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Object Search in Neovascular Age Related Macular Degeneration : The Crowding Effect.

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Running title : object search in macular degeneration

Key words: neovascular age related macular degeneration, anti-VEGF, visual search, object perception.

**Background:** Visual search, an activity that relies on central vision, is frequent in daily life. We investigated the effect of spacing between items in an object search task in participants with central vision loss.

**Methods:** Patients with neovascular age-related macular degeneration (nAMD), age-matched controls, and young controls were included. The stimuli were displays of 4, 6 and 9 objects randomly presented in a “crowded” (spacing 1.5°) or “uncrowded” (spacing 6°) condition. For each of 96 trials, participants were asked to search for a pre-defined target that remained on the screen until the response was recorded.. We recorded accuracy, search time, and eye movements (number of fixations and scan path ratio).

**Results:** Compared to older controls, accuracy decreased by 31% and search time increased by 61% in AMD participants. Aging also affected performance with a lower accuracy by 13.5% and longer search times by 46% in older compared to younger controls. Increasing the spacing between elements increased accuracy by +21% in AMD participants but it had no effect in older and younger controls. Performance was not related to visual acuity or to duration of neovascular AMD, but search time was correlated to the lesion size in the “crowded” condition.

**Conclusions:** Object search is ubiquitous in daily life activities. Our study shows that when visual acuity is irrevocably reduced, increasing the spacing between elements can reliably improve object search performance in patients.

Age-related macular degeneration (AMD) is the leading cause of blindness in developed countries.<sup>1</sup> Neovascular AMD accounts for most AMD-related severe vision loss. The prognosis of neovascular AMD has changed considerably with intravitreal injections of anti-VEGF<sup>2</sup> which results in visual acuity (VA) and morphological improvements.<sup>3</sup> Aflibercept and Ranibizumab show similar morphological outcomes, as assessed from retinal images (central retinal thickness, lesion size), and the dosing regimen of Aflibercept has the potential to reduce treatment burden and risks associated with frequent injections.<sup>4,5</sup>

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AMD has been found to cause a severity-dependent decrement in quality of Life (QoL). AMD patients suffer from greater social dependence, difficulties with daily living tasks, higher rates of clinical depression, increased risks of fall, premature admission to nursing homes, and suicide.<sup>6,7</sup>

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Although VA gain is obtained in the first year under anti-VEGF therapy in AMD, visual function may decline with time because of the natural course of age-related macular degeneration due to development of atrophy and/or fibrosis.<sup>8,9,10</sup> Vision-related functioning, which is important to patients and complementary to VA measurement, can be assessed either by QoL questionnaires or by a case control study of a visual task performance. The QoL is a patient-reported outcome measure which reflects aspects of daily life with AMD including psychological well-being, functional capacity, and the ability to perform daily activities.<sup>7,11</sup> The QoL (the NEI VFQ-25), classically used in clinical assessment of the patient's quality of life, is not AMD specific. Other outcome measures include computer based task-performance<sup>12-24</sup> and real world visual tasks that AMD patients accomplish every day.<sup>25</sup>

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Visual search is a frequent task in daily life. Indeed, everyone searches for something all the time in modern society, where a substantial amount of time is spent searching for computer icons or phone applications or shopping online, or simply search for objects to prepare meals. Human visual search involves multiple visual and cognitive functions, ranging from spatial vision, visual attention, oculomotor control, temporal integration of information across eye movements as search progresses, memory and decision making.<sup>30</sup> Using real world visual search tasks, visual search has been shown to be impaired in those with low vision.<sup>12,14,19,25,31,32</sup> In self-reported QoL questionnaires, AMD patients report difficulties in searching and finding things on a crowded shelf, suggesting that the spatial proximity of elements may have an impact on object search.<sup>33</sup>

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In natural environments objects are usually surrounded by other objects (e.g., on shelves of the supermarket or at home: books, clothes, food, etc), sometimes occluded, rendering visual search even more difficult. The crowding phenomenon describes the deleterious influence of

neighboring objects on the recognition of a target.<sup>34</sup> Crowding increases with eccentricity in normal vision.

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The impact of crowding is particularly relevant in central vision loss, as in patients with neovascular AMD with subfoveal choroidal neovascularization. Studies in reading have reported that vertical spacing (double interline) led to a small improvement in reading speed (+7 words/min or a gain of +16%)<sup>35</sup>, but when associated with horizontal spacing (double word/line spacing), reading speed increased by approximately +26% with high contrast texts and by +46% with low contrast texts in comparison to standard single spacing.<sup>36</sup> In our previous studies, AMD patients were able to quickly recognize objects and scenes.<sup>13,15,20-24</sup> In a realistic object search task, we found that AMD participants were able to accomplish the task with a performance of 75% correct detections, although they were 2 times slower (41.5s) than older controls (23.2s) and 5 times slower than young controls (8.7s). Errors were mainly due to false alarms resulting from confusion between the target object and another structurally similar object present in the scene.<sup>19</sup>

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Adaptive strategies, such as eccentric viewing and steady eye strategy, may be used to compensate for central vision loss secondary to AMD.<sup>26</sup> This preferred retinal locus for eccentric viewing is a well-defined retinal area used for fixation. Eccentric viewing is task-specific and is stable on repeated testing.<sup>27</sup> The fixation area can be measured either by static bivariate contour ellipse area (BCEA)<sup>28</sup> or by dynamic BCEA using microperimetry. The use of static BCEAs seems to offer a more accurate detection of fixation stability changes in patients with AMD.<sup>29</sup>

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In the present study, we aim to evaluate the crowding effect in object search performance in AMD participants. We hypothesize that, as in reading, crowding is deleterious on the performance and visual exploration of AMD participants.

## METHOD

### *Participants*

Three groups of participants were included patients with neovascular AMD, age-matched normally sighted controls, and young normally sighted controls. Inclusion and exclusion criteria are summarized in Table 1.

