Time course of eye and head deviation in spatial neglect

Monika Fruhmann Berger
University of Tübingen
Center of Neurology,
Hertie-Institute for Clinical Brain Research
Section Neuropsychology

Leif Johannsen
University of Birmingham
School of Psychology

Hans-Otto Karnath
University of Tübingen
Center of Neurology,
Hertie-Institute for Clinical Brain Research
Section Neuropsychology

Abstract

Spatial neglect is characterised by a deviation of the eyes and the head during both active search as well as at rest. Here we investigate the hitherto unknown relationship between these striking behaviours in the course of recovery. Gaze, eye-in-head, and head-on-trunk positions were recorded separately under two experimental conditions: (i) at rest (i.e. without any specific requirements, *doing nothing*) and (ii) during active exploratory search in a large visual array of 240° x 80° over a 10-months period. We observed a parallel decrease of eye and head (= gaze) deviation in both conditions, accompanied by a comparable decline in neglect severity. The results strengthen the view that the marked gaze deviation towards the ipsilesional side in patients with spatial neglect is due to a very elementary disturbance of human spatial information processing.

Keywords: Visual search; Eye and head deviation; Spatial neglect; Recovery; Stroke

Introduction

The most prominent impairment in patients with spatial neglect is their bias of active exploratory behaviour. When searching for targets, copying, or reading, such patients direct their eye and hand movements towards the ipsilesional side and neglect the contralesional side (Johnston & Diller, 1986; Karnath & Perenin, 1998; Karnath, Niemeier, & Dichgans, 1998). This exploratory bias is specific to patients with spatial neglect and is not observed in other stroke patients. Consequently, tasks requiring patients to search for targets became standard screening tests for the diagnosis of the disorder (see e.g. Weintraub & Mesulam, 1985). However, this ipsilesional bias of eye and head position is not only evident in tasks addressing the patients' *active* behaviour, namely when they are explicitly asked to explore or to draw something. It is also obvious in the spontaneous resting position of neglect patients (Fruhmann Berger & Karnath, 2005; Fruhmann Berger, Pross, Ilg, & Karnath, 2006). These latter studies recorded eye and head position of acute stroke patients at rest, i.e. while *doing nothing* – just sitting and relaxing in a chair. In this situation, the combined eye and head (= gaze) position in patients with spatial neglect was constantly deviated about + 30° towards the ipsilesional side, while it varied around the mid-sagittal body axis (0°) in stroke patients without the disorder.

In the acute stage of the stroke, the neglect patients' *passive* behaviour (i.e. the spontaneous gaze deviation at rest) thus seems to be as specifically related to spatial neglect as the patients' bias during *active* exploratory search. Apparently, both behaviours characterise the disorder at that time. However, to date it is still open whether these behaviours are independent or related symptoms of spatial neglect. Although few studies followed the spontaneous eye position by clinical inspection in the acute and subacute phase (De Renzi, Colombo, Faglioni, & Gilbertoni, 1982; Kömpf & Gmeiner, 1989; Steiner & Melamed, 1984; Tijssen, 1988), its progress was not related to the co-occurrence of spatial neglect.

Our present study thus measured the development of the spontaneous eye and head deviation at rest *and* during active visual exploration in patients with spatial neglect. We asked whether both phenomena dissociate over time, which would favour the assumption of independent, distinct symptoms, or whether they recover in parallel, i.e. appear to be tightly linked.

Methods

Subjects

Twelve consecutively admitted patients with spatial neglect (NEG) due to an acute right hemisphere stroke were investigated. During the follow-up period, two of these patients suffered a second stroke, two patients denied to be examined a second time, one patient was admitted to another hospital, and one patient had moved far beyond the catchment area. Thus, six neglect patients could be followed during recovery. They were compared with (i) six stroke patients who also suffered from acute right hemispheric lesions but did not show any signs of spatial neglect (RBD) and (ii) six patients without brain lesions (NBD) who were admitted with peripheral neurological disorders. All stroke patients (NEG, RBD) had acute circumscribed right-hemisphere brain lesions due to an ischaemic or haemorrhagic first-ever stroke demonstrated by diffusion-weighted and T_2-weighted fluid-attenuated inversion recovery magnetic resonance imaging or by spiral computed tomography. Patients with previous brain lesions, cerebral atrophy, tumours, diffuse or bilateral lesions were excluded.

