

# Contextual cueing impairment in patients with age-related macular degeneration

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Visual attention can be guided by past experience of regularities in our visual environment. In the contextual cueing paradigm, incidental learning of repeated distractor configurations speeds up search times compared to random search arrays. Concomitantly, fewer fixations and more direct scan paths indicate more efficient visual exploration in repeated search arrays. In previous work, we found that simulating a central scotoma in healthy observers eliminated this search facilitation. Here, we investigated contextual cueing in patients with age-related macular degeneration (AMD) who suffer from impaired foveal vision. AMD patients performed visual search using only their more severely impaired eye ( $n = 13$ ) as well as under binocular viewing ( $n = 16$ ). Normal-sighted controls developed a significant contextual cueing effect. In comparison, patients showed only a small nonsignificant advantage for repeated displays when searching with their worse eye. When searching binocularly, they profited from contextual cues, but still less than controls. Number of fixations and scan pattern ratios showed a comparable pattern as search times. Moreover, contextual cueing was significantly correlated with acuity in monocular search. Thus, foveal vision loss may lead to impaired guidance of attention by contextual memory cues.

## Introduction

Visual attention can be guided by past experience of regularities in the environment. One incidental form of visual context learning has been termed contextual cueing (Chun & Jiang, 1998). In contextual cueing, visual search is faster in repeated compared to random distractor arrangements. In this way, incidental learning of invariant spatial locations facilitates attentional guidance to the target position, as is evident in faster search times (e.g., Chun & Jiang, 1998), fewer fixations, and more direct scanpaths (Brockmole & Henderson, 2006; Geringswald, Baumgartner, & Pollmann, 2012; Manginelli & Pollmann, 2009; Peterson & Kramer, 2001; Tseng & Li, 2004).

What happens to contextual cueing if foveation is compromised? During the exploration of a scene, visual attention is closely linked to the fovea (Deubel & Schneider, 1996; Hoffman & Subramaniam, 1995) and in turn, foveating a stimulus increases its chance to be remembered explicitly (Hollingworth, 2006). If contextual cueing is a form of implicit learning (Chun & Jiang, 1998), it may not be affected at all by degraded foveal vision. Moreover, repeated distractor configu-

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rations can be learned even if they are ignored (i.e., not attentively processed; Jiang & Leung, 2005). The story may not be that simple, however. Learning in contextual cueing appears to be highly local (Brady & Chun, 2007; Olson & Chun, 2002) such that repetition of the distractors close to the target yields the highest search benefit. This may indicate that, during foveation of the target, a mental “snapshot” of the target and its surroundings is learned and used to guide search in invariant contexts. This process may well depend to some degree on foveal processing, like the advantage observed in explicit learning (Deubel & Schneider, 1996; Hoffman & Subramaniam, 1995), so it may be predicted that contextual cueing suffers in the presence of foveal vision impairment.

In normal-sighted observers, learning of contextual cues was diminished when only 3 out of 12 stimulus locations were repeated during learning, even when the whole display was repeated in a later test phase. Conversely, when the whole display was repeated during learning, repetition of only three or four items in a later test phase was sufficient to guide search efficiently in previously learned contexts (Song & Jiang, 2005). In visual search of patients with macular scotomata, parts of the search displays may not be perceived—or not perceived as well as in normal vision—even after eye movements. In analogy to the findings of Song and Jiang (2005), because patients with central vision loss may not perceive the whole context, learning of contextual cues and the establishment of robust visual memory traces for repeated displays may thus be impaired, in return reducing efficient guidance to target positions in previously encountered search arrays.

In line with this reasoning, no contextual cueing was observed in a group of normal-sighted young adults who searched in the presence of a gaze-contingent simulated central scotoma (Geringswald et al., 2012). However, visual search with a simulated central scotoma is a highly artificial situation and we cannot rule out that contextual cueing was absent because the observers needed to control the exploration of the search display voluntarily in order to compensate for the scotoma. Behavioral tasks in normal observers have shown that contextual cueing, particularly the use of learned memory traces, depends on attentional and working memory capacity (Jiang & Leung, 2005; Manginelli, Geringswald, & Pollmann, 2012; Manginelli, Langer, Klose, & Pollmann, 2013; Travis, Mattingley, & Dux, 2012; Vickery, Sussman, & Jiang, 2010). A cumbersome top-down controlled exploration of search displays forced by a simulated scotoma may leave not enough capacity to use contextual cues for attentional guidance in repeated displays.

This may be different in patients who suffer from progressive degeneration of the macula (age-related

macular degeneration, AMD), leading to diminished foveal vision (Arroyo, 2006; Nazemi, Fink, Lim, & Sadun, 2005), and, possibly, a central scotoma (Lindblad et al., 2009). On the one hand, one may expect AMD-patients to show at least as severe deficits in contextual cueing as young, normal sighted observers searching with an artificial central scotoma. On the other hand, patients with macular degeneration may use their remaining peripheral vision more efficiently because they have adapted their exploration behavior to eccentric viewing. This may lead to a more automatic search leaving more attentional and working memory capacity available for guiding search by contextual memory cues. One complicating aspect is the progressive deterioration of foveal vision in AMD. Therefore we would expect a beneficial effect of practice to occur in mild stages of AMD, when patients already had months or even years to become accustomed to explore their environment in the presence of impaired foveal vision, but before the development of a central scotoma leads to severe vision loss. The central aim of the present study was to investigate whether patients with AMD suffer from impaired contextual cueing. To our knowledge, this question has not been investigated previously. It is of practical importance, because impaired contextual cueing in AMD would be an additional burden for these patients beyond their basic visual deficits (for a review on psychophysical function in AMD see Neelam, Nolan, Chakravarthy, & Beatty, 2009). It is also of theoretical interest, because impaired contextual cueing following degraded foveal vision would indicate that contextual cueing does not occur automatically in the absence of attentional and working memory resources (Manginelli, Langer, Klose, & Pollmann, 2013).

We examined search behavior and eye-movements in AMD patients and closely matched healthy, normal-sighted controls. In the control group, we expected search time reduction in repeated displays, as it has been observed in healthy elderly observers (Howard, Howard, Dennis, Yankovich, & Vaidya, 2004). Furthermore, we expected this search facilitation in repeated displays to go along with a reduced number of fixations and more efficient scan paths in familiar search contexts, a pattern that has repeatedly been reported in younger observers (Brockmole & Henderson, 2006; Geringswald et al., 2012; Manginelli & Pollmann, 2009; Peterson & Kramer, 2001; Tseng & Li, 2004), but would be first demonstrated in elderly observers here. Because the severity of visual impairment in AMD often differs between both eyes, patients were tested with monocular and binocular vision. In the monocular condition, patients viewed the search displays with their more severely impaired eye. If contextual cueing depends on foveal vision, we expected selectively reduced search facilitation for repeated displays in search times and gaze parameters. Additionally, we expected the individual

amount of search facilitation to correlate negatively with the magnitude of visual impairment of the eye tested. In binocular vision, the central question was to what degree the better eye could compensate deficits in contextual cueing. One extreme might be that contextual cueing depends only on vision of the better eye. On the other hand, vision loss in the worse eye might interfere with contextual cueing even in binocular vision.

## Methods

### Participants

#### Patients

We tested 16 patients (seven females, nine males; one left handed) diagnosed with age-related macular degeneration. The average age of the patient group was 71 years, ranging from 67 to 76 years. The mean educational level of the patient group was 13 years of education, ranging from 8 to 19 years. Patients were recruited and diagnosed at the Ophthalmic Department of the University Hospitals of the Otto-von-Guericke University, Magdeburg. Subjects with narrow irido-corneal angle, glaucoma, ocular trauma, eye surgery (except cataract surgery), distinct cataract, diabetic retinopathy and other retinal diseases, high myopia ( $> 5$  dpt), amblyopia, cerebral blood flow disorder, and stroke were excluded. Macular degeneration was diagnosed based on an ophthalmic examination for both eyes, including slit lamp examination by an ophthalmologist, fundus photography, and optical coherence tomography. For each subject best corrected monocular decimal visual acuities were determined by an optician. Visual field defects were explored with standard static white-on-white perimetry (dynamic strategy; Goldmann size III; program: dG2; OCTOPUS® Perimeter 101, Haag-Streit GmbH, Wedel, Germany) complemented by fundus-controlled microperimetry with a Scanning Laser Ophthalmoscope (stimulus intensity: 0 db [ $71 \text{ cd/m}^2$ ] and 20 db; Goldmann size III; SLO, Rodenstock, Otto-brunn, Germany) or a micro perimeter (4-2 dB threshold strategy; Goldmann size III; MP-1, NIDEK CO., LTD., Gamagori, Japan) to determine the locus of fixation.