All participants underwent a complete ophthalmologic examination with recording of medical history, best corrected visual acuity (BCVA) using Early Treatment Diabetic Retinopathy Study charts at 4 m, slit lamp examination, intraocular pressure, and funduscopy. Basic cognitive abilities were assessed in neovascular AMD patients and age-matched controls using the French version of Mini Mental State Examination (MMSE).

### Neovascular AMD group:

Thirty-two patients with neovascular age-related macular degeneration, which was inactivated with at least 3 monthly intravitreal anti-VEGF injections (Aflibercept and or Ranibizumab), were included. Each patient had received at least 3 monthly intravitreal injection during de the loading phase. Then the patient was followed every month and treated as needed (“pro renata”).

Only one eye of each patient with logMAR visual acuity from 0.4 to 1 was tested for this study. In cases of bilateral AMD, we used the eye with the best corrected visual acuity. If both eyes had equal acuity, one eye was randomly selected and the other was occluded during testing. The diagnosis of neovascular AMD was confirmed by fluorescein angiography, indocyanine green angiography, and spectral domain optical coherence tomography (Heidelberg Retina Angiograph, HRA2; Heidelberg Engineering, Dossenheim, Germany). The areas of classic and occult choroidal neovascularization hemorrhage and serous pigment epithelial detachment were determined using fluorescein angiography and indocyanine angiography. The area of each lesion (mm<sup>2</sup>) and the greatest linear diameter of each lesion were measured from digital angiograms by outlining the lesion, using image analysis software (Eye Explorer, Heidelberg Engineering, Heidelberg, Germany).<sup>37,38</sup> Clinical assessment and the object search tasks for this study were performed during the same visit in the Ophthalmology Department.

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### Controls group

Age-matched controls, with normal visual acuity, were either relatives of participants with AMD or patients who underwent successful cataract surgery. Controls were tested monocularly according to the inclusion criteria. If both eyes had equal acuity, one eye was randomly selected.

A group of healthy young adults, students in medicine or in neuroscience, with normal vision were included as controls to dissociate the effect of aging from the effect of pathology. The tested eye was randomly selected for each participant.

The controls had normal vision without refractive error. As most of the AMD patients had already undergone cataract surgery, and spherical equivalence was lower than 0.5 D, the AMD group and the control groups had similar refractive error.

All participants were recruited from the ophthalmology department of Saint Vincent de Paul hospital, Lille, France. The study was approved by the ethical committee of Lille (N°EUDRACT 2010-101088-31), in accordance with the tenets of the Declaration of Helsinki. Written informed consent was obtained from all participants. As some participants with AMD exhibited excessive head movements, either poor validation during eye tracker calibration or loss of eye movement data occurred. Thus only 17/32 AMD patients and 17/19 older controls were included in the analyses of data. Demographic and clinical data of each group are summarized in Tables 2 and 3.

[Tables 1 and 2 about here]

#### ***Calibration of Eye Tracker and Fixation stability:***

Eye position was recorded with a SMI mobile eye tracker (Red-m Sensori-Motoric Instrument, Berlin, Germany) using Experiment Center software™. Using automatic eye-tracking and head movement compensation solutions, the infrared system provides reliable binocular gaze and “bright-pupil” data in a highly mobile and flexible way. This eye-tracker presents a high spatial resolution ( $<0.1^\circ$  according to the manufacturer) and high temporal resolution (120 Hz).

The experiment took place in a dimly illuminated room. The participants sat on a backed chair 60 cm from the center of a high-resolution display monitor (1600 x 900 pixels) and wore their best optical correction. No head immobilization by a chin rest or a forehead bar was used. Participants were asked not to move their head excessively. First, a gaze calibration with 5 points was conducted (black dots of 2x2 degrees on a white background). When the eye-tracker indicated that the calibration as “valid”, we considered the fixation as stable. In addition, we measured fixation stability using the method described by Crossland et al.<sup>28</sup> We asked the participants to fix a target (black dots of 2 x 2 degrees) in the center of the computer screen for 10 seconds.<sup>39</sup> Eye movement data were extracted with BeGaze 3.7 software™ and processed according to Crossland et al. criteria.<sup>28</sup> We obtained a BCEA (Bivariate Contour Ellipse Area) score in arcmin<sup>2</sup>. The calculation of BCEA provided a quantification of the fixation stability for each target in each participant. If the fixation was unstable or if more than 25% of the eye movements data were missing, the participant was excluded.

## ***Stimuli and Procedure***

### **Stimuli**

We used a commercial database of colored photographs of isolated objects (Hemera Photo Objects) to create our stimulus displays. Sixteen different objects were selected: 8 natural objects (various animals and vegetables) and 8 man-made objects (various tools and pieces of furniture). These 16 objects were used to create three display conditions: 9 objects (1 target and 8 distractors), 6 objects (1 target and 5 distractors) and 4 objects (1 target and 3 distractors) creating a set of 48 images (8x2x3). Within each display the objects (target and distractors) always belonged to the same semantic category and had similar colors in order to reduce a “pop out” effect of the target. We added two conditions of spacing between elements, “crowded” and “uncrowded”, resulting in a total set of 96 images (48x2). The size of each object varied between 5° and 6° horizontally and vertically, and the spacing between elements was 6° in the “uncrowded” condition and 1.5° in the “crowded” condition. Examples of stimulus displays are presented in Figure 1. Our displays measured 31.6° horizontally x 25.4° vertically at a viewing distance of 60 cm.

