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Spatial judgments in patients with retinitis pigmentosa

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ABSTRACT

Previous investigations into cortical plasticity in the presence of ocular disease have focused on central retinal damage. Perceptually, patients often report distortions of visual space which can be partially explained by perceptual filling-in. The mechanisms involved could also apply to peripheral field loss. Spatial interval discrimination was tested in 28 retinitis pigmentosa (RP) patients and a control group. When stimuli were presented to both hemispheres, bias did not differ whereas threshold was poorer in RP patients. When presenting the task to only one hemifield, bias was related to field asymmetry, but only in the left visual field, $r^2 = .59$. Brain laterality may be an important factor when examining changes in cortical function in response to peripheral system damage.

1. Introduction

Retinitis pigmentosa (RP) describes a group of hereditary genetic diseases that lead to photoreceptor death, resulting in progressive peripheral visual field loss and, in some cases, to blindness. Since RP is limited to cell death within the eye, the visual cortex should not be affected directly and should remain functionally organized in a retinotopic fashion. Even though progressive peripheral field loss is one of the hallmarks of RP, there has been a small number of studies addressing various components of spatial processing in central vision in RP, including space perception at various eccentricities (Temme, Maino, & Noell, 1985), relative space perception in 3D space (Turano & Schuchard, 1991) as well as in virtual environments (Fortenbaugh, Hicks, & Turano, 2008), symmetry perception (Szlyk, Seiple, & Xie, 1995; Wagemans, 1998) and spatial bisection (Turano, 1991). The most remarkable finding across these studies is the large variability in participant performance and the lack of clear evidence that clinical parameters such as field loss progression or disease state can predict performance.

One of the assumed consequences of progressive field loss would be a reduction of activity in primary visual areas of the cortex that used to receive stimulation from peripheral retina. Such changes have previously been summarized by Komatsu (2006) who reviewed studies on the retinotopic reorganization in primary visual cortex (V1) in the presence of central retinal scotomas and the associated visual distortions. The effects of central loss may be more easily observable at the cortical level since a larger proportion of primary visual cortex is dedicated to central vision (cortical magnification); however, the possibility of this occurring in the periphery as well has previously been suggested in the context of peripheral scotomas due to panretinal photocoagulation during the treatment of diabetic retinopathy (Dosso, Ustun-Yenice, & Safran, 2000). Work by Poggel et al. (ARVO E-Abstract 935, 2007) indicated that areas of V1 that would be expected to activate when processing peripheral visual stimulation show activation in RP patients when the central retina is stimulated. This result would point toward a certain amount of adaptability in the adult V1 with regard to retinotopic organization once peripheral retina has succumbed to cell death. The cortical areas that would be expected to remain silent due to loss of retinal input may be re-allocated to the processing of central information. This process has previously also been considered in the context of glaucoma but remains to be established with more certainty, specifically in RP patients (Duncan, Sample, Weinreb, Bowd, & Zangwill, 2007a; Duncan, Sample, Weinreb, Bowd, & Zangwill, 2007b).

Recently, Masuda and colleagues (2010) reported that cortical responses in V1 of RP patients show similar task-dependent activation as previously observed in patients with age-related macular degeneration (AMD) (Masuda, Dumoulin, Nakadomari, & Wandell, 2008). Masuda's team investigated whether passive viewing tasks, such as standard fMRI stimuli like drifting contrast patterns or

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reversing checkerboards, elicited different activation patterns across V1 when compared to more active testing paradigms, such as the judgment of consecutively presented visual stimuli (one-back task). Their findings indicated, in both AMD and RP patients, that cortical activity was much lower during passive stimulation and retinotopically predictable based on areas of healthy retina, whereas the active task engaged areas of V1 that were retinotopically not stimulated due to the presence of scotomas in AMD or peripheral field loss in RP. If cortical changes in retinotopic allocation of surface area in V1 are indeed occurring in patients with peripheral visual field loss, this re-distribution of activity could have behavioral consequences that should be measurable using psychophysical tests. The presence of such functional changes is of great importance for both clinicians and rehabilitation specialists, since they could be useful in diagnosis, disease progress, prognosis and skill training during rehabilitation.

The changes in visual perception that could result from retinotopic reorganization should be most apparent in basic visual domains, such as spatial vision. A small number of studies has investigated various aspects of spatial vision in RP; however, their findings are inconclusive as to whether or not the perception of visual space is changed in the presence of RP and which factors may be responsible for these effects. Temme et al. (1985) investigated the perception of stimulus eccentricity in three RP patients and four normal observers, using a Goldmann visual field perimeter. Participants were asked to monocularly view one III/4e Goldmann target at a time within the perimeter and then mark its perceived distance from fixation on a sheet of paper. When comparing the results of RP patients with controls, the data indicated that the perceived distance from fixation was overestimated by both groups, however, more so by RP patients. The authors concluded that these individuals with peripheral field loss experience a perceptual magnification of their central visual field, which results in overestimation of distances. This observed stretching of spatial information is consistent with a study by Dilks, Serences, Rosenau, Yantis, and McCloskey (2007) who described perceptual stretching of shapes presented at the border of quadranopic visual field loss. One could consider this perceptual phenomenon as *perceptual filling-out*.