All patients (except P08) were affected by AMD in both eyes. The progress of the disease was variable between patients as well as between individual eyes. One patient had dense central scotomata extending more than  $10^\circ$  of visual angle in both eyes. In five patients, dense macular scotomata had developed in one of their eyes with diameters ranging from  $5^\circ$  to  $\geq 60^\circ$ . Eight patients had developed relative scotomata, i.e., they showed reduced perceptual sensitivity at least in one of their eyes. For monocular testing, we measured the more severely affected eye in all but

three patients who were not able to perform the task with their most severely affected eye (see Table 1). Averaged across all patients, the logarithmic minimum angle of resolution (LogMAR) was 0.11 (decimal visual acuity 0.78) in the better eye and 0.65 (decimal visual acuity 0.22) in the worse eye. For the eye used for monocular testing average LogMAR was 0.42 (decimal visual acuity 0.38). For details of the patient sample see Table 1.

#### Controls

16 controls (seven females, nine males; one left handed) participated in the study. Their mean age was 68 years, ranging from 60 to 73 years. The mean educational level of the control group was 14 years of education ranging from 10 to 18 years. Controls were matched to patients individually considering sex, age, and years of education. Controls were examined at the Ophthalmic Department of the University Hospitals of the Otto-von-Guericke University, Magdeburg in order to ensure normal visual function, i.e., decimal visual acuity  $> 0.8$  and normal visual fields.

The procedures followed the tenets of the Declaration of Helsinki (World Medical Association, 2000) and the study was approved by the ethics board of the Medical Faculty of the Otto-von-Guericke-University of Magdeburg. Participants were not informed about the purpose of the study until they had completed all experimental sessions. Informed written consent was obtained prior to the experiment. Patients and controls received a compensation of €10 per hour. Additionally, AMD patients and their accompanying persons were compensated for travel costs to the laboratory.

#### Apparatus

Stimulus presentation and response recording were controlled using the Psychtoolbox (Brainard, 1997; Pelli, 1997) and the Eyelink Toolbox (Cornelissen, Peters, & Palmer, 2002) under Matlab on a PC with a 22 in. Samsung SyncMaster 2233RZ LCD monitor. The monitor was 474 mm (1680 pixels) wide and 296 mm (1050 pixels) high and the vertical refresh rate was 120 Hz. Responses were recorded with a ResponsePixx Handheld five button response box (VVPixx Technologies Inc.; <http://www.vpixx.com>). The stimuli were viewed binocularly by the controls and by the patients for the binocular condition. In the patients' monocular condition, observers viewed the stimuli monocularly with their more severely impaired eye when possible (see Table 1). The distance to the screen was kept constant at 85 cm leading to a pixel size of  $0.019^\circ$  or 1.14 arcmin of visual angle. The eye position of the left eye for binocular viewing and of the respective eye

Subject	Sex	Diagnosis		Age (years)	Visual acuity (logMAR, [decimal])		Scotoma diameter (horizontal°, vertical°)		Fixation	
		RE	LE		RE	LE	RE	LE	RE	LE
P01	M	AMD (dry)	AMD (wet)	75	0.2 (0.63)	0.3 (0.5)	–	r	c	c
P02	M	AMD (dry)	AMD (dry)	76	0.2 (0.63)	0.1 (0.8)	r	–	c	c
P03	M	AMD (wet)	AMD (dry)	73	0.6 (0.25)	0.0 (1.0)	r	–	e, t	c
P04	F	AMD (dry)	AMD (dry)	68	0.1 (0.8)	0.0 (1.0)	r	r	c	c
P05	M	AMD (wet)	AMD (wet)	70	0.8 (0.16)	0.2 (0.63)	7, 5	p	e, t	c
P06	M	AMD (dry)	AMD (dry)	68	0.6 (0.25)	0.6 (0.25)	11, 11	18, 20	e, t, d	e, t, v
P07	F	AMD (dry)	AMD (dry)	69	0.2 (0.63)	0.2 (0.63)	r	–	c	c
P08	M	–	AMD (dry)	70	–0.1 (1.25)	0.4 (0.4)	–	–	c	c
P09 <sup>a</sup>	F	AMD (dry)	AMD (wet)	76	0.0 (1.0)	1.3 (0.05)	–	30, 32	c	e, t, d
P10	M	AMD (dry)	AMD (dry)	68	1.2 (0.06)	0.2 (0.63)	5, 5 <sup>b</sup>	–	c	c
P11	F	AMD (dry)	AMD (wet)	75	0.1 (0.8)	0.7 (0.2)	r	r	c'	c'
P12	F	AMD (wet)	AMD (dry)	70	0.1 (0.8)	–0.1 (1.25)	–	–	c'	c'
P13	M	AMD (dry)	AMD (dry)	67	1.0 (0.1)	0.3 (0.5)	40, 45	r	e, t	c
P14 <sup>a</sup>	M	AMD (dry)	AMD (wet)	75	0.0 (1.0)	1.0 (0.1)	–	r	c	c
P15	F	AMD (wet)	AMD (wet)	74	0.6 (0.25)	0.0 (1.0)	r	–	c'	c'
P16 <sup>a</sup>	F	AMD (wet)	AMD (wet)	67	1.3 (0.05)	0.0 (1.0)	52, ≥60	–	e	c

Table 1. Patient characteristics. *Notes:* LogMAR, logarithmic minimum angle of resolution; RE, right eye; LE, left eye; AMD, age-related macular degeneration; –, no scotoma; r, relative scotoma; p, peripheral scotoma; c, central fixation; e, eccentric fixation; d, dorsal; v, ventral; t, temporal. <sup>a</sup> Three patients could not complete the experiment with their more severely affected eye in the monocular condition and were therefore tested with the better eye. <sup>b</sup> Patient with bilobed scotoma around the fovea. ', the locus of fixation was determined exclusively based on non-fundus controlled perimetry.

tested in the monocular condition was recorded using an Eyelink 1000 Desktop Mount (SR Research Ltd., Mississauga, Ontario, Canada), using corneal reflection and pupil tracking. The temporal resolution of the eye tracker was 1000 Hz. One patient (P08) was tested in the lab of Gisela Müller-Plath in Halle (Saale), Germany, in the monocular condition. In this setup, we used a 20 in. CRT monitor which was 400 mm (1600 pixels) wide and 300 mm (1200 pixels) high running at a vertical refresh rate of 85 Hz. The viewing distance was 55.1 cm leading to a pixel size of 0.026° or 1.56 arcmin of visual angle. We adapted all visual stimuli to match in size and eccentricity in degrees of visual angle as we had implemented in our lab. Eye position was recorded with an Eyelink II head-mounted gaze-tracking system (SR Research Ltd., Mississauga, Ontario, Canada) with a temporal resolution of 500 Hz. Head movements were minimized by stabilizing participants' head using a chin- and forehead rest. Visual acuity of patients was optimally corrected for the given viewing distance using a custom-made trial-frame and a full diameter (38 mm) perimeter trial lens set. Participants were tested individually in a dimly lit, sound-attenuated chamber.

## Stimuli

Each search display contained one target (90° or 270° rotated T) and eleven distractors (0°, 90°, 180°, 270° rotated L). The orientation of the target was randomly

chosen for each trial and did therefore neither correlate with the specific displays nor the experimental conditions. The orientations for the distractors were chosen such that each possible rotation was present not more than three times in a given configuration. Each item subtended 1.23° × 1.23° and was black presented on a gray background. The stimulus positions were randomly chosen on four imaginary concentric circles with radii of 2°, 4°, 6°, and 8° each containing 4, 12, 20, and 28 equidistant possible item locations, respectively. For each participant and each experimental session, 24 target positions were chosen randomly from the two intermediate circles before the beginning of the experiment. For 12 of those target positions, randomly assigned distractor configurations remained constant throughout the experiment ("repeated" condition). The other 12 target positions were combined with randomly generated distractor configurations for each experimental block ("novel" condition). Target positions were chosen equally often from each of the four display quadrants balanced across experimental conditions, thus for each quadrant there were three targets paired with repeated and three targets paired with novel distractor configurations respectively. Additionally, distractor positions were balanced across quadrants such that each quadrant of the search display always comprised three search items leading to an equal distribution of search items across the display for all configurations. The overall size of a search display in which search items were placed extended a circular area