### **Procedure:**

Only one eye of each participant was tested. A gaze calibration was validated by the software before the experiment. Each trial started with a central fixation cross (2x2°) displayed for 1 second, then the stimulus was displayed for a maximum duration of 30 seconds, followed by an inter-stimulus interval (black background) of 1 second. The task instruction was to find a target object, predefined verbally by the experimenter just before each trial, as quickly as possible. Participants were asked to fixate the target object and then validate the response by pressing the space bar of the keyboard. When the space bar was pressed the stimulus disappeared. The order of the images was semi-randomized: four blocks of images were determined by the computer and then randomly presented. [Figure 1 about here]

### ***Outcome measures***

The main outcome measures for this experiment were accuracy and target search time. The secondary outcome measures were the recorded eye movement parameters (number of fixations, scan path ratio). We also evaluated the relationship between object search performance (including eye movement parameters), and clinical parameters. The scan path ratio is a measure of how directly the eyes move to the target, as described previously in Brockmole and Henderson.<sup>40</sup> We



divided the total distance travelled by all eye movements arriving to the target by the linear distance between the initial fixation point and the target:

### ***Statistical analysis:***

Statistical analyses were conducted using Sigma Stat (13.0) on the BCEA score, accuracy (%) and search time (ms). Where the condition of homogeneity of variance was not fulfilled, a non-parametric ANOVA was conducted. Pearson's correlation coefficients  $r$  were calculated, and a  $p < .05$  was used to determine whether relationships between stability of fixation, task performance and logMAR visual acuity were significant. Statistical significance is reported as  $p < 0.05$ . The results are presented in Figures 2 and 3. Individual data are presented in Table 3.

## **RESULTS**

### ***BCEA (Stability of fixation):***

The effect of group on fixation stability was significant ( $H_2, F(2, 51) = 18.81, P < 0.001$ ). It resulted from a difference between younger and older controls (1614 vs 4238,  $P < 0.04$ ) and between younger controls and participants with AMD (1614 vs 8738;  $P < 0.001$ ). However, the average fixation stability of AMD patients, with  $8738 \pm 1422 \text{ arcmin}^2$  did not differ significantly from that of age-matched controls who had a score of  $4238 \pm 674 \text{ arcmin}^2, P = .14$ . No significant correlation was found between the BCEA score and visual acuity ( $r = 0.18, P = 0.49$ ), greatest linear diameter ( $r = 0.08, P = 0.75$ ) or the area of the lesion ( $r = 0.16, P = 0.55$ ) in the AMD group.

### ***Object search task performance***

#### Accuracy and search time

A main effect of group was found for accuracy ( $F(2, 48) = 179.12; P < 0.001$ ) and search time ( $F(2, 48) = 89.44; P < 0.001$ ). AMD Patients were less accurate than older controls (56.5% vs 80.8%,  $P < 0.001$ ) and older controls were less accurate than younger controls (80.8% vs 93.3%,  $P < 0.001$ ). AMD patients were also slower than older controls (4093ms vs 2530ms,  $P < 0.001$ ), and older controls were slower than younger controls (2530ms vs 1727ms,  $P < 0.001$ ).

#### Effect of "crowding" on object search

An effect of crowding was observed on object search accuracy ( $F(1, 48) = 24.48; P < 0.001$ ). Crowding interacted significantly with group ( $F(2, 48) = 5.85, P < 0.005$ ). The interaction

resulted mainly from the AMD group. In this group accuracy increased from 49.9% (“crowded”) to 63.0% (“uncrowded”,  $P < 0.001$ ). The difference between the “crowded” and “uncrowded” conditions was not significant in older controls (77.0% vs 84.5%) and in younger controls (91.6% vs 94.9%). The effect of crowding was significant on search time  $F(1, 48) = 14.1$ ,  $P < 0.001$  but there was no significant interaction with group ( $F(2, 48) = 1.47$ ,  $P = 0.24$ ).

#### Effects of the number of distractors on object search performance

There was an effect of the number of distractors on search time ( $F(1, 48) = 11.11$ ;  $P < 0.001$ ) with a significantly longer response time for 8 distractors compared to 5 (3265 vs 2621ms,  $P < 0.001$ ) and to 3 distractors (3265 vs 2465ms,  $P < 0.001$ ). The interaction between group and number of distractors was not significant ( $F(4, 96) = 1.3$ ,  $P = 0.25$ ). The effect of the number of distractors was not significant on accuracy ( $F(1, 48) = 2.49$ ;  $P = 0.08$ ) and there was no significant interaction between group and number of distractors ( $F(4, 96) = 0.30$ ,  $P = 0.87$ ). There was no significant interaction between group, crowding and number of distractors ( $F(4, 96) = 1.03$ ,  $P = 0.39$  for RTs and  $F(4, 96) = 1.5$ ,  $P = 0.20$  for accuracy).

[Figures 2 and 3 about here]

#### Eye movement's parameters

A video of eye movements recorded from a patient and an age-matched control is shown in supplementary data. A group effect was found in the number of fixations to find the target object ( $F(2, 48) = 15.19$ ;  $P < 0.001$ ). Younger controls made fewer fixations than older controls (7.6 vs 11.0,  $P < 0.001$ ) and fewer than AMD patients (7.6 vs 11.1,  $P < 0.001$ ). The number of distractors had an impact on eye movements ( $F(1, 48) = 4.55$ ;  $P < 0.01$ ). More fixations were made in displays containing 8 versus 3 distractors (11.0 vs 8.8,  $P < 0.008$ ). A group effect was observed on the scan path ratio ( $F(2, 48) = 24.36$ ;  $P < 0.001$ ). AMD Patients exhibited a lower efficiency of exploration than older (5.3 vs 3.4,  $P < 0.001$ ) and younger controls (5.3 vs 3.2,  $P < 0.001$ ). An effect of the number of distractors ( $F(2, 48) = 3.98$ ;  $P < 0.02$ ), but no effect of the spacing between objects ( $p = 0.97$ ), was found on the scan path ratio. The scan path ratio was less efficient, with 8 compared to 3 distractors (4.4 vs 3.5,  $P < 0.015$ ).