Spatial neglect was diagnosed when patients fulfilled the criterion in at least two of the following clinical tests: the *Letter cancellation* task (Weintraub & Mesulam, 1985), the *Bells test* (Gauthier, Dehaut, & Joanette, 1989), and a copying task (Johannsen & Karnath, 2004). Full details about the test procedure are described elsewhere (Fruhmann Berger & Karnath, 2005). RBD patients showed normal behaviour in all neglect tests. None of the subjects had a visual field defect or a history of vestibular or oculomotor abnormalities.

All patients with spatial neglect were investigated three times in a 10-months period. The initial examination (Exam 1) took place as early as possible after admission, i.e. once the patients could be mobilised in a wheelchair and were able to attend to an experiment over a period of approximately 30 minutes (*mean (M)* = 12.2 days, *standard deviation (SD)* = 5.3). The first follow-up examination (Exam 2) was carried out just before the patients were discharged and transmitted to a rehabilitation unit (*M* = 18.7 days, *SD* = 5.2). The second follow-up examination (Exam 3) took place in the chronic stage, i.e. not before six months had elapsed after stroke (*M* = 10.6 months, *SD* = 5.2). At this time, the patients had stayed in a rehabilitation unit for a median time of 70.2 days (*range* = 118 days). During this period, they had received a conventional therapy program including standard physiotherapy, occupational therapy, and neuropsychological training.

The two control groups without spatial neglect (RBD, NBD) were investigated once (RBD: *M* = 12.0 days since lesion, *SD* = 7.4). Table 1 gives an overview of the relevant demographic and clinical data of the three groups. All patients gave their informed consent to participate in the study, which has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

--- Table 1 near here ---

Apparatus

The present experimental set-up allowed for free, unrestricted gaze (= combined eye and head) movements within a large array that covered 240° of horizontal space (± 120° left and right of the trunk midline). Gaze, eye-in-head, and head-on-trunk positions were measured separately under two experimental conditions, (i) at rest ("passive behaviour") and (ii) during active exploratory search ("active behaviour") by using the magnetic field-search technique (Robinson, 1963). Full technical details of the set-up are described elsewhere (Fruhmann Berger & Karnath, 2005). In both conditions, head and eyes could be freely moved while the trunk was immobilised on the chair by a belt and shoulder straps. An unitary array of black letters on a white ground was presented in a rectangular area of 240° x 80°. There was no fixation target or any other hint indicating the objective straight ahead position (0°/0°). Gaze positions were measured by a 2D search coil (Skalar Medical, Delft, The Netherlands) adhered to the left sclera, head-on-trunk positions with a further solenoid attached to the forehead. Eye-in-head positions represent the difference between the corresponding gaze and head-on-trunk values and were determined by multiplying the rotation matrices of gaze with the inverse rotation matrices of head-on-trunk positions. Gaze positions represent the combined eye-in-head and head-on-trunk positions. Head-on-trunk and gaze co-ordinates 0°/0° were aligned with the patient's mid-sagittal body axis in the horizontal plane and the individual eye level in the sagittal plane. Eye-in-head co-ordinates were head-centred with co-ordinates 0°/0° aligned with the head's mid-sagittal axis at eye level. Positive values indicate right-sided positions, negative values those on the left.

