamine neurons is greater in the right compared with the left substantia nigra (Kempster et al., 1989), the question arises whether the observed alteration in directional bias in LPD is genetically related to the asymmetry of nigrostriatal dopaminergic pathways.

Using standard assessments for neglect there were no other signs for hemispatial neglect in this study. To our knowledge, the only study reporting signs of directional neglect at standard assessment in patients with IPD was published by Starkstein et al. (1987). These authors found a mild rightward deviation of patients with LPD at line bisection while the performance of patients with RPD did not differ from controls. Stronger degrees of symptom asymmetry in the patients of Starkstein et al. (1987) could be a possible reason for the contrast between their finding and the normal behaviour in line bisection of LPD patients in this series. Villardita et al. (1983) reported an increased number of omissions without signs of directional bias in target cancellation in some patients with LPD and thus a deficit of visuospatial processing that eventually reflects a non-directional aspect of neglect. The normal behaviour of our patients in this respect is possibly explained in terms of our more selective inclusion criteria, since major problems of visuospatial control were likely to provoke faulty responses in catch trials and thus lead to exclusion from evaluation in this study.

Experimental evidence for the role of dopamine in the mediation of directional attention

In experimental animals, unilateral damage of dopaminergic pathways projecting from the ventral tegmental area to neostriatal, mesolimbic and mesofrontal regions provokes changes of orientational behaviour which are considered as a model for neglect. Much evidence suggests that dopaminergic nigrostriatal projections regulate striatal output to the intralaminar thalamus via internal globus pallidus, to the superior colliculus, and to the mesencephalic reticular formation which are crucial areas for the mediation of attention (for review, see Heilman et al., 1993). While Carli et al. (1985) demonstrated that the response bias in rats with unilateral striatal dopamine depletion was due to a deficit in the initiation of contralesionally directed motor activities sensory inattention following lesions of dopaminergic pathways in monkeys was recently suggested by Schneider et al. (1992). These authors showed that monkeys made hemiparkinsonian by unilateral MPTP exposure not only showed signs of directional hypokinesia, but also extinction with double simultaneous stimulation. A subtle bias of initial spontaneous side preference without obvious failures of orientation was also found in their study: while no side preference in the choice of raisins arranged rightwards and leftwards from the midline was seen in healthy animals, monkeys with hemiparkinsonism using the unimpaired limb first, grasped for ipsilesional rewards before orienting to the contralesional hemispace. This phenomenon comes close to the atypical exploration behaviour found in neglect and in our patients with LPD.
Zimmerberg et al. (1974) and Glick and Cox (1978) have reported evidence for a role of dopamine in asymmetric orientative behaviour in experimental animals: in normal (unlesioned) rats, lateralized preferences in spontaneous turning have been described and this has been correlated with asymmetries of striatal dopamine content with the direction of turning being generally away from the side of greater striatal dopamine concentration. Although spontaneous asymmetric behaviour has also been observed in other species including primates (for overview, see Hellige, 1993) no further correlations of lateralized bias and dopaminergic transmission have been published to our knowledge.

Although neuroanatomical and neuropharmacological studies have provided evidence for asymmetrical distribution of dopaminergic systems in healthy humans (Waziri, 1980; Glick et al., 1982; Kooistra and Heilman, 1988) the consequences of these asymmetries for attentional processing are not yet established (for review, see Hellige, 1993). The alteration of initial visual exploration found in LPD patients in this study possibly suggests a role of dopaminergic nigral efferents for the regulation of directional attentional behaviour. Although we did not assess this issue systematically, the finding that untreated LPD patients showed a more pronounced rightward shift of IVE than treated cases is also in support of this hypothesis. A conclusive analysis of medication effects, however, is not possible due to the small number of subjects studied.

**Rightward shift of spontaneous visual exploration in LPD: a motor hypothesis**

To elucidate the mechanisms of asymmetrical visual exploration in pathological conditions, the results of the present study need to be discussed in the context of current concepts of the organization of attention. According to Heilman et al. (1993) and other authors (Mesulam, 1981; Weintraub and Mesulam, 1989; Posner and Dehaene, 1994), two attentional systems linked by direct pathways and by subcortical circuits can be differentiated. The anterior system, comprising dorsolateral frontal and mesolimbic structures, mediates executive and intentional aspects of attention while the posterior system located in inferior parietal and temporal regions exerts sensory representational functions without being directly related to motor processing. The dichotomy of this model has raised criticism (Bisiach and Vallar, 1988) and evidence from lesion studies in monkeys (Valenstein et al., 1982) and PET studies in humans (Baron et al., 1986; Fiorelli et al., 1991; von Giesen et al., 1994) suggests that specificity of the anterior system for motor neglect is only relative. However, its validity as an approximative concept is corroborated by a large body of experimental and clinical research (Wurtz et al., 1980; Deuel and Collins 1984; Posner et al., 1984; Deuel and Regan, 1985; Bisiach et al., 1990). Dysfunction of the anterior system only becomes apparent in the presence of overt motor activity whereas shifting of covert orientation is not affected (Posner et al., 1984). An important clinical manifestation of motor neglect is directional hypokinesia, i.e. delay or slowing of contralaterally directed movement which can occur in the contralesional but also in the otherwise unimpaired ipsilesional limbs (Watson et al., 1978; Heilman et al., 1985) and manifests predominantly in planned and goal directed behaviour (Heilman et al., 1985). Directional hypokinesia of eye movements is also thought to be relevant for deficits of visual exploration in neglect (Meador et al., 1989). In studying optomotor control in patients with hemiparkinsonism, Ventre et al. (1992) found that saccades to targets in the contralesional hemifield were delayed in LPD but not in RPD patients. This increase of saccade latencies was specific for predictable target stimuli and thus a condition where performance relied on appropriate preparatory motor planning, whereas reflexive saccades to random stimuli were not directionally impaired. Delayed saccades toward the contralesional hemispace were also reported for memory-guided eye movements in monkeys rendered hemiparkinson with MPTP (Miyashita et al., 1990).