## Relationship between object search and clinical parameters

We found a relationship between greatest linear diameter of the lesion and accuracy ( $r = -0.49, P < 0.04$ ) and between greatest linear diameter of the lesion and search time ( $r = 0.47, P < 0.05$ ) only when the objects were presented with the “crowded” condition. As can be seen from Figure 4 object search performance (accuracy and search time) was not related to visual acuity. There was no relationship between the duration of the disease and performance.

[Table3 about here]

[Figure 4 about here]

## **DISCUSSION**

Visual search is ubiquitous in daily life. Its reaction time is limited by retinal eccentricity, variability in the visual environment, stochastic neural processing, limitations of covert attention, and memory. Brain strategies, such as saliency, knowledge about the visual properties of the environment, knowledge of the target, contextual cues, target prevalence, and object co-occurrence, are used to optimize search performance in normal vision.<sup>30,41</sup> Most studies on visual search in patients have used optotypes: letters or Landolt rings.<sup>42,31,43</sup> Patients-based studies<sup>25,32,44</sup> with realistic visual search tasks are gaining more interest because of their resemblance to tasks that patients have to face in daily life.<sup>19,25,32</sup>

Our results can be summarized as follows: (1) Object search performance is affected by aging, with a decrease in accuracy (-13.5%) and an increase in search time (+46%) for older compared to younger normally-sighted participants. (2) Compared to age matched controls, those with AMD were less accurate, by -31%, and exhibited longer search time, by +61%. (3) For AMD patients, but for neither control group, reduced crowding improved visual search accuracy, by +21%, but not search time. (4) Adding distractors led to longer search times in all groups without any effect on accuracy. (5) Performance was not related to visual acuity or duration of neovascular AMD. (6) Object search time was positively correlated to the lesion size when objects were presented with the crowded condition.

A decline in selective attention is one of the sources contributing to age-related impairments of cognitive functions. Normal aging affects the efficiency and timing of early visual processing during multiple object tracking.<sup>45</sup> Older adults show slower response times, larger visual search slopes, and reduced cue-target association knowledge than do younger adults in guided visual

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search tasks.<sup>46</sup> This difference may explain the reduced object search efficiency in older controls compared to younger controls in our study.

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As expected, patients with AMD were less accurate and slower than age-matched controls in object search. Our results are consistent with previous reports showing that people with AMD need longer time to find a target than people without central scotomas. In a “search and identify” task using Landolt rings as stimuli, the presence of a central scotoma caused longer latencies by a factor of 1.75, and a weak correlation was found between visual acuity and task performance.<sup>31</sup> As the target often falls in the area of the scotoma the longer latencies may result from the multiple eye movements needed to relocate the target. In a visual search task for an item within digital photographs of indoor or outdoor scenes, mean search durations for patients with AMD and controls were respectively 15.3s and 8.3s.<sup>32</sup> There was a relationship between task performance and visual acuity in that search task which involved reading text within an image (e.g., the “price of an item” or the “street name”). Patients included in that study had dry AMD. Visual acuity, though reduced, fell within legal requirements for driving. These results highlight the burden of everyday tasks even with a relatively “preserved” visual acuity. In our previous work on object search in realistic panoramic scenes using binocular viewing, participants with bilateral dry or wet AMD were able to accomplish the task with high accuracy (75% correct detections) and their search time was longer than that of controls (41.5s vs 23.2s). Performance was not related to visual acuity in advanced AMD. In the present study that included exclusively neovascular AMD, with well-defined onset of the disease, and with inactivation of lesion under anti-VEGF therapy, object search performance was not related to visual acuity or to disease duration, but was correlated to the greatest linear diameter in the crowded condition.

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We found that crowding is deleterious in object search performance for neovascular AMD patients. When objects were clustered, object search accuracy was lower than when objects were separated by a blank space. This result is consistent with that of another study investigating the effect of contextual information in AMD.<sup>13</sup> Objects were presented within the context of their normal setting or isolated on a blank background. The study showed that separating the object from the scene background by a white rectangle facilitated performance in participants with AMD. The results of this study indicate that AMD increases the sensitivity to the effect of spatial masking and/or crowding. The effect of crowding was observed only in neovascular AMD patients and had no effect on older or younger controls in the present study. In normally-sighted people, a hallmark of crowding is its dependence on eccentricity. The critical spacing (i.e., the minimum distance between target and flanker stimuli that causes impaired identification of the target as eccentricity increases) is approximately a constant fraction which is half of eccentricity and is referred to as Bouma’s law.<sup>34</sup> Our neovascular AMD participants had a mean greatest linear diameter of 3.6mm,

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corresponding approximately to a 12° scotoma. A critical spacing between objects of 6°, as used here, is a useful knowledge for neovascular AMD since this spacing size improved accuracy by +21%. The improvement observed in the uncrowded condition contrasts with Wallace et al<sup>47</sup> who found that the critical spacing for crowding was not substantially different from that of controls. Our study is very different from that of Wallace. We used a visual search task in which participants explored the display to find the target. They asked participants to name a target closely surrounded by 2 flankers. The stimuli (target and flankers) were presented at the exact location of the preferred retinal location of their patients (2.9° for P1, 4.6° for P2 and 6.7° for P3) whilst the target location varied in each trial in the present experiment. Their 3 patients had substantial experience with psychophysics experiments whilst our patients were novice.

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Unsurprisingly, the number of distractors increased search time for all groups without any effect on accuracy. Adding more distractors degraded search time performance because visual coding is limited by stochastic neural processing.<sup>30</sup> We did not find any difference in the number of fixations to find the target and in the scan path ratio between groups. This result can be explained by the fact that we included only AMD patients with a good calibration. This similarity was also reported previously in Taylor's work, when the authors selected 16 AMD participants with good calibration and validation compared to controls. The number of distractors increased the number of fixations to identify each item in the display, resulting in longer search times.<sup>32</sup>

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Even with the limitations of monocular viewing and the use of a computer-based visual search task rather than a real-world task, this work highlights difficulties in object search encountered by AMD patients in daily activities. Although visual acuity is commonly used as the primary functional subjective endpoint in a clinical trial,<sup>48,49</sup> stabilization of a lesion size (neovascular AMD) and geographic atrophy area (atrophic AMD) is an objective, anatomic endpoint that is associated with a patient's ability to perform visual search tasks.