Procedure

Rest condition. The patients' spontaneous gaze, eye-in-head, and head-on-trunk position was measured at rest, i.e. without any specific requirements. Once the patients were seated in the chair and the coils were attached, they were informed that *it will be necessary to wait for a while until the preparations of the apparatus are finished and the experiment can start. Don't care about the prearrangements. Just relax, do nothing, until being informed that the experiment is ready to start*. No further communication took place and data were recorded right afterwards. The room light was switched off for 30 seconds, followed by 30 seconds in light. The cycle was repeated three times, such that the total recording period of the patients' passive behaviour in light was 90 seconds. After recording, the patients were told that *now all technical arrangements were completed and the experiment is ready to start*.

Active visual search condition. Subsequently, the patients' gaze, eye-in-head, and head-on-trunk movements were recorded during active visual search. We employed a task that resembles the clinical exploration task of Weintraub & Mesulam (1985) for the diagnosis of spatial neglect. The whole search array covered an area of 240° in the horizontal plane (120° right and left of the body's mid-saggital plane) and of 80° in the vertical plane (40° above and below the subject's eye level). Patients were blindfolded and told that a single target letter *A* would now be hidden *somewhere in the entire search array*. Immediately after the blindfold was removed, the task was *to actively search the whole array for this target letter A by looking thoroughly in all directions*. Data were recorded for 120 seconds under normal room light conditions. Subsequently, patients were blindfolded again.

In fact, during data recording no target letter was presented. This procedure was employed to prevent that a target stimulus attracts the patient's attention and thus influences the distribution of spontaneous exploratory gaze movements. To maintain the patient's motivation, an intermediate trial was implemented in which no data were recorded but the letter *A* was presented somewhere in the central area of the search array. If the patient did not find the target within 40 seconds, the experimenter identified its location by pointing on it. The active search behaviour of each patient was recorded in two out of three trials. The total recording period thus amounted to 240 seconds per patient.

Results

No differences were observed between the two groups of control patients with and without brain injury (RBD, NBD). Thus, they were merged into a single group of patients without spatial neglect (CON, n =12) which was compared to the stroke patients with spatial neglect (NEG, n = 6). The groups were comparable with respect to age (CON versus NEG: $t(16) = 1.17$, $p = .261$), time since lesion ($t(10) = 0.05$, $p = .965$), aetiology (Fisher's exact test: $p = 1.00$), and contralateral paresis (cf. Table 1).

Figure 1 illustrates the scan paths and Figure 2 the mean horizontal gaze (= combined eye and head) positions of the control and the neglect group during active visual exploration as well as at rest (*doing nothing*). In addition, Figure 2 shows the averaged neglect severity as obtained by the clinical neglect tests (see Methods section). In the acute stage of the disorder (Exam 1), we found marked differences between the patients with spatial neglect and the control group for both, active exploratory ($t(6.4) = 9.25$, $p < .001$) and resting behaviour ($t(5.3) = 4.51$, $p = .005$). In each case, the mean horizontal gaze position of the control patients was close to the mid-sagittal body axis (active search: M = - 2.7°, SD = 7.6°; resting: M = - 1.4°, SD = 4.2°), while it was markedly deviated towards the ipsilesional side by + 55.3° (SD = 14.4) during active visual search and by + 30.0° (SD = 16.8°) at rest in patients with spatial neglect. Correspondingly, the omissions made in the clinical neglect tests differed markedly between the two groups ($t(5.0) = 7.03$, $p = .001$).

--- Figures 1 & 2 near here ---

Development over Time

To analyse the development of active and of passive neglect behaviour as well as of neglect severity, we conducted a two-way repeated measures analysis of variance with *time* (Exam 1, Exam 2, Exam 3) and *condition* (active search, resting, severity) as within-subject factors. Degrees of freedom were corrected with the Greenhouse-Geisser epsilon. Post-hoc tests were adjusted using the Bonferroni procedure for multiple comparisons.

Analyses of the simple main effects indicated marked differences for both, the course of recovery ($F(2) = 64.35$, $p < .001$) as well as for the amount of the patients' neglect behaviour in the different conditions ($F(2) = 5.44$, $p = .025$). Post-hoc analyses revealed that neglect patients showed a more rightward deviation during active visual search than at rest in both, the acute as well as the subacute stage of the stroke (Exam 1: $t(5) = 4.53$, $p = .006$; Exam 2: $t(5) = 4.75$, $p = .005$).