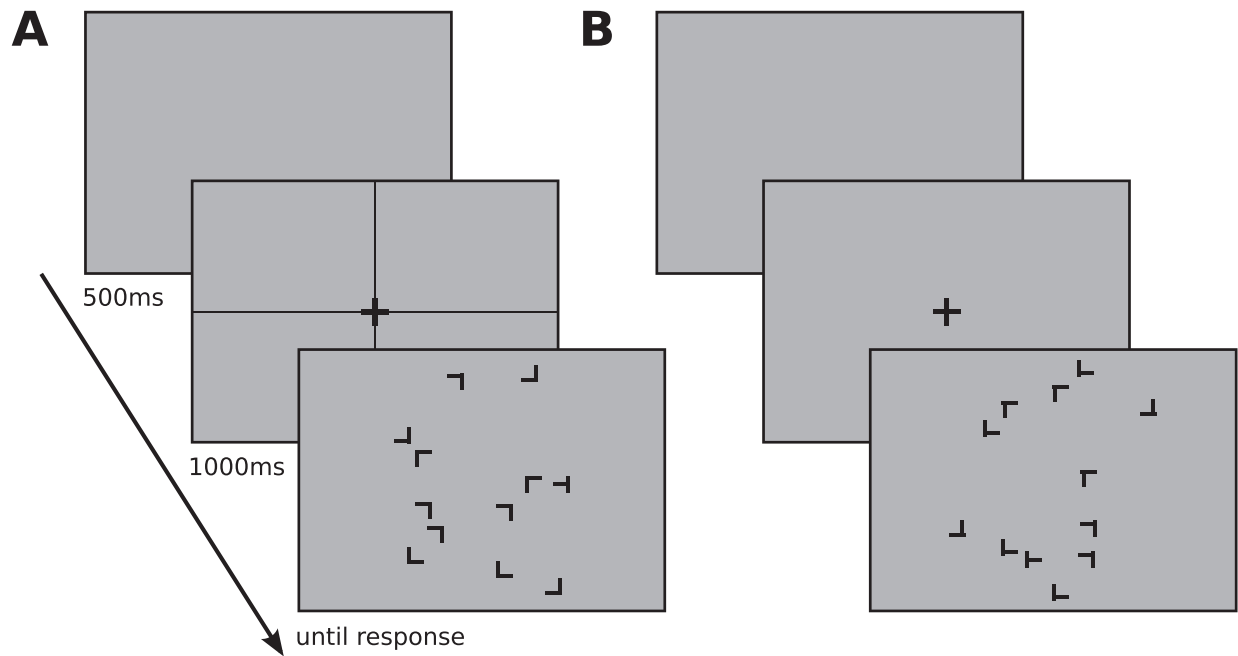


Figure 1. Schematic diagram of an experimental trial for patients (A) and controls (B). Each trial consisted of the presentation of a blank screen (500 ms) followed by a fixation cross (1000 ms) and the search display (presented until response). Displays used in the experiment in the patient monocular and binocular condition each contained one tilted target “T” and 11 randomly rotated distractor “L”s (A). In the control condition, search difficulty was increased by shifting the line segments of the distractors to make them perceptually more similar to the target (B).

with a diameter of  $17.23^\circ$ . Search difficulty for controls was increased by introducing an offset of  $0.13^\circ$  at the junction of the two line segments composing the distractor L-shapes, making them more similar to the target stimulus (Figure 1).

The fixation cross was composed of two black line segments which had a line width of  $0.62^\circ$  and a length of  $3.11^\circ$ . For the patients, we added one horizontal and one vertical line extending across the whole screen and intersecting at the center of the fixation cross in order to facilitate visibility of the fixation cross. In addition, we slightly changed the standard calibration targets implemented in the EyeLink Toolbox (Cornelissen et al., 2002) for testing the patients. We enlarged the calibration disks and added one horizontal and one vertical line intersecting at the center of the disks. This was done to increase visibility and facilitate eye tracker calibration in the patient group.

## Procedure

Participants searched for a left- or right-tilted T among L-shaped distractors and indicated its orientation with button presses of the left and right index finger. For the experimental sessions, patients’ visual acuity was corrected individually. Patients wore custom-made trial-frames and we adjusted trial lenses, based on results of the optical refraction, until patients

reported optimal visibility of stimuli on the computer screen. When necessary, e.g., because of wearing progressive lenses, we applied the same procedure to controls referring to their eyeglass prescription.

Patients performed visual search binocularly in their first session and were tested again approximately within two weeks using only their more severely affected eye. Each session started with a nine-point gaze calibration, followed by a short training to familiarize participants with the task, the actual search experiment, and a recognition test at the end of the session. One session lasted approximately 1 hr for controls and between 1 and 2 hrs for patients depending on the severity of the visual defect.

The training was composed of 24 trials containing randomly generated displays. Target positions of the training displays were not used in the experimental configurations. The main search experiment consisted of 20 blocks of 24 trials each. After each block participants were allowed self-determined breaks and the experimenter proceeded with the subsequent block when the participant was ready to continue. Every trial started with the presentation of a blank for 500 ms followed by the fixation cross for 1000 ms and the search display which remained on the screen until the participant responded (Figure 1). Auditory feedback was provided for correct (a 2000-Hz high-pitch tone) and wrong answers (a 500-Hz low-pitch tone). Participants were instructed to search for the target T as fast

and accurately as possible. They were further asked to follow their intuition and search for the target T passively, as suggested by Lleras and Von Mühlenen (2004). The recognition tests included the original 12 repeated and another 12 new randomly generated configurations presented in randomized order. Participants were asked to indicate by button presses whether they had seen the displays during the course of the experiment or not. No feedback about the correctness of the response was given.

## Data analysis

Response accuracy as well as search time analysis and all statistical tests were carried out using R (version 2.15.2; R Development Core Team, 2012). For the analyses of the contextual cueing effects, response times and gaze parameters were aggregated to four epochs, each containing five blocks, in order to increase statistical power. Analyses of variance (ANOVAs) were performed using type III sums of squares. We analyzed the data of patients and controls in joint three-way mixed-design ANOVA with the within subjects factors epoch (1–4) and configuration (novel, repeated) and the between-subjects factor experimental group. If the experimental group factor or interactions involving the experimental group factor became significant, we ran additional two-way within-subjects ANOVAs for each group, followed by planned comparisons between novel and repeated configurations for each epoch to detect significant contextual cueing if the factor configuration or the interaction became significant. These planned two-tailed *t* test comparisons were adjusted according to Holm (1979). For all statistical tests, the alpha level was set at 0.05.

Gaze data were analyzed with a custom-made Python script applying a velocity-based algorithm. We used the procedures described in Nyström and Holmqvist (2010) for filtering the data with the Savitzky-Golay (Savitzky & Golay, 1964) finite impulse response (FIR) smoothing filter algorithm with second-order polynomials and a filter length of 20 ms, the removal of invalid gaze samples due to eye blinks or signal losses and the calculation of adaptive velocity thresholds. We then identified saccade events by velocities that exceeded the adaptive peak velocity threshold. The saccade start was calculated as the first sample of monotonically increasing velocities trespassing the individual saccade velocity threshold before the velocity peak and the saccade end was calculated as the last sample of monotonically decreasing velocities falling below this threshold after the velocity peak. Fixations were then identified from the inter-saccadic events that exceeded a duration of 100 ms.

Two dependent measures were calculated from the fixation events. First, we measured the number of fixations required to find the target from the onset of the search display until a response button was pressed. The second measure of interest was the efficiency of the scan path toward the target which was calculated as the ratio between the total distance covered by the eye during search, i.e., the sum of distances between each consecutive fixation, and the shortest path possible, i.e., the distance between the first fixation and the target location (Brockmole & Henderson, 2006). Thus, more direct scan paths toward the target are characterized by lower scan pattern ratios.

## Data exclusion and spatial accuracy of gaze data

### Data exclusion

For the analysis of the reaction times and the gaze parameters, we excluded all erroneous responses from the data set. In a next step, we removed all trials in which the search time was shorter than 200 ms (two trials in the control condition). To detect and remove reaction time outliers, we applied the recursive procedure proposed by Van Selst and Jolicoeur (1994) for each participant and experimental session individually leading to the exclusion of 3.52% in the patient monocular, 2.01% in the patient binocular, and 2.59% in the control condition, respectively.

For the analysis of the gaze data we additionally excluded all trials in which more than 20% of the gaze samples were missing due to signal losses. Following this procedure we decided to exclude subjects from the gaze data analysis who had more than 20% of their gaze data identified as invalid. This led to the exclusion of two patients from the monocular (P06, 43.82%, and P08, 74.51% of invalid gaze data) and two patients from the binocular condition (P07, 35.82%, and P08, 27.60% of invalid gaze data). The average percentage of excluded invalid trials of the remaining participants was 4.48% ( $SD = 6.13\%$ ) in the patient monocular, 4.56% ( $SD = 5.86\%$ ) in the patient binocular, and 1.59% ( $SD = 2.64\%$ ) in the control condition.

### Spatial accuracy of gaze data

Measurement of eye movements required foveation of the calibration targets during the setup of the eye tracker. In AMD patients, this procedure is challenging because patients may not be able to foveate the targets, compromising spatial accuracy of the measured gaze. In order to test spatial accuracy, we computed the median distance of the last fixation to the center of the target stimulus, averaged for each participant across the experiment, between patients and controls. The average median distance of the last fixation was  $0.60^\circ$

( $SD = 0.20^\circ$ ) for the control condition. As expected, for the patients the distance of the last fixation was slightly larger. The average median distance was  $1.30^\circ$  ( $SD = 1.07^\circ$ ) in the patient monocular and  $1.44^\circ$  ( $SD = 1.75^\circ$ ) in the patient binocular condition. Of all last fixations in the control condition, 99.04% lay within an area surrounding the center of the target by  $3.0^\circ$  of visual angle. This was the case for 87.57% of fixations in the patient monocular and 86.96% in the binocular conditions. Thus, as expected, eye-tracking accuracies for patients were inferior to those of controls. However, the average deviations measured for the patients, i.e., the spatial accuracy of the measured gaze data, fell well within  $1.5^\circ$  of visual angle which can be considered as reasonable regarding the further analysis of the eye-movement data.

