

# Spatial and temporal crowding in amblyopia

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## Abstract

Spatial crowding is a well-known deficit in amblyopia. We have previously reported evidence suggesting that the inability to isolate stimuli in space in crowded displays (spatial crowding) is a largely independent component of the amblyopic deficit in visual acuity, which is typically found in strabismic amblyopia [Bonneh, Y., Sagi, D., & Polat, U. (2004a). Local and non-local deficits in amblyopia: Acuity and spatial interactions. *Vision Research*, 44, 3009–3110]. Here, we extend this result to the temporal domain by measuring visual acuity (VA) for a single pattern in a rapid serial visual presentation (RSVP-VA,  $N = 15$ ) for fast (“crowded”) and slow (“uncrowded”) presentations. We found that strabismic amblyopes but not anisometric amblyopes or normal controls exhibited a significant difference between VA under the fast and slow conditions. We further compared the “temporal crowding” measure to two measures of spatial crowding: (1) static Tumbling-E acuity in multi-pattern crowded displays ( $N = 26$ ) and (2) Gabor alignment with lateral flankers ( $N = 20$ ). We found that all three measures of crowding (one temporal and two spatial) were highly correlated across subjects while being largely independent of the visual acuity for a single isolated pattern, with both spatial and temporal crowding being high and correlated in strabismus and low in anisometropia. This suggests that time and space are related in crowding, at least in amblyopia.

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## 1. Introduction

A pattern can be difficult to identify when surrounded by a “crowd” of flanking patterns, a phenomenon called “crowding” (Stuart & Burian, 1962). A briefly flashed pattern can be difficult to identify when surrounded in time (before and/or after) by other patterns (Breitmeyer, 1984), forming a “temporal crowding” situation. This paper describes the possible relation between the two as studied in people with amblyopia.

The phenomenon of “perceptual crowding” was originally described as a reduction in letter acuity when the letter appears in a line, as compared to its acuity in isolation (Stuart & Burian, 1962). This reduction in acuity is due to an interference effect by the flanking patterns, sometimes termed “contour interaction”, and it depends on their dis-

tance from the central pattern (Flom, 1991; Flom, Weymouth, & Kahneman, 1963). The critical distance for crowding increases with eccentricity, extending as far as half the retinal eccentricity of the target (Bouma & Andriessen, 1970; Kooi, Toet, Tripathy, & Levi, 1994; Pelli, Palomares, & Majaj, 2004), and at the periphery it appears to be independent of the size of the target (Pelli et al., 2004; Tripathy & Cavanagh, 2002).

The related phenomena of “visual masking” refers to impaired performance regarding some judgment of a target stimulus when a mask stimulus is briefly presented before, during or after the target, at the same or at flanking locations (for a review, see Breitmeyer (1984), Breitmeyer & Ogmen (2000), Enns & Di Lollo (2000)). Within the literature on masking, the term “ordinary masking” is typically used to describe early interference, perhaps within the first stage of feature extraction in the visual cortex, e.g., in contrast detection experiments for a target surrounded by masks in space and time (Pelli et al., 2004). Masking, in

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general, depends on the target-flanker distance and on their temporal relations. A strong masking effect occurs when the mask appears within a time window of 100 ms or less relative to the target (Breitmeyer, 1984; Breitmeyer & Ogmen, 2000; Enns & Di Lollo, 2000; Francis, 2000; Gorea, 1987).

The relation between ordinary masking (typically studied in detection experiments) and crowding (typically studied in pattern identification experiments) is unclear. Studies in the spatial domain suggest that ordinary masking and crowding are related (Livne & Sagi, 2007; Petrov & McKee, 2006; Polat & Sagi, 1993), distinct (Parkes, Lund, Angelucci, Solomon, & Morgan, 2001; Pelli et al., 2004) or partially related (Bonneh, Sagi, & Polat, 2004a; Chung, Levi, & Legge, 2001). It is suggested that both crowding and ordinary masking are special cases of “masking,” which, in general, refers to any effect of a “mask” pattern on the discriminability of a target signal (Pelli et al., 2004). Although, masking is typically described in terms of suppression or early alteration of the target signal and crowding as “pooling” or over-integration of target and mask signals (Hariharan, Levi, & Klein, 2005; Pelli et al., 2004) or the inability to individuate a target among distracters (Tripathy & Cavanagh, 2002), both types of explanations could be applied to different experimental data. For example, we could discuss typical masking experiments in terms of pooling or attentional resolution and discuss typical crowding experiments in terms of signal suppression. Likewise, we can refer to some temporal masking effects as “temporal crowding” and investigate how the relationship between space and time affects the ability of humans to isolate items among distracters. Our approach is to investigate amblyopic observers who typically demonstrate very significant effects of spatial crowding at fixation (e.g. Bonneh et al., 2004a).