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**Conclusion and limitations:** Neovascular AMD patients have measurable difficulties in object search in a computer-based task. Our results demonstrate that aspects of ocular anatomy and visual function other than acuity influence performance on a visual task that resembles those tasks patients encounter in real life. For AMD patients in whom visual acuity cannot be improved, object search performance can be significantly improved by increasing the space between objects. The practical application of our results is to increase public awareness of spacing issues for the visually impaired. Increased spacing in all printed materials and in objects within a patient's environment can help patients more efficiently perform their daily tasks. There are several limitations in this study: (1) younger participants had a higher level of education than patients and age-matched controls.

Though the objects used were familiar this might have influenced performance in terms of higher accuracy and shorter search time. (2) All the objects (target and distracters) were from the same semantic category and therefore, were structurally similar and had a similar color. This might have increased the difficulty for participants with low vision. The detection of the target might have been easier for patients if the target was structurally and semantically different from the distractors. (3) Older participants (patients and age-matched controls) were significantly slower than young participants. This might result, in addition to the search time, from a motor slowing as the response was based on the space bar button press.

## REFERENCES

1. Klein R, Chou CF, Klein BE, et al. Prevalence of age-related macular degeneration in the US population. *Arch Ophthalmol* 2011; 129: 75-80.
2. Buckle M, Lee A, Mohamed Q, et al. Prevalence and incidence of blindness and other degrees of sight impairment in patients treated for neovascular age-related macular degeneration in a well-defined region of the United Kingdom. *Eye (Lond)* 2015; 29: 403-408.
3. Solomon SD, Lindsley K, Vedula SS et al. Anti-vascular endothelial growth factor for neovascular age-related macular degeneration. *The Cochrane Database of Systematic Rev* 2014, 8 :CD005139.  
<https://www.ncbi.nlm.nih.gov/pubmed/?term=10.1002%2F14651858.CD005139.pub3>
4. Sarwar S, Clearfield E, Soliman MK, et al. Aflibercept for neovascular age-related macular degeneration. *The Cochrane Database of Systematic Rev* 2016; 2 :CD011346.  
<https://www.ncbi.nlm.nih.gov/pubmed/?term=10.1002%2F14651858.CD011346.pub2>
5. Tran THC, Dumas S, Coscas F. Two-Year Outcome of Aflibercept in Patients with Pigment Epithelial Detachment due to Neovascular Age-Related Macular Degeneration (nAMD) Refractory to Ranibizumab. *J ophthalmol* 2017; 2017: 8984313.
6. Yuzawa M, Fujita K, Tanaka E et al.. Assessing quality of life in the treatment of patients with age-related macular degeneration: clinical research findings and recommendations for clinical practice. *Clin Ophthalmol* 2013; 7: 1325-1332.
7. Senra H, Ali Z, Balaskas K, Aslam T. Psychological impact of anti-VEGF treatments for wet macular degeneration-a review. *Graefe's Arch Clin Exp Ophthalmol* 2016; 254: 1873-1880.
8. Cohen SY, Oubraham H, Uzzan J, et al. Causes of unsuccessful ranibizumab treatment in exudative age-related macular degeneration in clinical settings. *Retina* 2012; 32: 1480-1485.
9. Danis RP, Lavine JA, Domalpally A. Geographic atrophy in patients with advanced dry age-related macular degeneration: current challenges and future prospects. *Clin Ophthalmol* 2015; 9: 2159-2174.
10. Boulanger-Scemama E, Sayag D, Ha Chau Tran T, et al. Ranibizumab and exudative age-related macular degeneration: 5-year multicentric functional and anatomical results in real-life practice. *J Fr Ophtalmol* 2016; 39: 668-674.
11. Matchar DB, Suner IJ, Samsa GP, et al. *Measuring Quality of Life for Patients with Age-Related Macular Degeneration*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2006 Feb. [AHRQ Technology Assessments](#).

Code de champ modifié

Code de champ modifié

12. Boucart M, Delerue C, Thibaut M, et al. Impact of Wet Macular Degeneration on the Execution of Natural Actions. *Invest Ophthalmol & Vis Sci* 2015; 56: 6832-6838.
13. Boucart M, Moroni C, Szaffarczyk S, et al. Implicit processing of scene context in macular degeneration. *Invest Ophthalmol Vis Sci* 2013;54: 1950-1957.
14. Corveleyn X, Lenoble Q, Szaffarczyk S, et al. What Is the Nature of the Reach and Grasp Deficit in Wet Age-related Macular Degeneration? *Optom Vis Sci* 2018; 95: 171-182.
15. Lenoble Q, Tran TH, Szaffarczyk S, et al. Categorization Task over a Touch Screen in Age-Related Macular Degeneration. *Optom Vis Sci* 2015; 92: 986-994.
16. Thibaut M, Delerue C, Boucart M, et al. Visual exploration of objects and scenes in patients with age-related macular degeneration. *J Fr Ophtalmol* 2016; 39: 82-89.
17. Thibaut M, Tran TH, Delerue C, et al. Misidentifying a tennis racket as keys: object identification in people with age-related macular degeneration. *Ophthalmic Physiol Opt* 2015; 35: 336-344.
18. Thibaut M, Tran TH, Szaffarczyk S, et al. The contribution of central and peripheral vision in scene categorization: a study on people with central vision loss. *Vis Res* 2014; 98: 46-53.
19. Thibaut M, Tran TH, Szaffarczyk S, et al. Impact of age-related macular degeneration on object searches in realistic panoramic scenes. *Clin Expl Optom* 2018; 101: 372-379.
20. Tran TH, Boucart M. Perception of objects and scenes in age-related macular degeneration. *J Fr Ophtalmol* 2012; 35: 58-68.
21. Tran TH, Despretz P, Boucart M. Scene perception in age-related macular degeneration: the effect of contrast. *Optom Vis Sci* 2012; 89 : 419-425.
22. Tran TH, Despretz P, Boucart M. Space representation in age-related macular degeneration. *Optom Vis Sci* 2014; 91: 1012-1020.
23. Tran TH, Guyader N, Guerin A, et al. Figure ground discrimination in age-related macular degeneration. *Invest Ophthalmol & Vis Sci* 2011; 52: 1655-1660.
24. Tran TH, Rambaud C, Despretz P, et al. Scene perception in age-related macular degeneration. *Invest Ophthalmol & Vis Sci* 2010; 51: 6868-6874.
25. Crabb DP, Taylor DJ. Searching for unity: Real-world versus item-based visual search in age-related eye disease. *Behav and Brain Sci* 2017; 40: e135.
26. Gaffney AJ, Margrain TH, Bunce CV, et al. How effective is eccentric viewing training? A systematic literature review. *Ophthalmic Physiol Opt* 2014;v34: 427-437.
27. Crossland MD, Engel SA, Legge GE. The preferred retinal locus in macular disease: toward a consensus definition. *Retina* 2011; 31: 2109-2114.