## Results

### Patients monocular

In the monocular condition, patients searched with their more severely affected eye and thus possible effects of foveal defects on contextual cueing should be most prominent under monocular search.

#### Response accuracy

Search accuracy was high, ranging from 87.29% to 100% (average 98.15%) in the patient, and from 97.08% to 99.79% (average 99.09%) in the control condition. We compared response accuracies between patients and controls using a mixed-design ANOVA with the within-subjects factor configuration (novel, repeated) and the between-subjects factor experimental group (patient, control). We did not observe any significant differences in accuracies between patients and controls, experimental group,  $F(1, 30) = 1.29$ ,  $p = 0.26$ ; configuration,  $F(1, 30) = 0.47$ ,  $p = 0.50$ ; experimental Group X configuration,  $F(1, 30) = 0.12$ ,  $p = 0.073$ , indicating that response accuracies were comparable between experimental groups and display configurations.

#### Search times

Averaged search times are shown in Figure 2, top row, and standardized search facilitation scores in Figure 3, green bars.

The three subjects who performed search with their better eye (see Methods, Participants) were excluded from this analysis as they may have profited from masking their worse eye. Results of the three-way mixed-design ANOVA are summarized in Table 2. Overall search times were comparable between patients

and controls, experimental group,  $F(1, 27) = 0.05$ ,  $p = 0.82$ . A significant main effect of epoch,  $F(3, 81) = 10.02$ ,  $p < 0.05$ , indicated general improvement over time. The significant main effect of configuration,  $F(1, 27) = 7.55$ ,  $p < 0.05$ , and significant Epoch X configuration interaction,  $F(3, 81) = 2.81$ ,  $p < 0.05$ , revealed significant contextual cueing. A significant three-way interaction between experimental group, epoch, and configuration,  $F(3, 81) = 2.81$ ,  $p < 0.05$ , suggested that contextual cueing differed between patients and controls. To further investigate the nature of this interaction, we ran separate repeated-measures ANOVAs with the factors epoch (1–4) and configuration (novel, repeated) for patients and controls, respectively. Results of these ANOVAs are summarized in Table 3. In patients, we observed a marginally significant effect of skill learning, epoch,  $F(3, 36) = 2.67$ ,  $p = 0.06$ , with decreasing response times from 2241 ms in the first to 2042 ms in the last epoch. However, patients did not additionally profit from repeated contexts as indicated by a nonsignificant main effect of configuration,  $F(1, 12) = 1.64$ ,  $p = 0.22$ , and a nonsignificant Epoch X configuration interaction,  $F(3, 36) = 0.43$ ,  $p = 0.73$ . Controls showed a pronounced effect of general skill learning reflected by a highly significant main effect of epoch,  $F(3, 45) = 9.79$ ,  $p < 0.05$ . Search times decreased from 2195 ms in the first epoch to 1955 ms in the last epoch. Additionally, responses to repeated displays were significantly faster than to novel search arrays as confirmed by a significant main effect of configuration,  $F(1, 45) = 7.22$ ,  $p < 0.05$ . The significant interaction,  $F(3, 45) = 6.07$ ,  $p < 0.05$ , furthermore indicated that this contextual cueing built up over the course of the experiment. Whereas response times were not significantly faster for repeated displays throughout Epochs 1 to 3, all  $t(15) < 2.08$ ,  $p_s > 0.16$ , responses were significantly speeded in the last epoch,  $t(15) = 4.11$ ,  $p < 0.05$ . Thus, in contrast to patients, we obtained robust contextual cueing in controls searching in displays that were matched for difficulty.<sup>1</sup>

If the successful use of contextual cues is related to foveal vision, contextual cueing should be more impaired in patients with greater foveal dysfunction. To test this prediction, we correlated the general visual performance, as indicated by logMAR visual acuity, and the normalized gain in repeated displays in the last epoch (Figure 4). We used Kendall's tau nonparametric rank order correlation and included all patients of the monocular condition. Normalized contextual cueing was obtained by individually calculating the difference in mean reaction times between novel and repeated displays and standardizing this absolute difference by the mean reaction time of novel displays. LogMAR visual acuity correlated negatively with the size of contextual cueing ( $\tau = -0.47$ ,  $p < 0.05$ ), implying that

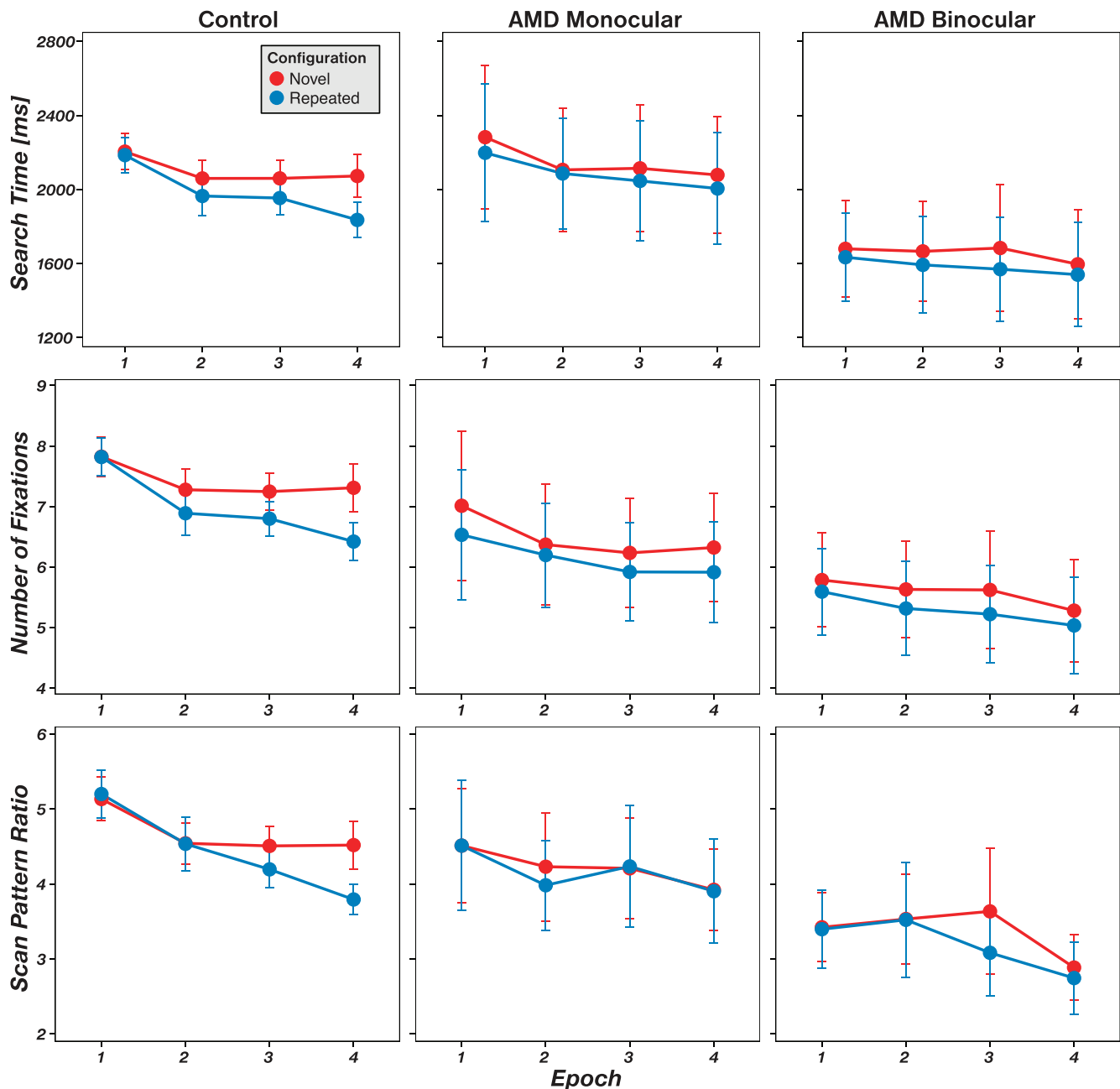


Figure 2. Averaged search times, numbers of fixations and scan pattern ratios for controls and AMD patients. Search times (top row), number of fixations (middle row), and scan pattern ratios (bottom row) were aggregated to epochs (each epoch containing five blocks) and are plotted for controls (left column), patients searching with their worse eye (middle column), and binocularly (right column). The three measures of visual search are plotted separately for repeated and novel displays (blue and red). Error bars depict the standard error of the mean.

patients with larger foveal impairments profited less from contextual cues and that, on the other hand, in mild cases contextual cueing was preserved to some extent.