Another relevant study on spatial perception in RP patients utilized a bisection task to investigate changes in central vision (Turano, 1991). The author asked 23 RP patients to monocularly view a stimulus display consisting of a central fixation bar and two equally spaced vertical flanker bars. The test stimulus was presented between either the upper or lower bar pair. At each 110 ms stimulus presentation, participants were asked to judge whether the test stimulus was located closer to the top, center or bottom reference bar. The resulting data provided information about both bias and threshold of the judgments. Surprisingly, the data on bias contradicted the findings by Temme et al. (1985) in some patients and showed values comparable to normal performance in others. Similarly, the threshold data exhibited great variability. The author then attempted to account for the variability in the data with clinical characteristics; however, much as in the study by Temme et al. (1985), neither disease duration nor progression were good indicators of performance levels.

2. Experiment 1 – symmetrical spatial interval discrimination

Based on these previous reports, it appears that the evidence for changes in spatial vision in RP patients remains sketchy. In part, these inconclusive findings may be based on small sample sizes and heterogeneity in the patient population; in part, the differences may be due to variations in methodological approaches. The study on bisection (Turano, 1991) only reported on monocular performance; however, most real-life tasks are executed binocularly. Measurements of binocular function may be affected both by summation as well as by interactions due to different levels of impairment in each eye. Therefore, it was decided to test both monocular and binocular spatial interval discrimination in individuals with RP, in order to investigate whether similar performance patterns could be found. Furthermore, the study by Turano (1991) focused on vertical judgments but no information using horizontal stimuli is presently available. This gap in the literature was addressed with the testing paradigm used in the present experiments and was applied to RP patients. Two effects were expected: (1) In line with the findings by Temme et al. (1985), the perceived point of spatial equidistance (bias) in spatial interval judgment would shift away from fixation in RP patients as a function of field loss, representing an expansion of visual space, and (2) slopes of the psychometric functions (threshold) would be shallower in RP patients, due to loss of partial visual information associated with random loss of photoreceptors.

2.1. Method

The protocol was approved by the Research Ethics Committee of the Center for Interdisciplinary Research in Rehabilitation of Greater Montreal (CRIR), the supervising research ethics board for the Institut Nazareth et Louis-Braille (INLB), and the Institutional Review Board of the SMBD Jewish General Hospital, Montreal, in accordance with the Canadian Tri-Council Policy Statement of ethical conduct for research involving humans.

2.2. Participants

Individuals with normal vision were recruited from the Department of Ophthalmology at the SMBD Jewish General Hospital, as well as among staff and members of the McGill Low Vision lab. The 29 participants ranged in age from 23 to 69 years ($M = 44$, $SD = 3$), with a minimum of five individuals per decade. Individuals with RP were recruited from the INLB Longueil. A chart review of patient files in September 2008 identified 614 individuals with a diagnosis of RP that were currently being followed. Of those, 68 persons fulfilled the recruitment criteria of visual acuity better than 20/60 in at least one eye and with at least one monocular horizontal visual field diameter larger than 5 dva. Closer examination of these files revealed that 19 participants were unsuitable for testing due to co-morbid conditions, such as Usher's Syndrome (15) or other ocular (2), physical (1) or cognitive (1) problems. Of the remaining 49 participants, a total of 27 were recruited into the study from the INLB between September 2008 and February 2009. The reasons for non-participation included inability to contact the person (13), the person was not available within the proposed testing schedule (5), or lack of interest (4). One additional participant was recruited at the SMBD Jewish General Hospital Department of Ophthalmology. Two of the participants were excluded because they were unable to complete the protocol due to insufficient acuity upon arrival at the testing session, resulting in analyzable data for a total of 26 RP patients (see Table 1 for patient characteristics). All participants were screened for the integrity of their cognitive status, using the Montreal Cognitive Assessment, which has been validated in English and French (Nasreddine et al., 2005).

2.2.1. Materials and procedure

The purpose and procedure of the experiment were explained and informed written consent was obtained before testing began. Participants were refracted with trial lenses when needed, using the NIDEK Autorefractor ARK-760A (VisionMedical, Montreal, Quebec, Canada). Both monocular visual acuities were tested using standard ETDRS charts at a distance of 4 m (Lighthouse

Table 1
Patient characteristics of participants with retinitis pignemntosa.

ID	Sex	Age	MoCA	Mths since last field	VA OD (log MAR)	OD		VA OS (log MAR)	OS	
						RVF (°)	LVF (°)		RVF (°)	LVF (°)
1	M	20	27	5	0.38	55.83	26.67	0.38	12.08	52.92
2*	M	22	30	16	0.16	5.42	5.00	0.22	8.33	6.25
3	F	22	29	25	0.28	12.50	7.92	0.38	7.92	10.83
4	F	26	28	31	0.32	12.92	12.50	0.24	13.33	13.33
5	M	27	28	14	0.58	7.50	7.92	0.50	8.33	8.75
6	M	27	29	4	0.16	10.83	7.08	0.22	10.83	7.08
7*	M	34	28	11	0.52	10.42	6.67	0.24	6.67	6.67
8*	M	36	26	45	0.30	5.00	3.33	0.42	4.58	5.83
9*	F	38	30	47	0.20	12.08	13.75	0.06	12.92	19.17
10*	M	39	26	1	0.42	6.67	7.92	0.30	6.25	10.83
11*	F	42	28	34	0.26	4.17	3.75	0.36	3.75	5.42
12	F	42	29	23	0.16	34.58	19.58	0.20	19.17	27.08
13	F	43	30	13	0.28	5.42	9.17	0.26	8.75	6.25
14*	F	46	27	35	0.22	13.33	12.92	0.24	14.58	11.67
15*	F	46	30	45	0.16	9.71	6.67	0.06	10.00	10.83
16*	F	48	30	22	0.40	8.33	7.92	0.34	7.50	10.42
17	M	50	27	9	0.38	8.75	9.17	0.30	10.00	7.08
18	M	51	28	9	0.36	7.50	13.33	0.38	14.58	7.92
19*	M	51	29	78	0.28	5.00	6.67	0.18	5.42	7.50
20	M	57	27	1	0.20	5.42	2.50	0.32	3.75	2.08
21*	F	57	28	5	0.20	9.58	10.00	0.08	10.42	10.00
22	F	57	28	15	0.11	8.75	9.58	0.00	8.33	10.00
23	F	58	29	13	−0.05	7.92	7.92	−0.06	9.17	6.25
24*	F	59	24	0	0.18	4.58	2.92	0.16	4.17	8.33
25	M	60	30	31	0.20	10.00	6.25	0.18	12.50	8.33
26	M	63	23	43	0.34	10.42	12.08	0.34	12.08	17.50
Avg		43	28	22	0.27	11.23	9.20	0.24	9.44	11.47
Low	M:14	20	23	0	−0.05	2.08	2.92	−0.06	3.75	2.08
High	F:14	63	30	78	0.58	34.58	26.67	0.58	19.17	52.92