Post-hoc comparisons on the time course of recovery showed a common decrease of the neglect patients' gaze deviation between the initial (Exam 1) and the follow-up (Exam 3) examination for active search ($t(5) = 9.23$, $p < .001$) and for resting ($t(5) = 5.14$, $p = .004$). At the chronic stage, the rest position had improved by approximately 83 percent of its initial amount (cf. Figure 2). Within the same time period the neglect patients' active search behaviour had decreased on average by 72 percent, as it was the case for neglect severity as well ($t(5) = 13.87$, $p < .001$).

Discussion

The present study investigated whether a bias during active visual search and at rest are independent or related symptoms of spatial neglect. Analysis of the course of recovery over a period of 10 month post stroke revealed a parallel decrease in both behaviours that was accompanied by a comparable decline in neglect severity. This common time course argues for a close relationship between active and passive neglect behaviour.

Based on qualitative observations it was assumed that an initial deviation of gaze position in patients with spatial neglect improves fast compared to traditionally measured active components such as cancellation or coping, favouring distinct rather than related phenomena (De Renzi et al., 1982). In clear contrast, our quantitative analysis revealed a parallel recovery of gaze positions in active and passive conditions as well as of neglect severity. The deviation of the eyes and the head did not recover faster. It was still obvious in some patients up to 10 months post stroke, though to a lesser degree than during active exploratory search. Apparently, the patients' deviation of eye and head position at rest is not a distinct symptom that may solely co-occur with traditionally defined "active" components of the neglect syndrome. Our findings rather argue for closely related symptoms, which both characterise spatial neglect behaviour and specify the disorder even beyond the acute post-stroke phase.

Of course, the observation of a shared development does not prove a *causal* relationship between active and passive neglect behaviour and also does not necessarily imply a common underlying mechanism since initial symptoms in various domains of brain function generally tend to improve during stroke recovery. This general tendency thus has to be taken into account as a potential alternative explanation of the present findings. Nevertheless, the parallel decrease in both behaviours is suggestive to assume a close relationship. In fact, it was observed in every single patient with spatial neglect of the present sample.

Previous studies followed the patients' spontaneous eye/head position by clinical inspection in the acute and subacute stage (De Renzi et al., 1982; Kömpf & Gmeiner, 1989; Tijssen, 1988). However, its progress was not related to the co-occurrence of spatial neglect. The average duration of eye deviation in these studies was estimated between 12.5 days (De Renzi et al., 1982) and 18.5 days (Kömpf & Gmeiner, 1989). Ringman, Saver, Woolson, and Adams (2005) conducted a post-hoc analysis on a data subset of a previous multicenter study. Three months post stroke, neither left nor right hemisphere patients showed a spontaneous deviation of the eyes. Yet, the authors did not relate their results to the recovery of spatial neglect in this sample. The study of De Renzi et al. (1982) investigated the co-occurrence of spatial neglect once between day 14 and 18. At this time, all patients with a clinically defined eye or head deviation showed neglect symptoms. However, the disorder was also found in some of those patients whose initial eye/head deviation had already recovered but who had not previously been investigated for spatial neglect. Although the results of De Renzi and co-workers (1982) are not strictly comparable with the present study (different procedures to detect gaze deviation and to test for spatial neglect, and so forth), they bear an interesting analogy, namely the gradual difference in the recovery of eye deviation compared to the recovery of other clinical neglect symptoms.