To summarize, we did not find evidence for contextual search facilitation in patients searching with their worse eye in the group analysis whereas matched healthy controls showed a significant development of contextual cueing over repeated searches. Additionally,

search facilitation covaried with the magnitude of foveal impairment.

### Gaze

Analogous to reaction times,<sup>2</sup> we investigated whether search facilitation for repeated displays was evident in eye-movement patterns. If contextual search facilitation for repeated displays emerged, this should



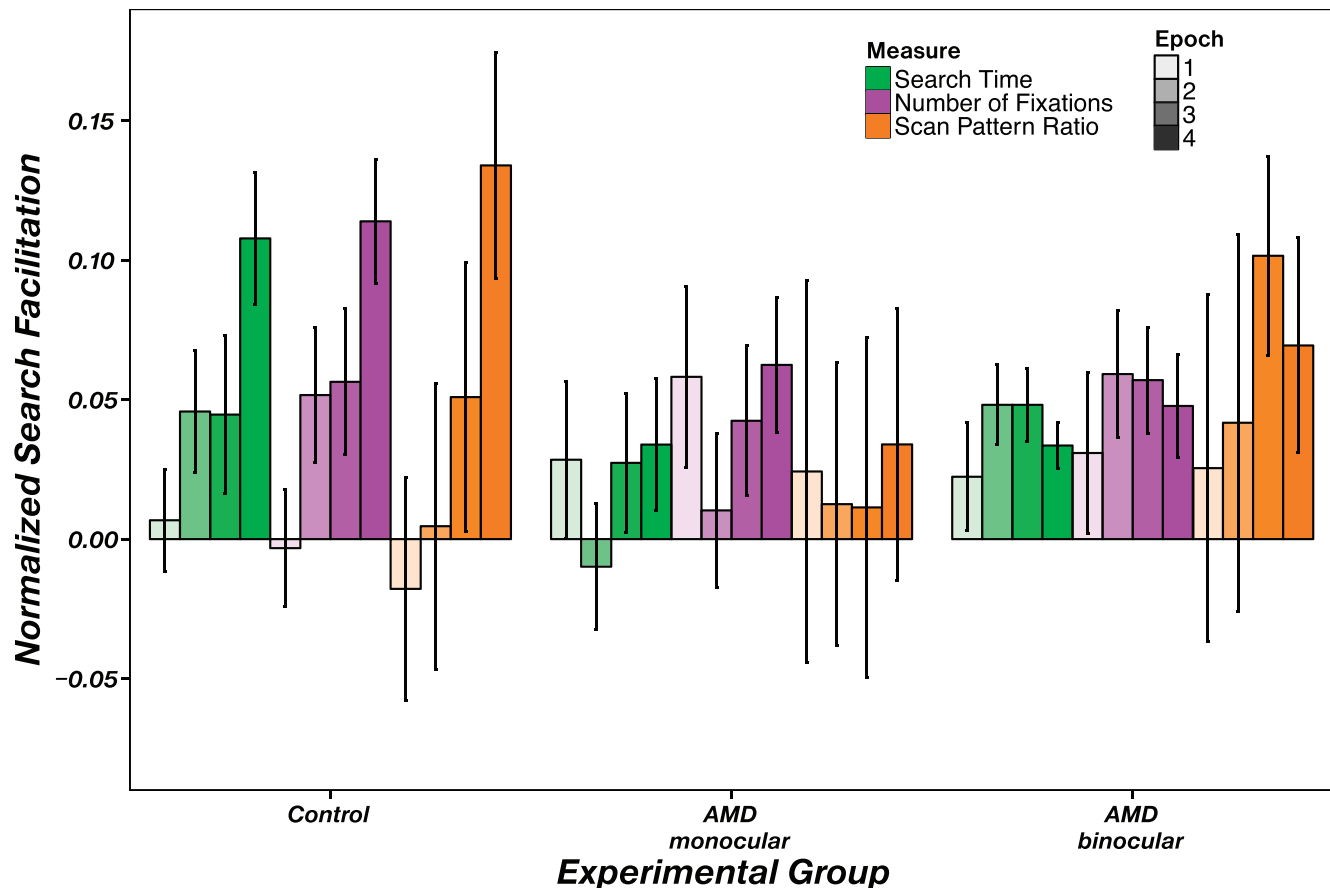


Figure 3. Averaged normalized search facilitation as a function of experimental group, broken down by measure (colors) and epoch (opacity). Normalized search facilitation was obtained by individually calculating the difference between novel and repeated displays and standardizing this difference by the mean of novel displays. Positive values indicate a benefit for repeated configurations. Error bars depict the standard error of the mean.

be reflected in a more efficient sampling of the search arrays, i.e., a reduction of number of fixations executed until the target is identified, compared to novel search arrays. In addition, the scan pattern ratio illustrates the efficiency of the placement of fixations on the search array by standardizing the summed distance the eye traveled across the display on the shortest path possible from the first fixation. Facilitation for repeated displays in contextual cueing is expressed by lower scan pattern ratios in repeated compared to novel search arrays. To our knowledge, search facilitation for repeated displays in eye movements have only been reported for younger observers (Brockmole & Henderson, 2006; Geringswald et al., 2012; Manginelli & Pollmann, 2009; Peterson & Kramer, 2001; Tseng & Li, 2004). We expected similar effects of contextual cueing in our older controls as well. In AMD patients, we expected a reduction of search facilitation in repeated displays.

*Number of fixations:* Figure 2, middle row, depicts the averaged number of fixations and average standardized search facilitation scores can be seen in Figure 3, purple bars. We again excluded the three subjects who

performed search with their better eye (see Methods, Participants). In addition, two patients dropped out due to significant amounts of missing gaze data (see Methods, Data exclusion).

The three-way mixed-design ANOVA yielded similar results as observed in response times (Table 2), showing a significant three-way interaction as well,  $F(3, 75) = 4.03, p < 0.05$ . The separate two-way repeated-measures ANOVA did not reveal any statistically significant effects in patients' number of fixations (Table 3), indicating that contextual cueing was impaired in this measure as well. In contrast to response times, we observed a nonsignificant trend towards less fixations in repeated compared to novel displays, configuration,  $F(1, 10) = 3.61, p = 0.09$ . We note, however, that we had to exclude two patients from the gaze analysis due to significant amounts of missing gaze data. One of them (P06) had a severe absolute scotoma such that the removal of this subject might have lead to higher general levels of contextual cueing within the patient group as observed in response times, presumably producing the nonsignificant trend towards general contextual benefits

Effect	Patient monocular versus control						Patient binocular versus control					
	Search time		Number of fixations		Scan pattern ratio		Search time		Number of fixations		Scan pattern ratio	
	F	p	F	p	F	p	F	p	F	p	F	p
Group	0.053	0.820	1.078	0.309	0.339	0.565	2.081	0.160	4.657	<0.05*	4.813	<0.05*
Epoch	10.020	<0.001***	10.900	<0.001***	7.947	<0.001***	8.145	<0.001***	15.358	<0.001***	8.278	<0.001***
Configuration	7.554	<0.05*	11.108	<0.01**	1.691	0.205	11.937	<0.01**	14.602	<0.001***	4.233	<0.05*
Group X Epoch	0.100	0.960	0.379	0.768	0.921	0.435	2.586	0.058'	2.443	0.070'	2.340	0.079'
Group X Config.	0.689	0.414	0.143	0.708	0.619	0.439	0.604	0.443	0.584	0.451	0.091	0.766
Epoch X Config.	2.812	<0.05*	3.307	<0.05*	1.184	0.321	4.055	<0.01**	4.424	<0.01**	2.534	0.062'
Group X Epoch X Configuration	2.815	<0.05*	4.029	<0.05*	1.907	0.136	3.932	<0.05*	3.582	<0.05*	1.291	0.283

Table 2. Statistical results of the group comparison for search time, number of fixations, and scan pattern ratio. Notes: ' p < 0.1; \* p < 0.05; \*\* p < 0.01; \*\*\* p < 0.001.

in the patient group. In contrast to patients, controls showed a pronounced effect of general skill learning as well as contextual cueing, building up over the course of the experiment. Whereas a similar amount of fixations was needed in repeated compared to random configurations in Epochs 1 to 3, all  $t_s(15) < 2.28$ ,  $p_s > 0.11$ , contextual cueing was significant in the last epoch,  $t(15) = 4.44$ ,  $p < 0.05$ ).

In more impaired patients, the foveal defect should be accompanied by a generally increased number of fixations to explore parts of the displays which may be covered by a scotoma. To test this relationship, we correlated the individual average number of fixations of all patients with the visual impairment. The correlation with logMAR visual acuity was significant ( $\tau = 0.59$ ,  $p < 0.05$ ), indicating that more severely impaired patients did indeed fixate more often during visual search.

*Scan pattern ratio:* The development of average scan pattern ratios is plotted in Figure 2, bottom row, and the standardized average search facilitation scores can be seen in Figure 3, orange bars.