28. Crossland MD, Sims M, Galbraith RF, et al. Evaluation of a new quantitative technique to assess the number and extent of preferred retinal loci in macular disease. *Vis Res* 2004; 44: 1537-1546.
29. Fragiotta S, Carnevale C, Cutini A, et al. Factors Influencing Fixation Stability Area: A Comparison of Two Methods of Recording. *Opt Vis Sci* 2018; 95: 384-390.
30. Eckstein MP. Visual search: a retrospective. *J Vis* 2011; 11(5). pii: 14. doi: 10.1167/11.5.14. Review.
31. MacKeben M, Fletcher DC. Target search and identification performance in low vision patients. *Invest Ophthalmol & Vis Sci* 2011; 52: 7603-7609.
32. Taylor DJ, Smith ND, Crabb DP. Searching for Objects in Everyday Scenes: Measuring Performance in People With Dry Age-Related Macular Degeneration. *Invest Ophthalmol & Vis Sci* 2017; 58 : 1887-1892.
33. Mangione CM, Lee PP, Pitts J, et al. Psychometric properties of the National Eye Institute Visual Function Questionnaire (NEI-VFQ). NEI-VFQ Field Test Investigators. *Arch Ophthalmol* 1998; 116: 1496-1504.
34. Bouma H. Interaction effects in parafoveal letter recognition. *Nature* 1970; 226: 177-178.
35. Calabrese A, Bernard JB, Hoffart L, et al. Small effect of interline spacing on maximal reading speed in low-vision patients with central field loss irrespective of scotoma size. *Invest Ophthalmol & Vis Sci* 2010; 51: 1247-1254.
36. Blackmore-Wright S, Georgeson MA, Anderson SJ. Enhanced text spacing improves reading performance in individuals with macular disease. *PloS One* 2013; 11:e80325. doi: 10.1371/journal.pone.0080325. eCollection 2013.
37. Querques G, Tran TH, Forte R, Querques L, Bandello F, Souied EH. Anatomic response of occult choroidal neovascularization to intravitreal ranibizumab: a study by indocyanine green angiography. *Graefes Arch for Clin Exp Ophthalmol* 2012; 250: 479-484.
38. Tran TH, Querques G, Forzy G, et al. Angiographic regression patterns after intravitreal ranibizumab injections for neovascular age-related macular degeneration. *Ophthalmic Surgery, Lasers & Imaging* 2011; 42: 498-508.
39. Bellmann C, Feely M, Crossland MD, et al. Fixation stability using central and pericentral fixation targets in patients with age-related macular degeneration. *Ophthalmology* 2004; 111: 2265-2270.
40. Brockmole JR, Henderson JM. Recognition and attention guidance during contextual cueing in real-world scenes: evidence from eye movements. *Q J Exp Psychol (Hove)* 2006; 5: 1177-1187.

41. Mack SC, Eckstein MP. Object co-occurrence serves as a contextual cue to guide and facilitate visual search in a natural viewing environment. *J Vis* 2011; 11: 1-16. doi: 10.1167/11.9.9.
42. Kuyk TK, Liu L, Fuhr PS. Feature search in persons with severe visual impairment. *Vis Res* 2005; 45: 3224-3234.
43. Geringswald F, Herbig A, Hoffmann MB, et al. Contextual cueing impairment in patients with age-related macular degeneration. *J Vis* 2013; 13. pii: 28. doi: 10.1167/13.3.28.
44. Taylor DJ, Hobby AE, Binns AM, et al. How does age-related macular degeneration affect real-world visual ability and quality of life? A systematic review. *BMJ Open* 2016; 6:e011504. doi: 10.1136/bmjopen-2016-011504.
45. Stormer VS, Li SC, Heekeren HR, et al. Normal aging delays and compromises early multifocal visual attention during object tracking. *J Cog Neurosci* 2013; 25: 188-202.
46. Hahn S, Buttaccio DR. Aging and guided visual search: the role of visual working memory. *Neuropsychol, Dev, and Cog. Section B, Aging, Neuropsychol and Cog* 2018;25(4): 535-549.
47. Wallace JM, Chung ST and Tjan BS. Object crowding in age-related macular degeneration. *J Vis* 2017; 17: 33. doi: 10.1167/17.1.33.
48. Altaweel MM, Daniel E, Martin DF, et al. Outcomes of eyes with lesions composed of >50% blood in the Comparison of Age-related Macular Degeneration Treatments Trials (CATT). *Ophthalmology* 2015; 122:391-398.
49. Grunwald JE, Pistilli M, Ying GS, et al. Growth of geographic atrophy in the comparison of age-related macular degeneration treatments trials. *Ophthalmology* 2015; 122: 809-816.