Note: *indicates individuals who participated in both Experiments 1 and 2.
OD = right eye, OS = left eye, VA = visual acuity, RVF = right visual field, LVF = left visual field, MAR = minimum angle of resolution.
M = male, F = female.

International, New York, NY). Acuities for the control group ranged from 20/14 to 20/32. All participants were corrected for testing distance, when needed, or wore their habitual glasses. Normally sighted participants were tested monocularly and/or binocularly, depending on their availability, and were compensated for their efforts by receiving $40 per testing session. RP patients were all tested monocularly and binocularly and received $80 in compensation for travel expenses.

2.2.2. Spatial interval discrimination test

Participants were seated facing a computer screen, placing their head in a chin- and forehead rest. Visual stimuli were presented on a RGB display powered by a PC (Intel Pentium 4 processor) at a viewing distance of 67 cm. Fig. 1a displays the spatial interval discrimination test-display used in Experiment 1. It consisted of two white circular dots (130 cd/m^2) presented around a small fixation target on a grey background (33 cd/m^2). Dot size was defined by the Gaussian function, whereby 2 SD fell within 1° of visual angle (dva), making the visible diameter of the dot appear at approximately 1 dva. Dot size was held constant at all testing eccentricities. Stimuli were presented at 1, 3, and 5 dva eccentricity horizontally from fixation. At each eccentricity, one flanker target was at the respective fixed eccentricity while the opposite flanker varied within a predetermined set of five distances, ranging ±20% of the eccentricity at 5% intervals (method of constant stimuli). For example, at 1° eccentricity for the fixed flanker dot, the test eccentricities were 0.8, 0.9, 1.0, 1.1 and 1.2 dva for the variable flanker dot. Each variable test eccentricity was presented 20 times and was randomly intermixed with trials of the opposite trial set (reversed fixed flanker and variable flanker dots). The fixed flanker varied from trial to trial; therefore, from the participants' perspective, both dots moved within one trial set, consisting of 200 trials per set. Participants were asked which dot appeared closer to the central fixation spot and responded by pressing one of two keys on a keyboard. Participants were allowed to take rest breaks as needed. The protocol required approximately 3 h of testing per eye for normally sighted participants; therefore, those who were available for monocular and binocular testing returned twice on separate days to complete the testing sessions. For RP participants, the testing duration depended on the size of their visual field but did not exceed 3 h, including breaks.

2.2.3. Dependent variables

The data collected from the spatial interval discrimination test were analyzed by fitting psychometric curves (Weibull function) to the proportional responses as a function of eccentricity. The two dependent variables of interest were the *midpoint* of these functions (bias) and the *slope* at the midpoint (threshold). Using MATLAB R2006b Version 7.3 (Mathworks, Novi, MI), both bias and threshold values were calculated and imported into SPSS for further statistical analysis. In order to be able to analyze bias scores on a comparable scale across eccentricities, bias was defined as midpoint values expressed as a percentage of the absolute eccentricity at which the stimuli were presented, using the following formula:

$$\text{bias} = \frac{\text{Midpoint} - \text{Eccentricity}}{\text{Eccentricity}} * 100$$

Positive values in this conversion indicate the retinal position of the perceived point of equidistance shifted towards the visual periphery away from the fovea. Threshold values were transformed by taking the logarithm to the base 10 in order to assure normal distribution of the data.