A further argument for a close relationship between active and passive neglect behaviour is provided by recent anatomical findings. Singer, Humpich, Laufs, Lanfermann, Steinmetz, and Neumann-Haefelin (2006) studied brain lesions in patients with a *passive* deviation of the eyes. They described a network of structurally affected regions in the right hemisphere, including the temporoparietal junction and the basal ganglia as well as perfusion deficits in the right inferior parietal cortex, the supramarginal gyrus, the middle and superior temporal cortex, as well as parts of the insula. Interestingly, these regions are known to be structurally injured in patients with spatial neglect (Heilman, Watson, Valenstein, & Damasio, 1983; Karnath, Ferber, & Himmelbach, 2001; Karnath, Fruhmann Berger, Küker, & Rorden, 2004; Mort et al., 2003; Vallar & Perani, 1986) as well as to be malperfused though structurally intact in cases of subcortical neglect (Karnath, Zopf, Johannsen, Fruhmann Berger, Nagele, & Klose, 2005).

The present study revealed that both, passive and active neglect behaviour, have a parallel time course that starts at a different level of impairment. One obvious explanation for these gradual differences at stroke onset may be the task difficulty of our exploration task. It required to search for a non-existing target in a very dense array of distractors that covered 240° of horizontal space. Previous studies on active tasks have shown that the rightward bias is reduced by decreasing the number of stimuli in search displays (DeRenzi, Gentilini, Faglioni, & Barbieri, 1989; Husain & Kennard, 1997; Kartsounis & Findlay, 1994; Rapcsak, Verfaellie, Fleet, & Heilman, 1989) or during visual exploration in darkness (Hornak, 1992; Karnath, Fetter, & Dichgans, 1996). Thus, it is feasible that less complex visual exploration tasks would provoke eye/head shift amplitudes that are more comparable in extent to those at rest.

In conclusion, our present finding on a parallel development of active and of passive neglect behaviour strengthen the view that the characteristic feature of the disorder, namely the marked deviation towards the ipsilesional side, might be due to a very elementary disturbance of those transformation processes that convert the multimodal sensory input (visual, vestibular, neck proprioceptive, etc.) into internal representations of space, providing us with redundant information about the position and motion of our body relative to external space (Karnath, 1997; Karnath & Dieterich, 2006). In consequence of this disturbed co-ordinate transformation, patients with spatial neglect show a specific bias that might represent a pathological default position of the eyes and the head at a new origin on the ipsilesional side under both rest and active task conditions. In fact, this lateralised behaviour was observed while "doing nothing" as well as during active search. This shift may be understood as a pathological adjustment of the subject's normal resting position at a new, spatially lateralised location on the ipsilateral side.

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Author Notes

Monika Fruhmann Berger and Hans-Otto Karnath, Section Neuropsychology, Center of Neurology, Hertie-Institute for Clinical Brain Research, University of Tübingen, Tübingen, Germany; Leif Johannsen, Behavioural Brain Sciences Centre, School of Psychology, University of Birmingham, Birmingham, U.K.

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Correspondence concerning this article should be addressed to Monika Fruhmann Berger, Center of Neurology, Hertie-Institute for Clinical Brain Research, University of Tübingen, Hoppe-Seyler-Str. 3, D-72076 Tübingen. Fax: ++49-7071-295957, E-Mail: monika.fruhmann@gmx.de

Table 1

Demographic and clinical data of the right hemisphere stroke patients with spatial neglect and the control patients without spatial neglect.