Amblyopia is a developmental disorder of spatial vision characterized by reduced visual acuity, which cannot be improved by refractive correction, and is not due to ocular pathology. In addition to the main symptom of abnormal optotype acuity measured with static charts, amblyopia is also associated with reduced contrast sensitivity (Bradley & Freeman, 1981; Hess & Howell, 1977; Levi & Harwerth, 1977), grating and Vernier acuity (Bradley & Freeman, 1981; Levi & Klein, 1982a, 1982b; McKee, Levi, & Movshon, 2003), spatial distortions (Bedell & Flom, 1981, 1983; Sireteanu, Lagreze, & Constantinescu, 1993), and abnormal spatial interactions (Bonneh et al., 2004a; Ellemberg, Hess, & Arseneault, 2002; Kovacs, Polat, Pennefather, Chandna, & Norcia, 2000; Levi, Klein, & Hariharan, 2002c; Mussap & Levi, 2000; Polat, Sagi, & Norcia, 1997; Polat, Ma-Naim, Belkin, & Sagi, 2004; Polat, Bonneh, Ma-Naim, Belkin, & Sagi, 2005; Poppel & Levi, 2000).

Crowding is an important deficit in amblyopia. It has been known for several decades that people with amblyopia have better letter acuity for an isolated letter than when this letter appears in a line of letters (Stuart & Burian, 1962). The reduction in acuity is due to an interference

effect by the flanking patterns and depends on their distance from the central pattern (Flom, 1991; Flom et al., 1963). Thus, the extent of crowding (at least for broadband stimuli, e.g. lines or letter) appears to be proportional to the uncrowded acuity and thus amblyopes were considered to have normal crowding relative to their acuity (Flom et al., 1963; Hess & Jacobs, 1979; Levi & Klein, 1985; Simmers, Gray, McGraw, & Winn, 1999). However, several recent studies showed that crowding in strabismic amblyopes extends over greater distances for broadband stimuli even when expressed relative to the uncrowded acuity (Bonneh et al., 2004a; Hess, Dakin, Tewfik, & Brown, 2001) or for narrow-band stimuli, e.g. Gabor patches (Levi, Hariharan, & Klein, 2002a), even when tested with size and spatial-frequency comparable (via scaling) to the normal fovea. Thus, the fault is unlikely to be in the first filtering stage, and it was suggested that it is due to abnormal second stage integration or pooling, which extends over a large spatial distance (Levi et al., 2002a).

Another view proposed by Polat et al. (1997) is that the amblyopic deficit in spatial vision, and hence crowding, may stem, at least in part, from abnormal development of long-range spatial interactions. Psychophysical and physiological studies provide evidence, in normal vision, for early mechanisms of lateral integration, possibly mediated via long-range connections in the primary visual cortex (Bonneh & Sagi, 1998; Gilbert, 1998; Polat & Sagi, 1993; Polat, Mizobe, Pettet, Kasamatsu, & Norcia, 1998). The first indication that amblyopic subjects fail to show facilitation of local contrast detection in the presence of high-contrast collinear flankers (Polat et al., 1997) was recently supported by other studies (Bonneh et al., 2004a; Ellemberg et al., 2002; Levi et al., 2002a; Polat et al., 2004, 2005). However, the relationship between the abnormal lateral suppression and crowding is still not fully understood.

Amblyopia is also associated with a temporal deficit, which includes deficits in perception of motion-defined form, temporal integration and asynchrony discrimination, as well as increased latency of response for stimuli presented to the amblyopic eye (see Asper, Crewther, & Crewther (2000) for a review). Steinman, Levi, and McKee (1988) found that in strabismic amblyopia, the temporal asynchrony detection thresholds for each eye were proportional to the grating resolution for that eye, which suggests a common mechanism for the losses in resolution and temporal processing. The increased latency in amblyopia has been measured psychophysically, manifested as increased reaction times (RTs) (Hamasaki & Flynn, 1981; Loshin & Levi, 1983) and saccadic latencies (Ciuffreda, Kenyon, & Stark, 1978) as well as prolonged neural latencies in the form of longer VEP latencies (Davis et al., 2003; Levi & Harwerth, 1978). The RTs for the amblyopic eye were found to be correlated with visual acuity in strabismic amblyopes (Hamasaki & Flynn, 1981), but at the same time were related to contrast sensitivity because latencies are known to decrease with contrast (Ciuffreda, Levi, &