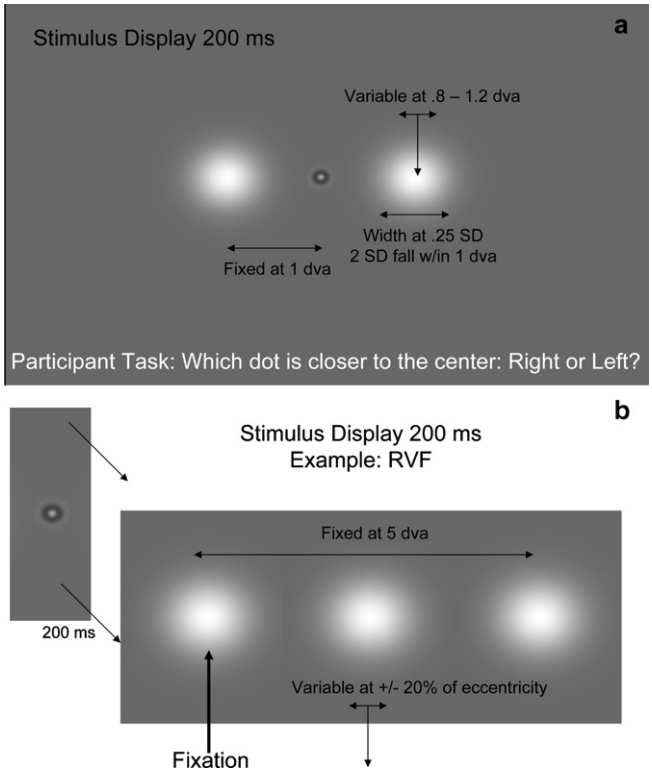

Fig. 1. The spatial interval discrimination test displays for Experiment 1 (1a-top) and Experiment 2 (1b-bottom). 1a displays an example stimulus at 1° eccentricity. Participants fixated at the central fixation target (continuous presentation) and made judgments about which of the two flanker dots appeared closer to the central target. 1b displays an example of the display shifted into one hemifield. Participants fixated on the same target as in 1a but in its place one of the flanker targets would appear (see text for details). ms = milliseconds, dva = degrees of visual angle, SD = standard deviation.

2.3. Results

Statistical significance was set at an alpha level of .05 for all analyses. Complete monocular and binocular data were only available for 11 normally sighted participants. In order to maintain the maximum number of possible data points for the various analyses, data from separate eyes were pooled according to retinal or hemispheric visual field location. Age was entered as a covariate for all analyses of covariance in this experiment. However, this variable did not reach statistical significance as a covariate, indicating that neither accuracy nor precision was affected by chronological age. This variable was, therefore, dropped from the analyses and only the results of analyses of variance (ANOVAs) are reported here.

In order to adhere to the necessary data distribution of mixed ANOVA designs, for the monocular viewing condition, RP participants were divided into two groups: those with larger visual fields who were able to complete the testing procedure out to 5 dva ($n = 6$), and those with smaller fields who were only able to provided data for up to 3 dva ($n = 7$). However, the analysis of data obtained from RP patients with smaller fields did not differ in a meaningful way from those with larger fields. Therefore, only the results from the latter group are reported in detail here. The data were separated by stimulus presentation to either the temporal or nasal side of either retina. For participants where both eyes were tested, the two scores were pooled. For the purpose of graphical display, the data were collapsed across retinal or hemispheric location since this variable did not reveal significant effects.

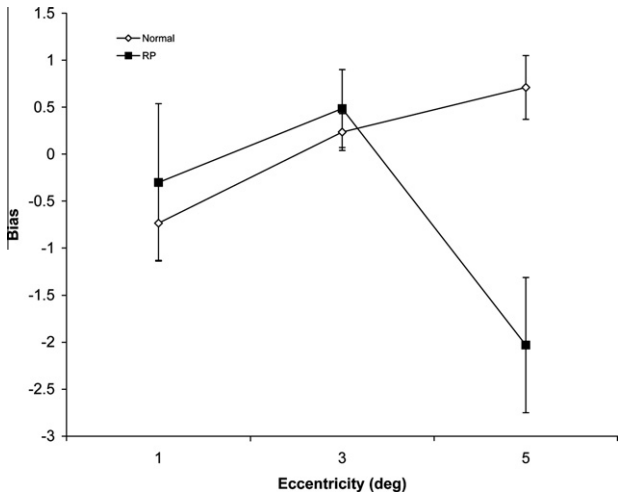

Fig. 2. Bias as a function of eccentricity for the monocular viewing condition for retinitis pigmentosa (RP) patients with larger visual fields and normal observers. Error bars represent one standard error of the mean.

2.3.0.1. Analysis 1. Monocular viewing: retinal eccentricity × location × ocular health

This analysis examined the effects of eccentricity (1, 3, 5 dva), retinal location (nasal/temporal) and ocular health (normal/RP) on bias and threshold under monocular viewing. A 3 × 2 × 2 within-between ANOVA on bias scores revealed a statistically significant interaction of eccentricity and ocular health state when comparing RP patients to normal observers, $F(2, 62) = 6.01$, $p < .004$, $\eta^2 = .17$. Post-hoc analysis indicated that bias scores were more negative in RP patients, however, only at the furthest eccentricity of 5 dva, $p < .001$ (Fig. 2). For threshold values, neither the triple nor the dual interactions were statistically significant. For the main effects, the ANOVA indicated that thresholds were only statistically significantly affected by ocular health state, $F(1, 31) = 22.13$, $p < .0001$, $\eta^2 = .42$. Post-hoc analysis indicated that scores for RP patients were smaller across all eccentricities, $p < .05$ (Fig. 3).

2.3.0.2. Analysis 2. Monocular viewing: retinal eccentricity × visual field × ocular health

The statistical effects detected in this analysis are mathematically identical to the comparable effects in Analysis 1. This is due to the fact that the same data were re-analyzed, under different pooling conditions. This difference in pooling the data did not reveal different effects.