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**Table 1:** Inclusion and exclusion Criteria for participants

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Inclusion criteria	
AMD group	Neovascular AMD well defined with subfoveal involvement confirmed by fluorescein and indocyanine angiography Best corrected visual acuity between 20/40 and 20/400 in the eye to be studied Refraction between +3D and -3D
Controls group	Normal vision (visual acuity of 20/25 to 20/20)

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Exclusion criteria	
	History of any neurological or psychiatric disease History of ophthalmologic disease other than AMD that might compromise its VA or peripheral vision during the study (amblyopic, uncontrolled glaucoma, optic neuropathy, diabetic retinopathy, uveitis) Insulin-dependent diabetes Unable to communicate (deafness) Mental deterioration with MMSE < 24

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MMSE, Mini-Mental State Examination; VA, visual acuity.

**Table 2:** Demographic and clinical data of AMD participants, older and younger controls

<b>nAMD participants</b>	N=17
<b>Age (mean in years <math>\pm</math> SD, range)</b>	78.1 $\pm$ 4.2 (71-86)
<b>Gender (M/F)</b>	3M/14F
<b>MMSE (mean <math>\pm</math> SD, range)</b>	28.3 $\pm$ 2.5 (26-30)
<b>VA (mean in LogMAR<math>\pm</math> SD)</b>	0.64 $\pm$ 0.33
<b>Greatest linear diameter (mean in mm<math>\pm</math> SD, range)</b>	3.6 $\pm$ 1.6 (0.5-6.5)
<b>Area of the lesion (mean in mm<sup>2</sup><math>\pm</math> SD, range)</b>	7.4 $\pm$ 6.8 (0.4-25.7)
<b>Age-matched control participants</b>	N=17
<b>Age (mean in years <math>\pm</math> SD, range)</b>	76.9 $\pm$ 7.2 (62-86)
<b>Gender (M/F)</b>	6M/11F
<b>MMSE (mean <math>\pm</math> SD, range)</b>	29.1 $\pm$ 1.2 (26-30)
<b>VA (mean in LogMAR<math>\pm</math> SD)</b>	0.03 $\pm$ 0.04
<b>Young adult participants</b>	N=17
<b>Age (mean in years <math>\pm</math> SD, range)</b>	23.8 $\pm$ 2.3 (21-27)
<b>Gender (M/F)</b>	9M/8F
<b>VA (mean in LogMAR<math>\pm</math> SD)</b>	1.00 $\pm$ 0.00

MMSE, Mini-Mental State Examination; F, female; M, male; VA, visual acuity

**Table 3:** Individual clinical data and object search performance in the crowded and the uncrowded conditions

Num ber /Gend er /Age	Test ed Eye	MM SE score	ETD RS score	Durati on of nAMD D (mont hs)	CN V typ e	Anti- VEGF therapy	GL D (m m)	SA (mm 2)	Object search performance			
									Crowded condition		Uncrowded condition	
									Accura cy (%)	Respo nse time (ms)	Accura cy (%)	Respo nse time (ms)
1/F/8 2	OR	27	55	42.4	typ e 2	Ranibizu mab	341 7	6.97	37.5	4096	47.6	3135
2/F/7 8	OR	28	65	45.7	typ e 1	Afliberce pt	305 8	4.8	45.8	3089	54.2	6347
3/F/8 2	OR	30	65	76.1	typ e 1	Ranibizu mab	292 5	4.91	42.9	3382	52.9	3822
4/F/8 0	OR	30	35	74.2	typ e 2	Ranibizu mab	337 5	8.9	45.8	4136	62.5	2801
5/F/8 0	OR	29	45	13.8	typ e 1	Ranibizu mab	353 2	9.57	37.5	5108	44.0	5708
6/F/8 3	OR	28	65	14.4	typ e 1	Ranibizu mab	258 6	2.82	41.7	2677	62.5	4939
7/F/8 0	OR	30	5	3	typ e 1	Ranibizu mab	652 5	25.7 4	55.2	2751	41.7	2751
8/F/7 7	OR	28	65	27.3	typ e 1	Ranibizu mab	162 3	1.39	62.5	3677	75.0	2665
9/F/7 7	OR	30	55	7.5	typ e 1	Ranibizu mab	283 1	4.21	54.2	3688	52.4	2852
10/F/ 81	OR	30	33	73.2	typ e 2	Ranibizu mab	589 6	21.2 1	39.3	8449	77.2	6816
11/F/ 79	OR	30	65	7.9	typ e 3	Ranibizu mab	384 384	0.4	62.5	3633	83.3	3137
12/F/ 71	OR	29	70	9.1	typ e 1	Ranibizu mab	175 8	2.83	50.0	2251	70.8	1903
13/F/ 81	OR	30	45	60	typ e 2	Ranibizu mab	491 0	9.79	39.3	7714	56.3	8077
14/F/ 86	OR	30	68	41	typ e 3	Ranibizu mab	855 855	0.42	62.5	3859	66.7	3700
15/F/ 74	OS	27	50	1.8	typ e 3	Afliberce pt	300 6	5.3	59.5	4500	61.1	5847
16/F/ 73	OR	30	65	98	typ e 1	Afliberce pt	266 9	3.64	66.7	2554	87.5	2484
17/F/ 73	OR	26	40	41	typ e 2	Ranibizu mab	468 1	10.6 5	50.0	3911	75.4	3791

CNV: choroidal neovascularization, F: female, OS: left eye, OR: right eye M: male, F: female, VA: visual acuity, GLD: Greatest Linear Diameter ( mm), SA:Surface Area ( mm<sup>2</sup>).