The observations on oculomotor behaviour in LPD suggest that intentional executional deficits for contralesionally directed eye movements and thus dysfunction of the anterior attentional system might have contributed to the rightward shift of IVE in LPD patients. This assumption is further supported by the fact that no signs of delayed covert orientation which is thought to reflect attentional neglect due to posterior dysfunction are found in IPD (Wright et al., 1990). Similarly, seven of our LPD subjects with rightward IVE showed no direction specific increase of latencies or susceptibility to unvalid cueing during testing of covert orientation by the technique described by Posner (1980) even after a drug-free interval of 12 h (unpublished results).

The apparent contrast between neglect-like behaviour in our assessment and the facilitation of disengagement in covert orientation in IPD might be due to a differential involvement of the anterior and posterior system in the disease process (Clark et al., 1989; Wright et al., 1990).

**Asymmetric spontaneous exploration in LPD: hypoarousal of a right-hemispheric network?**

In spite of the evidence for a contribution of motor factors to the rightward bias in LPD, several observations suggest that the assumption of directional hypokinesia due to dysfunction of the anterior attentional system cannot account completely for all aspects of the explorative bias in our subjects.

Leftward bias of spontaneous exploration is consistently found in healthy individuals (Gainotti et al., 1991; Hättig, 1992), but a physiological delay of initiation for rightward saccades in normals has not been reported.

Rightward bias of attention after clinical recovery from neglect is also seen in paradigms which are not influenced
by motor factors, i.e. double simultaneous stimulation (Karnath, 1988).

An important characteristic of orientative preference is its susceptibility to priming of lateralized hemispheric arousal (Heilman and Watson, 1978; Kinsbourne, 1987; Robertson, 1989; Ishiai et al., 1994). This phenomenon has been demonstrated for our IVE approach by Härtig (1992), who found a decrease of leftward bias in normal controls when a verbal task ('left-hemispheric arousal') immediately preceded exploration of the texture arrays.

Taken together, these observations suggest that activity of a complex network rather than strictly confined neuronal loops might be critical for spontaneous exploration. Heilman et al. (1993) proposed a network reciprocally connecting anterior and posterior attentional system, thalamic relays and the mesencephalic reticular activating system, to account for global hemispheric hypoarousal. Lesions of one of these structures tend to involve the whole network. This network hypothesis is corroborated by PET studies in neglect patients demonstrating frontoparietal hypometabolism in thalamic strokes (Baron et al., 1986) and combined frontoparietal hypometabolism in motor neglect due to frontal lesions [Fiorelli et al. (1991) versus von Giesen et al. (1994)]. Evidence for widespread cortical hypometabolism in IPD stems from PET studies showing reduced regional cerebral blood flow and local cerebral oxygen utilization in frontal (Wolfson et al., 1985) and parietal (Lenzi et al., 1979) regions contralateral to the side of greater clinical involvement.

Compatible with our findings and the network approach is a model of neglect presented by Karnath (1988) who suggested that distinct components of neglect are operative at successive stages of exploration, i.e. (i) a directionally specific, spontaneous and stereotypical orienting to the side ipsilateral to the lesion leading to primary analysis of ipsilateral information, (ii) a directionally specific deficit to reorient attention contralateral and (iii) a directionally non-specific deficit of information processing by sequential analysis.

According to Karnath, component (ii) recovers quite rapidly, while rightward bias of initial orientation [component (i)] and complex deficits of visual processing [component (iii)] are far more persistent. A similar concept is supported by De Renzi et al. (1989), although in contrast to Karnath these authors hold that oculomotor factors are the primary origin of perceptual bias. Early automatic orienting to the ipsilesional side is thus considered as a milder and residual manifestation of gaze-deviation as seen in acute neglect syndromes.

**Conclusion**

The results of our study call for elucidation of two critical issues. First, the mechanisms underlying rightward IVE in LPD need to be corroborated by means of assessments which explicitly differentiate motor from representational aspects of neglect since both mechanisms could account for lateralized bias of initial visual exploration. Sophisticated clinical procedures (e.g. Karnath, 1988; Bisiach et al., 1990; Tegnér and Levander, 1991), simultaneous registration of saccade parameters during IVE testing and PET activation studies are encouraged to distinguish between directional hypokinesia and sensory representational bias. Furthermore, since rightward IVE was already present in all six de novo LPD patients with recent onset of disease, it remains to be determined whether IVE testing and other (Levin et al., 1989; Cooper et al., 1991; Ebersbach et al., 1994) assessments sensitive for initial cognitive alterations can contribute to early diagnosis in IPD. Another point raised by our findings is the question as to whether differences in LPD and RPD behaviour need to be taken into account considering other assessments. If hemispheric arousal in Parkinson’s disease is biased away from the side of predominant dopamine depletion, performance in other tests not only of visuospatial but also of motor, emotional and cognitive behaviour might possibly reflect LPD/RPD differences. Secondly, together with two case reports suggesting effectiveness of dopamine agonists for the treatment of neglect in humans (Ross and Stewart, 1981; Fleet et al., 1987), our results encourage systematic investigations on medication effects on neglect phenomena.

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