2.3.0.3. Analysis 3. Binocular viewing: retinal eccentricity × visual field × ocular health

The third analysis examined the effects of eccentricity (1, 3, 5 dva) and visual field location (right/left) on bias and threshold, however now under a binocular viewing condition. Data were available for 11 normal observers and 13 RP patients. The sample size for RP patients was larger compared to the previous analyses because several patients only had sufficient visual field sizes for this task under the binocular viewing condition since the overlap of both monocular fields allowed them to perceive a larger stimulus display. ANOVA did not reveal any statistically significant main- or interaction effects for bias scores, indicating that eccentricity, visual field and ocular state did not affect performance under binocular viewing. For threshold, the ANOVA did reveal that values were statistically significantly different according to ocular health state, $F(1, 22) = 9.83$, $p < .005$, $\eta^2 = .31$. *Post-hoc* analysis

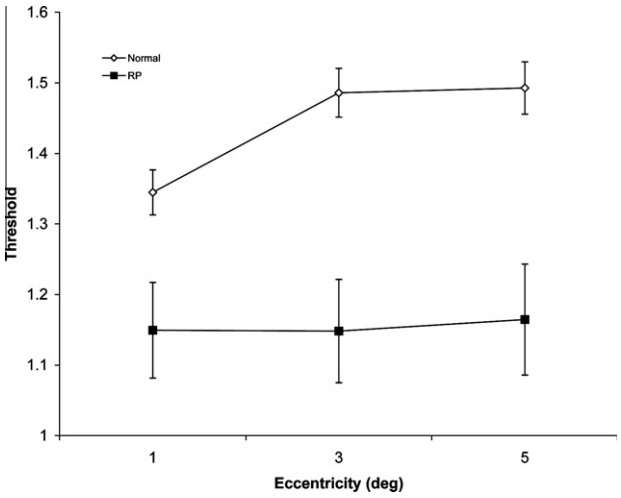

Fig. 3. Threshold as a function of eccentricity for the monocular viewing condition for retinitis pigmentosa (RP) patients with larger visual fields and normal observers. Error bars represent one standard error of the mean.

indicated that scores for RP patients were smaller across all eccentricities, $p < .05$ (pattern similar to Fig. 3 in Analysis 1).

2.3.0.4. Analysis 4. Correlation of visual field ratio and bias ratio

The bias variable can have positive and negative values, indicating a shift of the psychometric function away or towards fixation, respectively. In order to examine whether these shifts are related to the extent of the visual field diameter in RP patients, an analysis was conducted that correlated the ratio of the right and left monocular and binocular field diameters, as measured by Goldmann perimetry, with the bias scores obtained at the maximum possible eccentricity on the spatial interval discrimination task. The calculation of ratios was conducted as follows: Field ratio = RVF diameter/LVF diameter. Values of 1 indicated symmetrical visual fields, values larger than 1 indicated visual fields that were larger on the right, and values smaller than 1 indicated that visual fields were larger on the left. The calculation of bias ratios followed the same logic. However, during this transformation, it must be considered that bias scores could be either positive (shift away from fovea) or negative (towards fovea). Therefore, the absolute values of these ratios were of less interest. More importantly, ratio values that were positive indicated that bias scores in the two hemispheres were either both positive (shift of the function away from fixation in both hemispheres = perceptual expansion of visual space) or both negative (shift of the function towards fixation in both hemispheres = perceptual compression of visual space). When the bias ratios were negative, either one of the bias values must have been negative, indicating that the visual field shifted away from fixation in one eye and towards in the other. For OD and OS, 77% of the bias ratios were negative while for OU 84% of the bias ratios had negative values, $\chi^2(1, n = 22) = 6.54$, $p < .025$ and $\chi^2(1, n = 25) = 11.56$, $p < .005$, respectively. These results indicate that visual space is shifted in the same horizontal direction in patients with visual field loss, independently of their visual field diameter, as measured by Goldmann perimetry.

2.4. Discussion

The purpose of this experiment was to evaluate whether bias and/or threshold on a task of perceived spatial judgments would be influenced by the presence of peripheral visual field loss due to RP, the cortical hemisphere which processed the spatial information, and/or at which retinal eccentricity the task was presented. The first point of interest in the data set regarding accuracy is the small and similar range of bias scores in RP and normal observers, indicating that spatial interval discrimination may not differ in a functionally relevant way for RP patients. When examining the directional differences in monocular bias scores, RP patients with larger fields demonstrated a shift of spatial judgments towards fixation closer to their visual field border. This result would indicate a compression of visual space compared to performance of normal observers at the same eccentricity and is in direct contradiction to the reports by Temme et al. (1985) whose data indicated expansion of field perception. However, Temme's team presented stimuli on one side of the visual field at a time whereas in the present experiment the comparator reference stimulus was presented in the opposite visual field. If space perception in the present sample was indeed contracted, then both the test- and the reference-stimulus should be equally shifted by this effect (this question is further considered in Experiment 2).

When analyzing the data by either pooling across retinal locations or across visual field hemisphere, the results failed to show any significant differences between normals and both groups of RP patients. In part, this may be due to the smaller range of tested eccentricities in RP patients and the associated reduced sample size when comparing with data from normal observers. The results regarding thresholds of performance revealed that, regardless of monocular/binocular viewing, hemispheric processing or eccentricity, normal observers overall demonstrated higher threshold values when compared to RP patients with either smaller or larger visual fields. This decrease in the presence of RP could be due to factors such as random central photoreceptor loss which could reduce sampling of visual information (Reme, Grimm, Hafezi, Iseli, & Wenzel, 2003), changes in receptive fields of ganglion cells that reorganize based on changes in bipolar cell activity (Marc et al., 2007), or changes in fixation behavior and stability of RP patients (Luo, Vargas-Martin, & Peli, 2008), which could contribute further to uncertainty when executing spatial interval discrimination judgments.