			Neglect Acute stage		**Neglect** Chronic stage	**No Neglect** Acute stage	
			Exam 1	**Exam 2**	**Exam 3**	**RBD**	**NBD**
Number of patients			6			6	6
Sex			6m			4m, 2f	4m, 2f
Age (years)		*Mean (SD)*	62.7 (12.4)	62.7 (12.4)	63.5 (12.3)	51.8 (13.5)	59.8 (8.3)
Aetiology		Infarct	5			4	
		Haemorrhage	1			2	
Time since lesion (days)		*Mean (SD)*	12.2 (5.3)	18.7 (5.2)	317.2 (156.0)	12.0 (7.4)	
Contralateral paresis		% present	100	83.3	83.3	100	0
Lesion location			NEG1 Bg			RBD1 P	
			NEG2 F, P, T, I			RBD2 Bg, I	
			NEG3 Bg			RBD3 Bg	
			NEG4 F, P, T, I, Bg			RBD4 T, I, P	
			NEG5 F, P, T, I, O, Bg			RBD5 F, P	
			NEG6 F, T, I, Bg, Th			RBD6 P, O, Th	
Visual field defect		% present	0	0	0	0	0
Spatial neglect							
Letter cancellation (hits)	Left	*Mean (SD)*	2.8 (4.0)	8.7 (10.0)	23.3 (7.3)	29.7 (0.8)	
	Right	*Mean (SD)*	16.0 (10.0)	20.3 (11.1)	29.8 (0.4)	29.3 (0.5)	
Bells test (hits)	Left	*Mean (SD)*	0.7 (0.8)	3.0 (4.3)	10.0 (3.9)	14.2 (0.8)	
	Right	*Mean (SD)*	8.5 (5.4)	10.7 (4.8)	14.7 (0.5)	15.0 (0.0)	
Copying (% omitted)		*Mean (SD)*	60.4 (27.9)	43.8 (40.1)	25.0 (27.4)	0.0 (0.0)	

Note. NEG = right brain damage with spatial neglect, RBD = right brain damage without spatial neglect, NBD = non brain damage, f = female, m = male, *SD* = Standard deviation, F = frontal, P = parietal, T = temporal, O = occipital, I = insula, Th = thalamus, Bg = basal ganglia.

Figure 1

Scan paths (= gaze) of the patients with spatial neglect during active visual search (black lines) as well as at rest (grey lines) for each time of examination (upper three panels) compared to the group of control patients without neglect (panel four). In the acute stages of the disorder (Exam 1 & 2), the neglect patients showed a marked bias of their active and their passive behaviour towards the ipsilesional, right side (Exam 1 > Exam 2). In the chronic stage (Exam 3), both performances converged towards those of patients without the disorder (panel three).

Figure 2

Mean horizontal gaze position of the patients with spatial neglect during active visual search (closed circles) and at rest (closed triangles) for each time of examination (Exam 1 to 3) compared to the performances of the patients without the disorder (visual search: open circle, rest position: open triangle). In addition, the averaged neglect severity as measured by the clinical neglect tests is given (closed squares). The doted horizontal line represents the position of the mid-sagittal body axis (0°).