Results of the three-way mixed-design ANOVA are summarized in Table 2. Neither the factor configuration nor any interaction involving configuration was significant, suggesting that contextual cueing affected neither patients' nor controls' scan paths, Group X Epoch X configuration,  $F(3, 75) = 1.91$ ,  $p = 0.14$ . Thus, we decided to conduct follow-up repeated-measures ANOVAs for each group (Table 3) to investigate whether contextual cueing was completely absent in controls albeit Figure 2 and 3 suggest that contextual benefits emerged over time. Overall search benefits for repeated search arrays were not significant in controls, however, contextual cueing developed over the course of the experiment. Whereas similar scan pattern ratios were observed in repeated compared to random configurations in Epochs 1 to 3, all  $t_s(15) < 1.27$ ,  $p_s > 0.68$ , contextual cueing was significant in the last epoch,  $t(15) = 3.22$ ,  $p < 0.05$ . In patients, we did not find any evidence for contextual cueing. None of the effects were significant (all  $F_s < 1.22$ ,  $p_s > 0.32$ ).

Thus, facilitation of scan path efficiency in repeated displays was impaired in patients searching with their worse eye. To some extent, contextual cueing also appeared reduced in controls. Possibly, contextual benefits stabilized only late in the experiment and were more variable between participants than search times and number of fixations, thereby leading to nonsignificant interactions involving the factor configuration in the three-way ANOVA.

### Patients binocular

We next examined contextual cueing in binocular viewing in patients. In this condition, patients might

Group	Effect	Search time		Number of fixations		Scan pattern ratio	
		<i>F</i>	<i>p</i>	<i>F</i>	<i>p</i>	<i>F</i>	<i>p</i>
Patient monocular	Epoch	2.666	0.062'	2.577	0.072'	1.214	0.322
	Configuration	1.644	0.224	3.605	0.087'	0.153	0.704
	Epoch X Configuration	0.430	0.733	0.736	0.539	0.217	0.884
Patient binocular	Epoch	1.170	0.332	5.613	<0.01**	2.327	0.090'
	Configuration	4.716	<0.05*	6.866	<0.05*	2.284	0.155
	Epoch X Configuration	0.981	0.410	0.448	0.720	0.843	0.479
Control	Epoch	9.794	<0.001***	11.361	<0.001***	12.561	<0.001***
	Configuration	7.224	<0.05*	8.574	<0.05*	2.261	0.153
	Epoch X Configuration	6.073	<0.01**	7.903	<0.001**	4.250	<0.01**

Table 3. Statistical results of the within-group analyses for search time, number of fixations, and scan pattern ratio. Notes: '  $p < 0.1$ ; \*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$ .

partially accommodate visual deficits of their worse eye and might be more amenable to context repetitions. This might result in generally higher amounts of benefits from contextual cues in the group statistics. Concomitantly, binocular viewing has a higher ecological validity and may reflect patients' visual behavior in everyday life to a greater extent.

**Response accuracy**

Patients' performance was again very high, ranging from 97.08% to 100% (average 99.02%). It was not significantly different from controls' performance and comparable between display configurations, experimental group,  $F(1, 30) = 0.06, p = 0.80$ ; configuration,  $F(1, 30) = 0.72, p = 0.40$ ; experimental Group X configuration,  $F(1, 30) = 3.12, p = 0.09$ .

**Search times**

The three-way mixed-design ANOVA yielded similar results as for the comparison between patients' monocular search and controls (see Table 2). Overall search times were comparable between patients and controls and the significant three-way interaction,  $F(3, 90) = 3.93, p < 0.05$ , suggested differences in contextual cueing. General skill learning was not significant in patients (Table 3), performance improved from 1657 ms in the first to 1568 ms in the last epoch. However, in contrast to monocular search, patients could use repeated configurations to speed up search by 72 ms,  $F(1, 15) = 4.72, p < 0.05$ . The nonsignificant interaction between epoch and configuration suggested that the magnitude of contextual benefits did not differ across experimental epochs. Planned comparisons between novel and repeated configurations for each epoch indicated that patients benefited from repeated

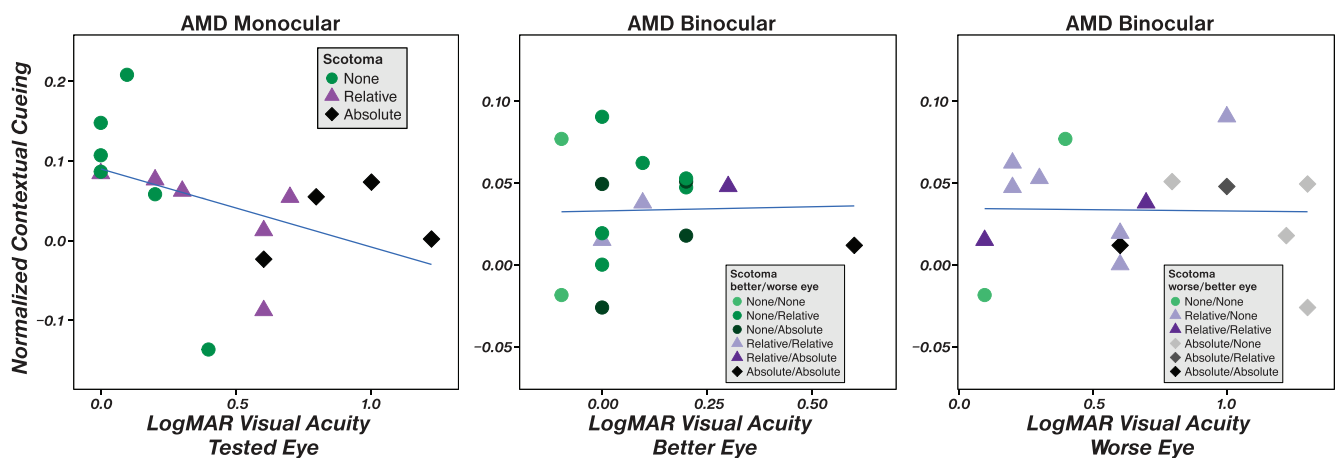


Figure 4. Relationship between the degree of foveal impairment in AMD (logMAR visual acuity) and normalized contextual cueing in search time in the last epoch in monocular (left panel) and binocular search considering the better (middle panel) or worse eye (right panel). Normalized contextual cueing was obtained by individually calculating the difference in mean reaction times between novel and repeated displays and standardizing this absolute difference by the mean reaction time of novel displays. Rank correlations were quantified using Kendall's tau. The blue line depicts the linear regression for the purpose of visualization.

search displays early in the experiment. While response times to repeated and novel search displays were comparable in the first epoch,  $t(15) = 0.96$ ,  $p = 0.35$ , responses were significantly faster for repeated displays in the second,  $t(15) = 3.10$ ,  $p < 0.05$  as well as in the last epoch,  $t(15) = 2.99$ ,  $p < 0.05$ . This difference failed to reach significance in the third epoch,  $t(15) = 1.79$ ,  $p = 0.19$ , indicating that contextual cueing may have an early onset, but also be less stable in patients. In addition, a comparison of the magnitude of contextual cueing effects in the last epoch with controls suggests that search facilitation was significantly reduced in patients searching binocularly, Welch two-sample  $t$  test,  $t(18.13) = -2.98$ ,  $p < 0.05$ . On average, patients' contextual cueing amounted to 56 ms compared to 237 ms in healthy controls. Although average search times between patients and controls did not differ significantly, Figure 2 suggests that search might have been slower in controls, inflating contextual cueing. Thus, we carried out an additional Welch two-sample  $t$  test comparing normalized contextual cueing effects between patients and controls. This test confirmed decreased search facilitation in patients,  $t(18.49) = -2.96$ ,  $p < 0.05$ . Facilitation accumulated to 3.36% in patients and to 10.78% in controls.

To test whether the individual amount of contextual search facilitation was related to visual impairment, we correlated the visual impairment of the better and worse eye with the normalized magnitude of contextual cueing of the last epoch. We did not find any significant relationships between contextual cueing and logMAR visual acuity (Figure 4) of the better ( $\tau = 0.06$ ,  $p = 0.74$ ) or worse eye ( $\tau = 0.04$ ,  $p = 0.82$ ).

## Gaze

### Number of fixations

The three-way mixed-design ANOVA yielded overall similar results as for search times, with a significant three-way interaction indicating differences in contextual cueing between patients and controls (Table 2). In contrast to search times, the main effect of experimental group was also significant, with a reduced number of fixations committed by patients (on average 5.44 fixations) compared to controls (on average 7.20 fixations). Different from search times, patients showed significant general skill learning in the number of fixations (Table 3). Performance improved from 5.69 in the first to 5.16 fixations in the last epoch. As observed before, patients overall benefited significantly from repeated contexts, making on average 0.29 fixations less in repeated configurations. The magnitude of these contextual benefits did not differ significantly between epochs. Planned comparisons between novel and repeated configurations for each epoch did not reach statistical significance. However, in accordance with

search times, we observed a trend for significant contextual cueing in Epochs 2,  $t(13) = 2.65$ ,  $p = 0.08$ , and 4,  $t(13) = 2.62$ ,  $p = 0.08$ , but not for the first,  $t(13) = 0.97$ ,  $p = 0.35$ , and third epoch,  $t(13) = 1.98$ ,  $p = 0.14$ . The magnitude of contextual cueing effects in the last epoch was significantly smaller compared to controls regarding absolute benefits, Welch two-sample  $t$  test,  $t(21.11) = -2.91$ ,  $p < 0.05$ , as well as normalized contextual cueing,  $t(27.64) = -2.29$ ,  $p < 0.05$ .