Possibly the most intriguing finding of this experiment was the exploratory analysis of the distribution of visual field ratios and bias ratios. The large majority of both monocular and binocular bias ratios were negative, independently of the level of visual field asymmetry. The negative sign of the bias ratios indicated that one of the two bias values was positive while the other was negative before the ratio was calculated. Functionally, this should translate into a shift of the entire visual field in one direction only, meaning, if perception was altered towards one side of the visual hemisphere, it was shifted towards the same side in the other hemisphere. This finding contradicts previous reports whereby the visual field generally contracted or expanded (Fortenbaugh et al., 2008; Temme et al., 1985; Turano, 1991; Turano & Schuchard, 1991). The nature of the present data analysis did not, however, allow for a direct demonstration of the direction in which this shift actually occurred. In order to examine this phenomenon in more detail and to address the methodological limitation of symmetric stimulus presentation in both hemispheres simultaneously, Experiment 2 was designed to tease some of these issues apart.

3. Experiment 2: asymmetric spatial interval discrimination

While the study by Turano (1991) utilized a symmetrical stimulus display around fixation, much like in Experiment 1, the study by Temme et al. (1985) has been the only one to provide information based on a testing paradigm that relied on stimulus presentation in one half of the visual field at a time (asymmetrical), thereby examining differences in hemispheric spatial perception of patients with RP. Within the central 20 dva, RP patients responded

with the same level of accuracy as normal observers; however, stimuli that were presented beyond that eccentricity and which thereby approached the limits of their visual fields, were generally perceived further away from fixation. This was the case for both the nasal and temporal side of the fields tested. The authors interpreted these findings as support for their hypothesis that visual space is perceived as magnified toward the limits of the field; however, asymmetries in the field loss were not considered in their study.

Given the variable results of previous studies and the shortage of information about binocular spatial perception in RP patients, the second experiment was designed to examine both monocular and binocular spatial interval discrimination in one visual field at a time. In line with the findings by Temme et al. (1985), it was hypothesized that binocular bias scores in each hemifield of RP patients would be larger and more positive (shift away from fixation) as eccentricity increased and stimulus location approached the limit of the visual field.

3.1. Method

The protocol for this experiment was covered within the ethics approvals for Experiment 1. Twelve participants from Experiment 1 were contacted and invited to return for an additional testing session. They have been identified with a "*" next to their ID code in Table 1.

3.1.1. Materials and procedure

The testing materials and the stimulus parameters of the spatial interval discrimination test were identical to Experiments 1. However, the placement of the fixation target and the stimuli were changed in such a way that one of the flanker dots now appeared in the fixation location (see Fig. 1b). The middle target and the opposite flanker dot appeared both either to the right or the left of fixation. In this protocol, both flanker dots remained stationary for every stimulus presentation, while the central dot was displaced on each trial with the same proportional difference as in Experiment 1. When, for example, the outside flanker dot was presented at 4 dva, the middle target appeared randomly at one of seven locations, within ±30% of the middle eccentricity. In this case, the middle target appeared at 1.4, 1.6, 1.8, 2.0, 2.2, 2.4 or 2.6 dva from fixation. Therefore, bias was calculated in relation to the center of the flanker dots. Given the diameter of the test and flanker stimuli, the smallest testable eccentricity for the outer flanker target was 3 dva. Participants completed trial sets monocularly in both the right and left visual field, at their field limits. In addition, all possible eccentricities were tested binocularly in each visual field.

3.2. Results

Statistical significance was set at an alpha level of .05 for all analyses. The first analysis included all 12 participants since they were all able to complete the testing for an eccentricity of up to 5 dva for the outer flanker target. A factorial 2×3 (hemifield $\times$ eccentricity) within-subjects ANOVA for bias did not reveal any statistically significant main- or interaction effects. When the data set was reduced to participants who were able to view the flanker target out to 7 dva ($n = 9$), a factorial 2×5 (hemifield $\times$ eccentricity) within-subjects ANOVA also did not reveal any statistically significant effects. These results indicated that bias did not increase (or decrease) as a function of eccentricity in RP patients under binocular viewing conditions.

Any possible relationship between bias and the extent of visual field asymmetry was investigated by correlating the bias scores with the ratio of visual field diameter, by dividing the diameter of the RVF by the measurement in the LVF. A value of 1 would indicate perfect field symmetry. When correlating monocular bias scores with monocular field ratios, none of the correlation coefficients were statistically significant. Under the binocular condition, there was no statistically significant relationship for data in the RVF ($r^2 = .02$) but the values were significantly correlated for data in the LVF, $r^2 = .59$ (see Fig. 4). This result indicated that, if the LVF was larger, bias scores in the LVF were shifted away from fixation while, if the LVF was smaller, bias scores in the LVF were shifted toward fixation.

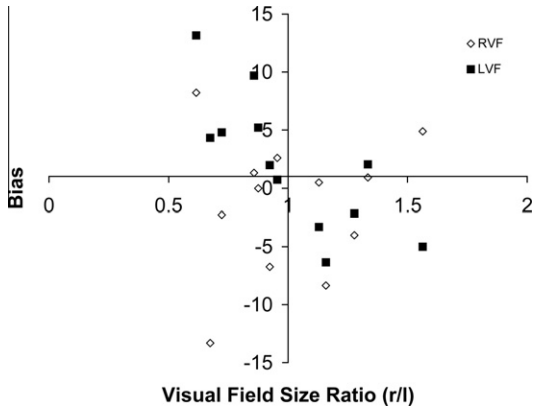

Fig. 4. Bias as a function of visual field size ratios for binocular viewing in the right and left visual field of RP patients. For the LVF, a significant correlation was detected, $r^2 = .59$, indicating that bias scores in the LFV were shifted away from fixation (spatial magnification) when the LVF was larger, whereas scores were shifted towards fixation (spatial contraction) when the LVF was smaller. LVF = left visual field.