**Figure legend:**

**Figure 1:** Example of stimuli used in the experiment in 6 different conditions: one target among 8 distractors (right), 5 distractors (middle) or 3 distractors (left), in the crowded condition (top) and the uncrowded condition (bottom).

**Figure 2:** Accuracy (%) of the target search as a function of group (AMD, older controls, younger controls), crowding (C= crowded vs U = uncrowded) and number of distractors (3, 5, 8).

**Figure 3:** Search time (sec) of the target as a function of group (AMD, older controls, younger controls), crowding (C= crowded vs U = uncrowded) and number of distractors (3, 5, 8).

**Figure 4:** Accuracy and search time for the crowded and the uncrowded conditions as a function of acuity (LogMar) in ascending order for the 17 patients.

Figure 1

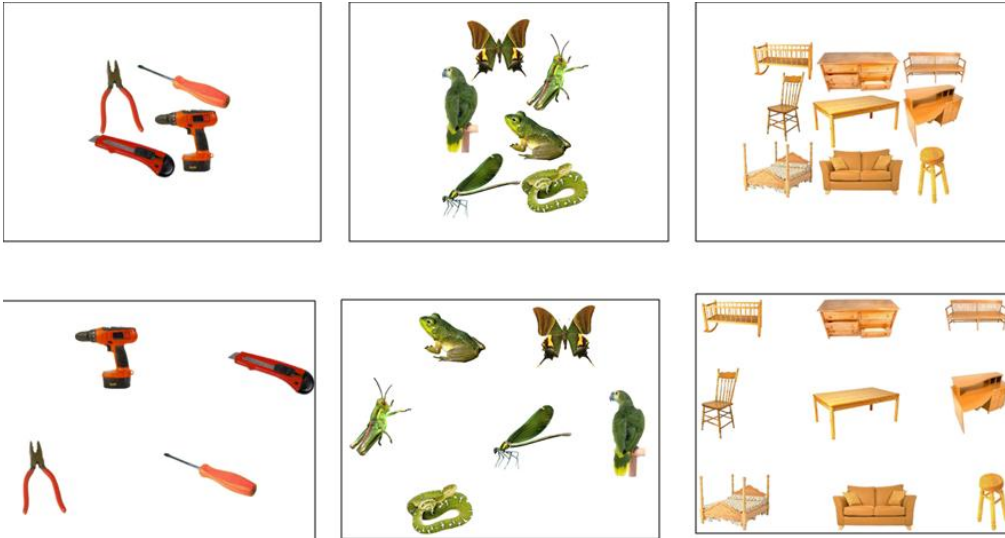




Figure 2

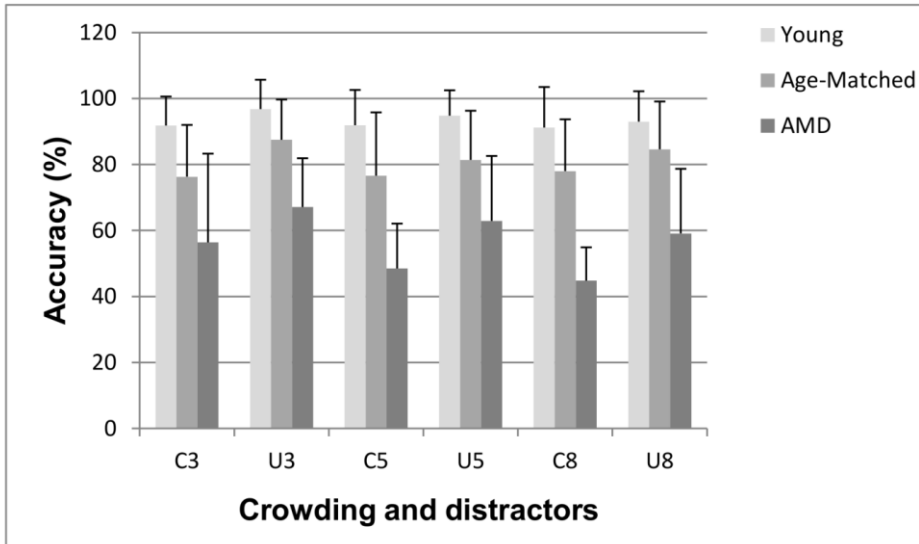


Figure 3

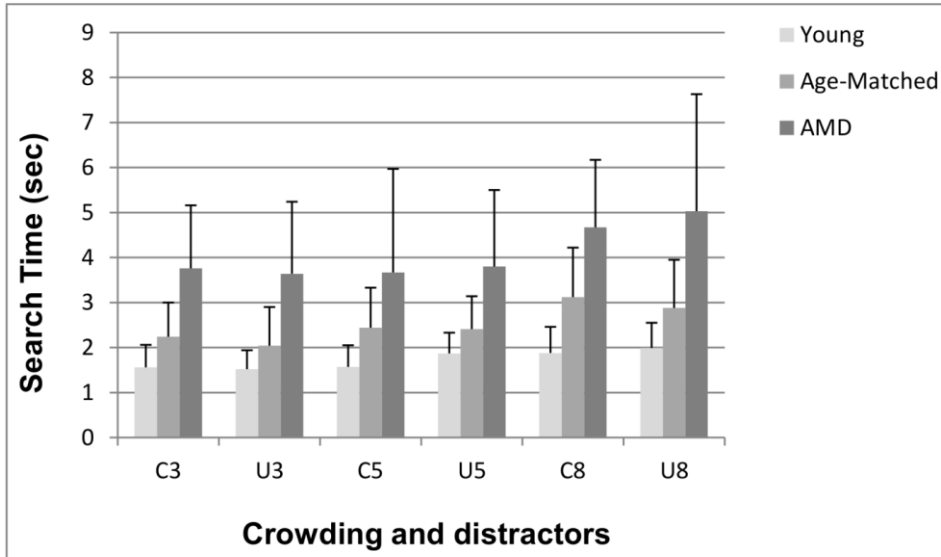


Figure 4