Selenow, 1991) and lower contrast sensitivity is typically found in amblyopia (Bonneh et al., 2004a; Bradley & Freeman, 1981; Hess & Howell, 1977; Levi & Harwerth, 1977). It was also found, although for a small number of amblyopes, that when stimuli are equated relative to the contrast detection threshold, the RTs become similar (Loshin & Levi, 1983). Hence, it was suggested that the increased RTs as well as VEP latencies do not reflect a fixed neural delay, but rather reflect the contrast-threshold deficit of the amblyopic eye (Ciuffreda et al., 1991).

Our recent study of crowding in a large number ( $N > 50$ ) of amblyopic subjects (Bonneh et al., 2004a) shows that spatial crowding constitutes a major component of the strabismic (but not anisometric) acuity deficit, which is largely independent of (not correlated with) the acuity of a single pattern at fixation. Moreover, this non-local effect is manifested in a correlated manner in different paradigms: static Tumbling-E pattern identification and contrast detection in the presence of a Gabor flanker (lateral masking) along the horizontal axis in a side-by-side configuration. This intriguing correlation between the crowding effects measured in very different types of paradigms, which are not correlated with the acuity of an isolated pattern, inspired us to consider the idea that the general difficulty of strabismic amblyopes to select or individuate a pattern among distracters in space (Sharma, Levi, & Klein, 2000) may also be generalized to the temporal domain. The results reported in the current study support this idea by measuring “temporal crowding” in rapid serial presentations (RSVP). The results show that strabismic but not anisometric amblyopes have a greater reduction in VA under conditions of fast RSVP (temporal crowding) than normal controls. Moreover, the temporal crowding effect was correlated across subjects with two different types of spatial crowding paradigms, with all crowding effects being largely independent of the acuity for a single pattern. This work was previously reported in an abstract (Bonneh, Polat, & Sagi, 2004b).

## 2. Methods

### 2.1. Subjects

The study population comprised 26 subjects between 17 and 55 years old, who had been diagnosed with unilateral amblyopia secondary to strabismus or anisometropia or both. The subjects were divided into two categories: (a) anisometric, (b) strabismic, or combined (strabismic anisometropes). There were three tasks, which were performed by subgroups of the amblyopic subjects: Task 1 (RSVP, temporal crowding) by  $N = 20$ , Task 2 (EVA) by  $N = 26$  and Task 3 (alignment) by  $N = 15$ . There was an overlap of  $N = 15$  subjects between tasks 1 and 2,  $N = 9$  between Tasks 2 and 3 and  $N = 20$  between Tasks 1 and 3 (see Table 2, bottom). The VA data (an average of two measurements) for all the subjects as well as the number and VA group average for each experiment and category are summarized in Table 1. Among the strabismic subjects ( $N = 16$ ), there were subjects with severe amblyopia ( $VA > 0.7$ ,  $N = 6$ ), while the rest of the strabismic subjects ( $VA < 0.7$ ;  $N = 10$ ) were verified to have steady and central fixation (measurement accuracy of about  $0.5^\circ$ ). In addition to the amblyopic subjects, we had a separate control group in monocular viewing for each of the experiments:  $N = 10$  for Task 1 (RSVP),  $N = 30$  for Task 2 (EVA), and  $N = 10$  for Task 3 (alignment). The controls were between 20 and 30 years old, with normal or corrected-to-normal vision.

### 2.2. Optotype visual acuity (VA)

Optotype acuity was measured with a Bailey–Lovie LogMAR chart, as has been done in most recent amblyopia studies (e.g. McKee et al., 2003). Observers viewed the chart with their best visual correction at a distance of 3 m. Two tests were administered, one at the beginning and one at the end of the sequence of masking experiments reported elsewhere (Polat et al., 2004) in order to accommodate possible VA improvements.

### 2.3. Apparatus

Stimuli were displayed on a 17” CRT monitor controlled by dedicated software running on a Windows PC. The video format was true color (RGB), a 100-Hz refresh rate, with  $1024 \times 768$  pixels resolution occupying a  $12^\circ \times 9^\circ$  area from 1.5 m. Luminance values were  $\gamma$ -corrected. The sitting distance was 1.5 m in all tasks except from task 1, and all experiments were administered in the dark. In all experiments involving Gabor signals, as well as the RSVP experiment, the mean luminance was  $40 \text{ cd/m}^2$ .