3.3. Discussion

The goal of the second experiment was to determine whether binocular bias of RP patients on the asymmetric version of the spatial interval discrimination task reflected the monocular spatial expansion previously reported by Temme et al. (1985). The data, however, did not support the hypothesis, as bias did not increase as a function of eccentricity. First, this lack of support for their findings may be based on the difference in monocular and binocular viewing conditions. Monocular measurements may reflect spatial distortions that disappear due to summation when binocular viewing is engaged. Second, methodological differences could be responsible for the contradictory results. Viewing time was not limited by Temme et al., whereas stimulus presentation was reduced to 200 ms in the present experiment. Perceived distance could be affected by factors that are influenced through temporal summation. However, a case could be made that this summation would aid judgments whereas, here, bias scores were more accurate under limited display time. Third, patient characteristics differed between the two studies. Temme et al. tested participants who were in earlier stages of the disease with larger field diameters than those of the participants in this study. Furthermore, they presented stimuli using a Goldmann perimeter, which allowed them to test eccentricities far beyond the limits of the computer display utilized herein. Temme et al. reported that spatial judgments within the central 20 dva did not differ from those of normal observers. Given that stimulus presentation in the present experiment did not exceed 7 dva on either side of fixation, the findings concur with those of Temme et al. The difference lies in the fact that several RP patients in this experiment did not have fields much larger than 20 dva. Even though it was expected that shifts in bias scores may be present towards the field limits, the absence

of these changes in spatial vision may be based on differences in receptive-field sizes within the central 20 dva as compared to larger eccentricities. Progressive loss of peripheral vision in areas with larger receptive fields could be more susceptible to spatial distortions.

In order to investigate changes in bias in relation to visual field diameter, an exploratory analysis considering field asymmetry was conducted. The results indicated that, in cases where the left visual field was larger than the right field, bias scores were shifted away from fixation, towards the left. This shift is equivalent to spatial magnification of visual space in the LVF. Similarly, in patients whose LVF was smaller, bias scores were shifted towards fixation in the LVF, towards the right. This shift is equivalent to contraction of visual space in the LVF. However, these respective effects were not apparent in the RVF. These results open the question as to whether perception in the two halves of the visual field could differ and why.

4. General discussion

The presented experiments were designed to examine spatial vision judgments in patients with RP. The first experiment evaluated spatial interval discrimination using a symmetrical stimulus presentation paradigm. The results indicated that bias in RP patients is largely preserved at a level comparable to that of normal observers; however, threshold scores are generally lower. This finding indicates that, even though the ability to make spatial judgments seemed unaffected by peripheral vision loss, the way in which RP patients arrive at this performance level differs from normally sighted individuals; they execute the task with more variability.

The second experiment focused on whether the ability to make spatial interval judgments is maintained when the paradigm is altered to asymmetrical presentation, whereby the entire stimulus display is presented within only one hemifield. The results indicated that, in the presence of asymmetrical field loss in RP patients, bias scores were affected in a systematic way that reflected the asymmetry of the remaining visual field; however, this was only the case in the LVF that corresponds to the cortical hemisphere believed to be more specialized in tasks involving spatial vision. The measured asymmetries in performance indicated that, if the LVF was smaller in relation to the right field, spatial distance judgments in the left field were shifted toward fixation. Such a shift could be interpreted as a contraction of visual space in the remaining area. If the field asymmetry was reversed, the opposite was the case, indicating that spatial vision in the left field was expanded when the left field was larger than the right. This observed effect accounted for 59% of the variability in the data.

It is remarkable that the majority of RP participants performed as well as they did on the spatial interval discrimination test, considering that the anatomical integrity of their retinas should be compromised to some level. Numerous visual functions have been demonstrated to decline as a result of RP, even in earlier phases of disease progression; however, the participants generally managed to perform within small ranges of bias across experiments. These findings were paralleled in a study on space perception in the context of time-to-collision judgments by RP patients (Jones, 2006). Based on data from 10 legally blind participants, the author concluded that their ability to estimate the time to the collision with a traveling object approaching on a computer screen did not differ significantly when compared with performance by normally sighted observers. This maintenance of functional ability is noteworthy and must have some underlying reasons. At the same time, the general decline in performance threshold by RP patients across experiments indicated that some deficits were present. Translated into real-life behavior, this would be comparable to being able to decide successfully where to pass between two parked cars but the confidence in where this central path lies would be much more variable. An argument could be made that the maintenance of a functional *status quo* in the presence of declining ocular integrity is behavioral evidence for some type of plasticity that goes beyond learning or temporary adaptation. However, in order to support the idea that this involves plasticity in the visual cortex, brain imaging studies would be required in order to examine changes in cortical processing during behavioral tasks that involve spatial judgments.

In vision, lateralization has been shown in tasks involving stereopsis (Carmon & Bechtold, 1969), word recognition (Bub & Lewine, 1988), reaching and grasping (Fisk & Goodale, 1988), face processing (Broad, Mimmack, & Kendrick, 2000; Puce, Allison, Asgari, Gore, & McCarthy, 1996; Rossion, Joyce, Cottrell, & Tarr, 2003), object processing (Brown & Kosslyn, 1995), and visual memory (Laeng, Overvoll, & Ole Steinsvik, 2007). In addition, there is evidence that receptive-field sizes differ between the hemispheres (Gabibov, 1993), which results in differences when processing spatial frequency information (Ivry & Robertson, 1998). The left hemisphere (RVF) seems to demonstrate more specialization when it comes to the processing of high spatial frequency information, whereas the right hemisphere (LVF) shows a preference for low frequency information. This becomes of particular importance when interpreting the results of the second experiment since the spatial frequency of the dots used was low at 0.5 dva. It is possible that the changes in spatial interval discrimination observed on this task in the LVF may, in part, be influenced by this preference. Evidence of laterality of function in spatial vision generally indicates that the right hemisphere (LVF) is faster (Tsagareli, 1995) and more accurate in processing spatial information (Laeng, Chabris, & Kosslyn, 2003). This applies specifically to coordinate spatial processing when making judgments about location in space (Meadmore, Dror, & Bucks, 2009).