### Scan pattern ratio

Results of the three-way mixed-design ANOVA were similar to the number of fixations (Table 2). Patients (ratio on average 3.28) searched the displays overall more efficiently than controls. The interaction between experimental group, epoch, and configuration failed to reach significance,  $F(3, 84) = 1.29$ ,  $p = 0.28$ . A finer analysis of the patient data, including the factors epoch and configuration, did not reveal any significant effects (Table 3).

### Fixation duration

Patients found the target with fewer eye movements than controls. On average, they made 5.44 fixations during search, that is 1.76 fixations less than controls, and this difference was statistically significant in the above analyses. Concomitantly, scan paths were significantly more efficient in the patient group. However, search times did not differ significantly between patients and controls. One possible reason for this inconsistent result may be that patients had an increased fixation duration. Increased fixation durations have been reported, e.g., in artificial scotoma simulations, increasing with the size of the scotoma (Cornelissen, Bruin, & Kooijman, 2005). To test this possibility, we calculated the median fixation duration for each patient and control across the whole experiment. A Welch two-sample  $t$  test on median fixation durations indicated a nonsignificant trend towards longer fixation durations in patients,  $t(22.56) = -1.60$ ,  $p = 0.12$ . Patients fixated on average for 234 ms, controls for 215 ms. The individual median fixation duration was significantly correlated with the logMAR visual acuity of the better eye ( $\tau = 0.47$ ,  $p < 0.05$ ), but not with the visual acuity of the worse eye ( $\tau = -0.01$ ,  $p = 0.96$ ). Thus, patients with a greater visual impairment in their better eye fixated longer than less affected patients.

### Recognition test

Mean recognition accuracy in the patient monocular condition was 55.73% ( $SD = 10.42\%$ ). Patients correctly classified repeated displays as old (the hit rate) on

52.60% ( $SD = 22.71\%$ ) of trials and falsely reported 41.15% ( $SD = 21.83\%$ ) of novel displays as old (the false alarm rate). A paired  $t$  test on hit and false alarm rates was significant,  $t(15) = 2.20$ ,  $p < 0.05$ , indicating that patients may have become aware of display repetitions when they searched monocularly. Howard et al. (2004) found that contextual cueing was disrupted in older individuals who became aware of the display repetitions and linked these results to the use of different search strategies in aware compared to unaware participants. In order to test whether such a relationship was also present in our data, we carried out correlation tests between response accuracy as an indicator of awareness and the individual normalized contextual cueing of the last epoch in reaction times, using Kendall's tau nonparametric rank order correlation. The correlation between the normalized magnitude of contextual cueing and awareness did not reach significance ( $\tau = -0.22$ ,  $p = 0.25$ ).

Mean recognition accuracy in the patient binocular condition was 49.48% ( $SD = 10.53\%$ ) with a mean hit rate of 52.08% ( $SD = 20.30\%$ ) and a mean false alarm rate of 53.13% ( $SD = 23.35\%$ ). A paired  $t$  test on the hit and false alarm rates was not significant,  $t(15) = -0.20$ ,  $p = 0.85$ , indicating that the patient group was generally not aware of the display repetitions. Recognition accuracy and normalized contextual cueing in search times did not correlate significantly ( $\tau = -0.09$ ,  $p = 0.65$ ).

In the control difficult condition, mean recognition accuracy accumulated to 56.77% ( $SD = 11.17\%$ ) with a mean hit rate of 61.98% ( $SD = 21.72\%$ ) and a mean false alarm rate of 48.44% ( $SD = 21.78\%$ ). A paired  $t$  test on the hit and false alarm rates was significant,  $t(15) = 2.43$ ,  $p < 0.05$ , indicating that controls became aware of the display repetitions. The correlation between recognition accuracy and normalized contextual cueing in search times did not reach significance ( $\tau = -0.24$ ,  $p = 0.22$ ).

## Discussion

We investigated whether the loss of foveal vision in AMD affects efficiency of visual search in repeated contexts. To this end, we examined search performance in patients with AMD in the contextual cueing paradigm. The central finding was that search facilitation in repeated displays was reduced in AMD-patients, while it was preserved in closely matched healthy controls (Howard et al., 2004). In the patients, reduced or absent contextual cueing was observed in search times as well as in the number of fixations and the efficiency of the scan path.

Overall, the successful use of contextual information was related to the amount of visual impairment in AMD patients. Under monocular viewing, we found a correlation of visual acuity and contextual cueing. Particularly patients with mild acuity deficits profited from contextual cues. Under binocular viewing, we found evidence for contextual cueing in AMD patients, which, however, was reduced in comparison to the control group and did not increase over time, as would be typical for contextual cueing.

Previous studies have shown that contextual cueing increases with search difficulty, by minimizing attentional allocation to irrelevant items (Chun & Jiang, 1998, Jiang & Chun, 2001). In order to match search difficulty between visually impaired patients and controls, we used perceptually more demanding search displays for controls. Response times clearly indicate that this matching was successful, i.e., that the difficulty of the task was comparable between patients and controls. The drawback, however, was that patients and controls searched different items. When controls were given the same search displays as patients, significant contextual cueing developed in controls, however, as expected, the absolute contextual benefits were smaller than in the difficult displays. It is a dilemma often observed in patient studies that on the one hand, presentation of identical tasks requires increased effort from patients and, on the other hand, equalizing effort affords unequal task parameters. We think that equalizing search difficulty was important for a fair comparison between patients and controls. However, we acknowledge that there is a remaining uncertainty in how far the different search displays affected the size of contextual cueing in unknown ways. Future studies might try to minimize this dilemma by using search difficulties that are intermediate between the presently used searches, so that they are not too difficult for patients and not too easy for controls.

Another caveat concerns potential order effects. Patients were first tested binocularly, then monocularly. We hoped that the easier binocular condition would lead to general learning of the experimental setup (unrelated to contextual cueing) that may help the patients to carry out the more difficult monocular task. Likewise, controls were first tested with the easier search task. Both patients and controls showed evidence for explicit recognition in the second testing session, possibly due to greater experience with the task or the explicit recognition test at the end of the first session. However, explicit recognition did not correlate with size of contextual cueing—neither in patients nor controls—so that it is unlikely that task order had a systematic influence on the contextual cueing data. One reason not to randomize task order in the present study was that the sample was too small to assess possible interactions between patient factors such as severity of

visual impairment and task order. However, if larger sample sizes become available in future studies, randomizing the order of binocular and monocular search would be clearly preferable.

Notably, the size of the contextual cueing did not correlate with the acuity of the better or worse eye in binocular search, in contrast to the correlation between acuity and contextual cueing in monocular search. This may hint at an interaction of the worse eye's vision on vision with the better eye. For example, it has been shown that unequal damage to the retina in both eyes may lead to binocular inhibition in some AMD patients (Faubert & Overbury, 2000; Posner, Snyder, & Davidson, 1980; Quillen, 2001; Valberg & Fosse, 2002). The new finding is that interference between unequal vision in both eyes might also affect high-level visual functions such as visual learning and memory.

Brady and Chun (2007) showed that the local context information close to the target location contributes most to contextual cueing. In AMD patients, this “snapshot” of the target and its surrounding distractors may be compromised either because of acuity loss in mild cases or due to a central scotoma, requiring peripheral “fixation” in more severe cases. Brady and Chun (2007) also observed a contribution of global regularities to contextual cueing. Consistent with this global contextual cueing, van Asselen and Castelo-Branco (2009) found intact contextual cueing in participants who had to keep central fixation and perceived search stimuli only in their visual periphery, and contextual cueing remains intact when search displays are presented only briefly, curtailing eye movements (Chun & Jiang, 1998). These results challenge the idea that central vision is necessary for contextual cueing. We know from the spatial cueing experiments developed by Posner et al. (1980) that covert spatial attention can be moved away from central fixation. This may be one mechanism that mediates guidance of attention in contextual cueing when eye movements are restricted. However, the reverse appears to be impossible, i.e., making a saccade without a concomitant shift of attention (Deubel & Schneider, 1996; Hoffman & Subramaniam, 1995). Thus, when eye movements are necessary in visual search, like in our experiment, elimination of foveal sight impairs contextual cueing.