Table 1  
Statistical data on subjects’ visual acuity (VA) as measured in a LogMAR optotype acuity chart

Experiment	Group	# of Subjects	VA (LogMAR)	Range
RSVP-VA (temporal crowding)	All patients	15	$0.45 \pm 0.08$	0.18–0.99
	Aniso	6	$0.33 \pm 0.05$	0.18–0.60
	Strab	9	$0.55 \pm 0.12$	0.18–0.99
	Controls	10	$\sim 0$	$\sim 0$
Tumbling-E VA	All patients	26	$0.44 \pm 0.06$	0.18–0.99
	Aniso	10	$0.31 \pm 0.06$	0.18–0.6
	Strab	16	$0.53 \pm 0.08$	0.18–0.99
	Controls	30	$\sim 0$	$\sim 0$
Gabor alignment	All patients	20	$0.46 \pm 0.06$	0.18–0.99
	Aniso	7	$0.31 \pm 0.06$	0.16–0.48
	Strab	13	$0.54 \pm 0.08$	0.24–0.99
	Controls	10	$\sim 0$	$\sim 0$

Subjects were divided into two groups according to the amblyopia type: (a) anisometric, (b) strabismic, or combined (strabismic anisometropes). Subjects were also grouped by the different experiments, since not all subjects performed all the experiments. The number of “overlapping subjects” that participated in each pair of experiments appears in Table 2, bottom.

#### 2.4. Task 1: Temporal crowding in RSVP displays

This new paradigm attempts to measure “crowding” in the time domain, i.e. the loss of visual acuity when stimuli are close together in time. It could be thought of as a subset of the attentional blink paradigm (Raymond, Shapiro, & Arnell, 1992) with only one target, and with a novel manipulation of pattern size used to measure visual acuity (see Chung (2004) for a manipulation of size in a reading speed test with spatial crowding). The paradigm is illustrated in Fig. 1a.

##### 2.4.1. Stimuli

A rapid sequence of visual presentation (RSVP) of nine black digits on a gray background generated by removing different segments of a rectangular pattern forming the shape of an eight, and presented in two modes: slow (“uncrowded”) with SOA = 400 ms and fast (“crowded”) with SOA = 200 ms between the onsets of each digit. One of the digits appearing fourth or fifth was smaller (70%) and was the target for identification.

##### 2.4.2. Procedure

Subjects were seated 0.7 m from the screen and viewed the stimuli with their good eye covered by an opaque lens (left eye covered for the controls);

they were required to identify the smaller digit in the sequence (chance level of 15%). The size of the patterns was changed in 0.1 Log MAR (log units) steps. There were 10 trials per size and sizes were arranged from large to small. The sequence of sizes for each time condition was repeated 2–4 times, and the threshold was estimated from the psychometric curves as the pattern size that leads to 50% correct identification given in Log MAR-equivalent acuity units. There were separate runs for the slow (“uncrowded”) and fast (“crowded”) conditions, and the RSVP-VA elevation (crowding effect) was calculated from the difference between the acuities in the fast and the slow conditions. This measure of crowding parallels the measure obtained in the Gabor alignment task, which was also based on subtracting the uncrowded acuity from the crowded one at a fixed flanker distance.

#### 2.5. Task 2: Spatial crowding in static Tumbling-E patterns (EVA)

This paradigm was identical to that described in our previous paper (Bonneh et al., 2004a) and its description was introduced here for convenience. We applied it here for correlation purposes in order to investigate the general properties of crowding across paradigms. It is a Log MAR chart equivalent, monitor-based paradigm that used E patterns presented statically until there was a response.