Bowers and Heilman (1980) proposed that bisection judgments at midline exhibited a perceptual shift towards the left and were generally more accurate in left hemispace. Considering this pseudo neglect in normal observers, these findings provide support to the idea that the LVF receives different visuo-spatial attention than the RVF (Corbetta, Miezin, Shulman, & Petersen, 1993). There are additional reports in the literature regarding hemispheric differences in cortical processing, which have been the topic of several books (Davidson & Hugdahl, 1995; Hugdahl & Davidson, 2003; Kinsbourne, 1978). Each of these publications contains specific sections in the domain of spatial vision. Studies in the area of localized brain lesions indicated that higher levels of spatial perception are disrupted in patients with right hemisphere temporal lobe brain injury (Teuber & Weinstein, 1954; Weinstein, 1962). Carmon and Bechtold (1969) demonstrated that the right hemisphere (LVF) is dominant in processing stereoscopic information. These results were later supported in a study by Danta, Hilton, and O'Boyle (1978). Exploration and stimulus localization in space, as well as spatial perception have been shown to be impaired with right hemisphere damage (De Renzi, 1978), while deficits in reaction on spatial tasks in patients with right hemisphere lesions have been reported (Carmon, 1978). These studies provide the basis for the possibility that spatial vision in the LVF and its processing in the right cortical hemisphere may be uniquely different in patients with RP. Given the specialization for spatial vision in the right hemisphere, this cortical area may have different capabilities for compensation when spatial vision is affected by loss of partial as well as asymmetrical retinal input.

One main limitation of the field-ratio analysis is the fact that fields were measured with Goldmann III/4e targets at the rehabilitation agency whereas the stimulus presentation within the experiment used a calibrated computer screen. The parameters of

these two stimulus displays differ greatly, whereby Goldmann III/4e targets (when properly calibrated) are 4 mm^2 in size and appear at 318 cd/m^2 on a background of 10 cd/m^2 (Grosvenor, 2007; Heijl & Patella, 2002; Tate & Lynn, 1977). Such high luminance levels are not possible with a computer display and were approximately three times as bright at the spatial interval discrimination test display, even though stimulus size was similar. It must, therefore, be assumed that the functional fields of RP patients for the spatial test in these experiments were generally much smaller than the Goldmann field diameters, since visual field measures generally decrease with decreased luminance parameters. These smaller fields, however, were never mapped in detail, neither monocularly nor binocularly. The correlation of Goldmann field diameters with bias scores at the field limits of the spatial interval discrimination task may, therefore, not necessarily hold. Field limits of RP patients are not always clearly defined and can include transitional regions in which function is relatively reduced or impaired, not absolutely lost. In addition, sensitivity within the visual field borders mapped by Goldmann perimetry may not necessarily be homogenous; therefore, it is possible that islands of reduced sensitivity may interfere with encoding of spatial information, an aspect that was not measured within the present experimental conditions.

The interpretation of the results within the framework of cortical involvement may not necessarily be the most parsimonious approach. Turano (1991) has previously reviewed alternate explanations for changes in bisection judgments of RP patients in more detail, including the possible effects of macular edema, early cataract, problems with photoreceptor alignment and positioning as well as changes in neural signaling at the retinal level. Any of these factors, or a combination thereof, may indeed explain part of the variability in the present data. Interestingly, Turano (1991) also mentioned the possibility of cortical remapping, an idea that was still young at the time and has since then received more attention. Overall, our study results indicate that the perceptual shifts in asymmetric spatial judgments of RP patients are not easily explained by factors such as visual field diameter or disease progression. Regarding field asymmetries, the data indicated that a possible factor in perceptual adjustments of space could be the relative relationship of visual field size between the two visual hemispheres. This would support the idea that the LVF (right cortical hemisphere) may adjust spatial position perception according to field asymmetries. Given previous reports about hemispheric specialization of the right cortical hemisphere with regard to spatial information, it is possible that, in RP patients, the right hemisphere engages in altered spatial processing in response to asymmetric visual field loss in a more systematic way than its left counterpart. This possibility could be investigated in the future in more detail with brain imaging studies in order to localize differences in hemispheric processing both in the visual field and the corresponding cortical hemispheres.

The presented experiments provide insight into a potentially important direction of research in the area of spatial vision in RP. Research paradigms in previous investigations have largely ignored the idea that spatial visual processing can have a lateralization bias toward the right hemisphere. This consideration, however, may play an important role when examining perceptual data and may provide the ability to detect subtle changes in visual perception that may go unnoticed when global large-scale effects are the focus of analysis. Even though the experience of vision loss is unfortunate for the affected patients, their willingness to participate in research studies such as these provides a unique opportunity for vision scientists to examine the processes and mechanisms of vision when the system is undergoing changes due to disease. Particularly in the area of cortical reorganization after retinal damage, ethical considerations prevent researchers from using paradigms commonly used in animal research; however, work with ophthalmic patients can overcome these obstacles and provide insights from those whose sight is failing.

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