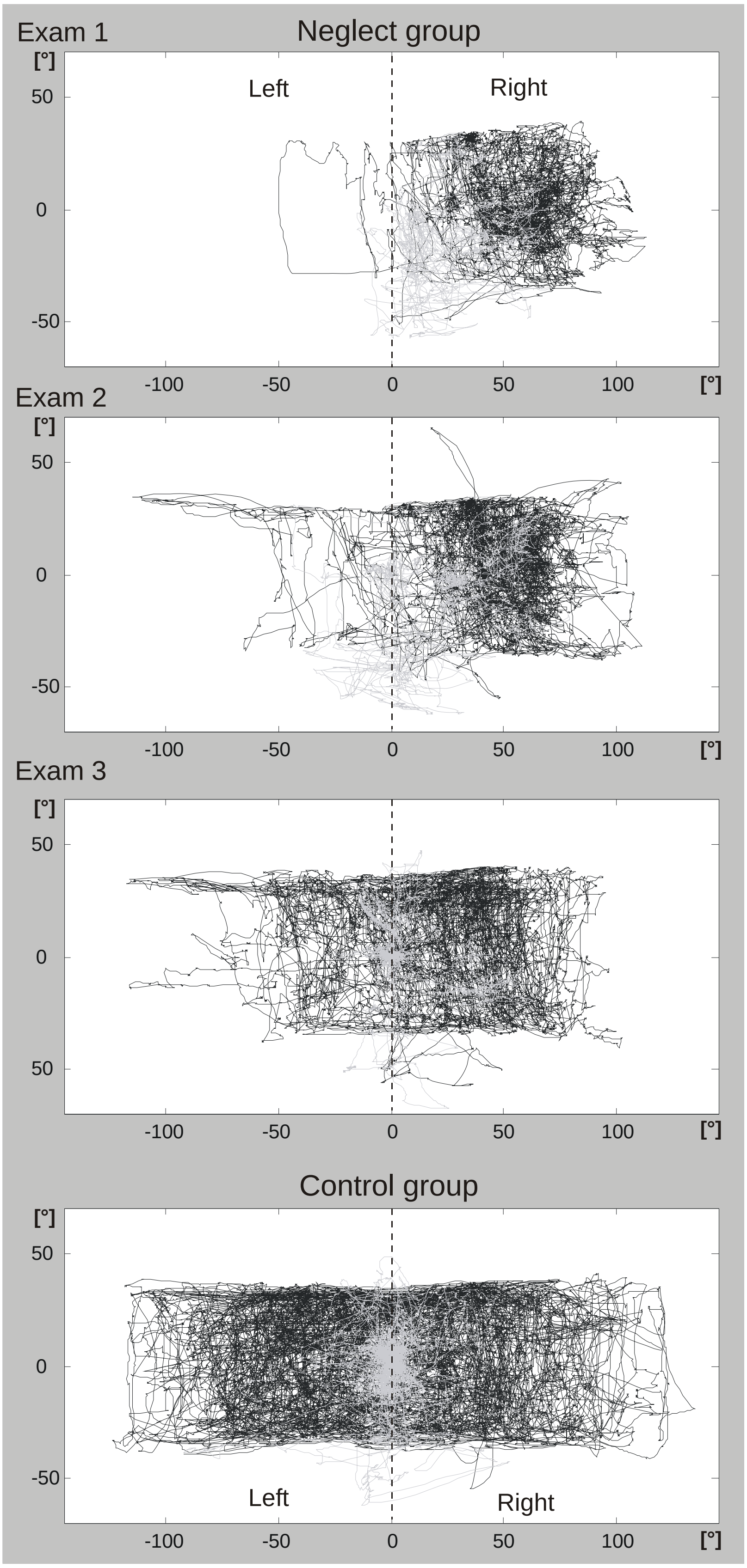

Fig. 1. Active and passive neglect behaviour

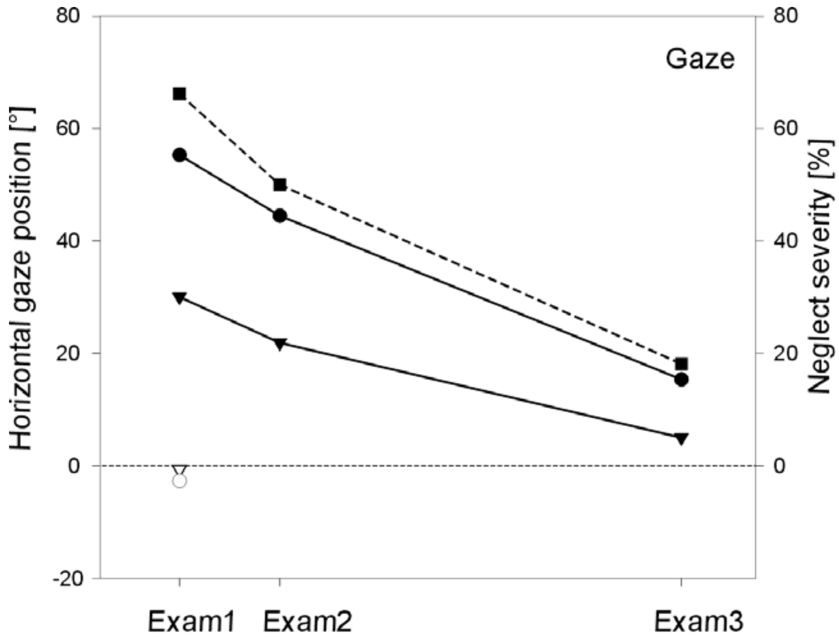

Fig. 2. Active and passive neglect behaviour