The above suggests that it may be advantageous for AMD patients, to make as few eye movements as possible and to rely more on global regularities, minimizing the demands of exploring the search array. In contrast to the studies by van Asselen and Castelo-Branco (2009) or Chun and Jiang (1998) however, patients with central visual impairment will not perceive the whole stimulus configuration uniformly as the macular scotoma will cover parts of the search array. For example, in van Asselen and Castelo-Branco

(2009), attention may be shifted peripherally between search items while the search array itself remains static, facilitating the learning of spatial relations between search items. If patients with central vision loss do not move their eyes, the strength of memory representations of spatial configurations should be reduced in such displays because less visual information is available to them, compared to unimpaired controls. On the other hand, if patients want to encode information covered by the scotoma, exploration via eye movements is mandatory and may result in reduced contextual cueing as observed in our study. Consequently, for larger central vision loss due to AMD more eye movements should be needed to explore the scotomized area and a larger loss of contextual cueing should be evident.

Previously, we observed reduced contextual cueing with simulated central scotomata in healthy observers (Geringswald et al., 2012). In comparison, our AMD patients benefited more from contextual cues than the students with a simulated central scotoma, who showed virtually no contextual cueing. A likely explanation is that the patients have learned to adapt scene exploration to the presence of their vision loss, requiring less attentional resources for the top-down controlled exploration of the search displays, for instance for inhibiting foveation of the to be inspected parts of the display, as in untrained search with a simulated scotoma. Thus, a more stimulus-driven search in patients may allow for contextual cueing, as observed in the binocular condition (Lleras & Von Mühlenen, 2004). There is a caveat, however, in that the mild cases among the patients had less foveal vision loss than that introduced by the simulated scotoma in our previous study. Further simulation studies with varying degree of foveal vision degradation will be needed to address this question.

Even if patients may search more automatically than students with artificial scotomata, contextual cueing was at least significantly reduced compared to healthy controls. The link between the deployment of attention to and subsequent foveation of a visual target appears to be an automatic process, which is so dominant that it takes AMD patients several months to adapt the oculomotor system to eccentric fixating (Crossland, Culham, Kabanarou, & Rubin, 2005) and may not be complete even years after the onset of the disease (Crossland, Culham, & Rubin, 2004; Tarita-Nistor, González, Markowitz, & Steinbach, 2008; White & Bedell, 1990; Whittaker, Cummings, & Swieson, 1991). The attentional resources needed to suppress foveation and explore search displays with peripheral vision are thus not available for contextual cueing. Search facilitation in repeated displays, especially the retrieval and use of learned contextual cues, depends on attending to the display items (Jiang & Chun, 2001;

Jiang & Leung, 2005) and on free visuospatial working memory capacity (Manginelli et al., 2012, 2013; Travis et al. 2012; Vickery et al., 2010). Converging evidence comes from fMRI data showing that parietal and occipital areas that are modulated by visual working memory capacity are also involved in contextual cueing (Manginelli, Baumgartner, & Pollmann, 2013). Due to their foveal vision loss, AMD patients suffer from increased attentional demands on the programming of eye movements during the exploration of search displays. This may lead to impairments in the deployment of selective attention to the environment and thus interfere with attentional guidance in familiar environments. Similarly, the planning and execution of eye movements in AMD patients may require visuospatial working memory capacity which may make the match between search templates from long-term memory and the current search display more difficult, thereby reducing contextual benefits observed in healthy controls. With the patient data, it is difficult to discriminate between potential causes of impaired contextual cueing, i.e., (a) direct interference of foveal vision loss with learning contextual cues or (b) competition for working memory resources between top-down controlled display exploration and memory-guided search. Further studies with simulated scotomata could selectively address the influence of scotoma size, duration of practice with a central scotoma, or scotoma presence in learning versus test phases in a more controlled setting than is possible with patient data.

Learning of contextual cues can be dissociated from more general skill learning, which occurs over time for repeated and novel displays alike. Patients failed to show general learning in search time data. This lack of general skill learning appeared more pronounced in the binocular than in the monocular condition, although eye movements became more efficient during search. In patients, the eye movements are more costly in terms of programming and execution. A more optimized search strategy would thus be the reduction of eye movements and a more peripheral processing of search items during each fixation. The trend of longer fixation durations in patients' binocular search supports this idea. Due to reduced peripheral acuity (compared to foveal search), patients may have needed longer to discriminate the target from distractors (e.g., longer dwell times) than controls, leading to longer overall search times. Contextual benefits were completely absent in the efficiency of the scan path in patients, although less fixations were placed in repeated displays in binocular search, which further supports the idea that processing of search items was more peripheral compared to controls.

Patients searching monocularly and control participants appeared to be not completely unaware of the

display repetitions in our experiments. Initially, it was thought that contextual cueing was a form of implicit learning (Chun & Jiang, 1998; Chun & Phelps, 1999; Manginelli & Pollmann, 2009). More recent studies with more sensitive explicit memory tests, however, provided evidence that explicit memory of context repetition may at least be present for a subset of repeated displays (Geyer, Baumgartner, Müller, & Pollmann, 2012; Geyer, Shi, & Müller, 2010; Schlagbauer, Müller, Zehetleitner, & Geyer, 2012; Smyth & Shanks, 2008). In these studies, the size of the contextual cueing effect was not related to explicit or implicit learning. We found no significant correlation of contextual cueing and explicit memory, in contrast to Howard et al. (2004) who reported that contextual cueing was reduced in older individuals who became aware of the context repetitions.

It may be surprising, that patients showed reduced or absent contextual cueing in our experiments, given that an efficient utilization of global regularities should be prioritized by the visual system to improve visual exploration of the environment, possibly by reducing costly eye movements to a minimum. However, we demonstrated impaired contextual cueing in AMD using abstract stimuli in a semantically not very meaningful environment. A question that thus remains to be investigated is whether AMD patients show similar deficits in the use of contextual information in more realistic scenes or whether they would be more efficient in using much richer semantic relations between objects in a scene to improve visual search. Patients might additionally profit from more realistic scenes as the transfer of exploration strategies from everyday behavior should be easier than in search for rather nonmeaningful objects as in standard contextual cueing tasks.

## Conclusions

In summary, our results demonstrate that the loss of foveal vision in AMD impairs contextual cueing in visual search. This deficit was correlated with the degree of visual impairment when patients searched monocularly with their worse eye. In binocular search, patients overall benefited from contextual cues; however, this search facilitation was reduced compared to age-matched controls. Thus, loss of foveal vision in AMD severely interferes with search facilitation in familiar environments, an effect that transcends the immediate consequences of foveal vision loss. Future research is needed to investigate whether learning of contextual cues depends on foveal vision or whether the use of previously learned contextual memory cues is

impaired following foveal vision loss, possibly due to competition for visuospatial working memory capacity.

*Keywords:* contextual cueing, visual search, visual attention, visuospatial working memory, age-related macular degeneration, macular scotoma

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## Footnotes

<sup>1</sup>In an additional experiment, controls performed visual search in displays identical to those of patients. This was done in order to exclude the possibility that contextual cueing observed in controls was specific to the perceptually more demanding displays. We expected controls to show general skill learning as well as contextual cueing over the course of the session. A highly significant main effect of epoch confirmed general learning in the easy condition,  $F(3, 45) = 23.20$ ,  $p < 0.05$ . Performance improved from 1194 to 1071 ms in the first and last epoch. The main effect of configuration was not significant,  $F(1, 15) = 0.80$ ,  $p = 0.39$ . However, the significant interaction,  $F(3, 45) = 4.47$ ,  $p < 0.05$ , confirmed that contextual cueing in controls was not specific to the more difficult search displays. Similarly to the difficulty-matched condition, responses to repeated displays were significantly faster in the last epoch,  $t(15) = 4.02$ ,  $p < 0.05$ ; all other  $t(15) < 1.42$ ,  $ps > 0.35$ .

<sup>2</sup>Before we carried out the analyses on gaze parameters, we reanalyzed search times including only those subjects and those trials, which were not discarded from eye-movement analyses due to invalid or missing gaze data. This was done to ensure that the pattern of results for search times remained comparable to results of the gaze data. The main pattern of results remained similar. Search times were comparable

between patients' monocular search and controls, experimental group,  $F(1, 25) = 0.08$ ,  $p = 0.77$ , and the three-way interaction was significant,  $F(3, 75) = 2.97$ ,  $p < 0.05$ . Patients neither showed significant general learning,  $F(3, 30) = 1.93$ ,  $p = 0.15$  nor contextual cueing, configuration,  $F(1, 10) = 2.74$ ,  $p = 0.13$ ; interaction,  $F(3, 30) = 0.87$ ,  $p = 0.47$ ) whereas this was the case for controls (all  $F$ s  $> 5.97$ ,  $ps < 0.05$ ). Under binocular viewing, patients' response times did not differ significantly from controls,  $F(1, 28) = 1.37$ ,  $p = 0.25$ . The three-way interaction just missed significance,  $F(3, 84) = 2.68$ ,  $p = 0.05$ , most likely due to decreased statistical power. In patients, the main effect of epoch was not significant,  $F(3, 39) = 1.27$ ,  $p = 0.30$ , and the main effect configuration was marginally significant,  $F(1, 13) = 3.78$ ,  $p = 0.07$ .

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