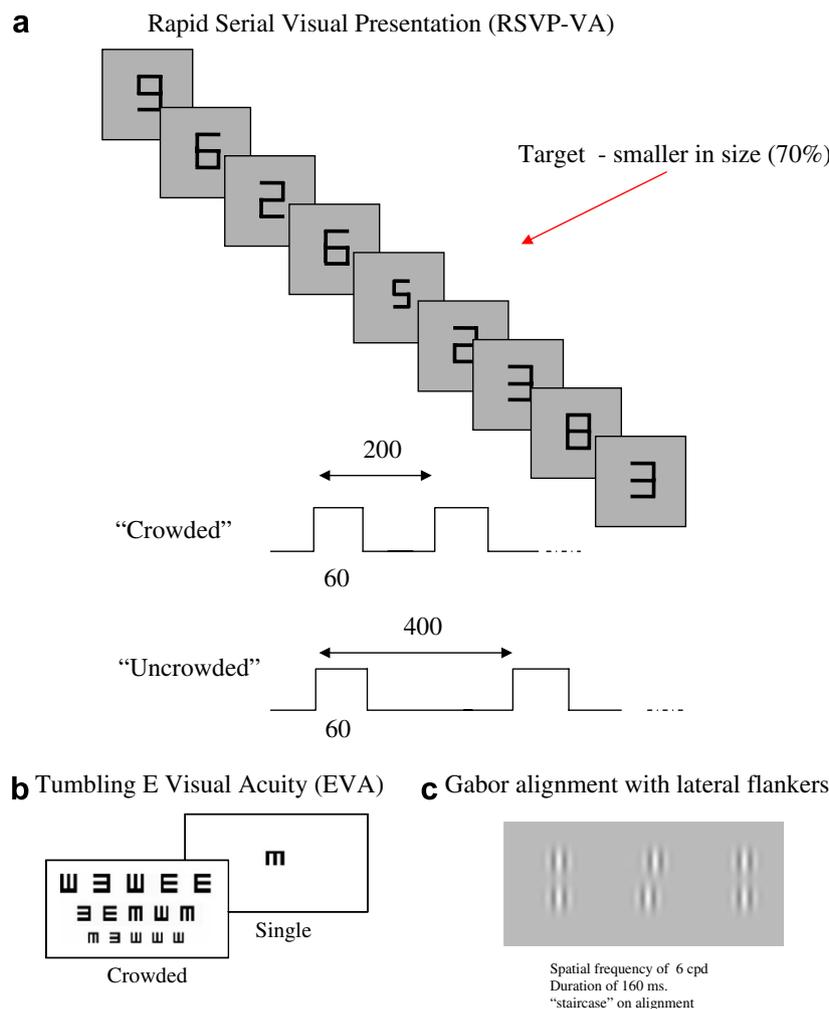


Fig. 1. A schematic description of three experimental paradigms used. (a) Typical stimuli used in the “temporal crowding” experiment. The target was a smaller (70%) digit among a rapid sequence of digits presented rapidly (SOA = 200 ms; “crowded” condition) and slowly (SOA = 400 ms; “uncrowded” condition), with varied digit size to determine threshold acuity. (b) Typical stimulus displays used in the EVA experiment for single and crowded conditions. (c) A typical stimulus display for the Gabor alignment experiment in which the subject had to determine the alignment of the two central patches, with the two flanking pairs of patches used to generate “crowding” at different distances.

### 2.5.1. Stimuli

A sample stimulus appears in Fig. 1b. Three rows of five E patterns each, facing one of four directions, with a 0.1-log unit size difference between the rows were presented. These stimuli correspond to a subset of the LogMAR chart, with a baseline (EVA = 0) pattern size corresponding to baseline (i.e. 6/6 vision) of the LogMAR chart. The central pattern (center of the middle row) was always the target for identification. The patterns were black on a white background, with a maximum luminance of 100 cd/m<sup>2</sup>, and the viewing distance was 1.5 m.

### 2.5.2. Procedure

On each trial the task was to determine the direction of the central E (the target) presented until there was a response. An adaptive procedure in which the pattern size and spacing were modified in 0.1 log unit steps was used to determine the size for 50% correct (chance was 25%). Different auditory feedbacks were given for correct and incorrect responses.

### 2.5.3. Analysis

To determine crowding, we used separate runs for the target alone (EVA single) and crowded (EVA crowded) conditions. We then computed the EVA value as EVA = average (single, crowded) and the crowding effect given by EVA elevation = crowded – single (difference on a log scale), i.e. normalizing the crowded condition by the acuity of a single pattern.

## 2.6. Task 3: Spatial crowding in Gabor alignment

We used a Gabor alignment task similar to previous studies (Popple, Polat, & Bonneh, 2001) with additional flankers that generate a crowding effect similar to a paradigm previously used to measure line acuity under crowding (Levi & Klein, 1982c).

### 2.6.1. Stimuli

A sample stimulus appears in Fig. 1c. The stimuli consisted of even symmetric Gabor patches ( $\sigma = \lambda$ , Gaussian envelope given by  $\exp(-x^2/\sigma^2)$ , where  $\lambda$  is the wavelength) as previously used (Polat & Sagi, 1993), with spatial frequencies of 6 cpd, presented for a duration of 160 ms. A central pair of vertical patches was used as the target, and two flanking pairs of patches were used to generate “crowding”; these flanking pairs of patches appeared at different target-to-flanker distances in separate blocks during a session: 5, 6, 8, 10, 12, 14, and 18 wavelengths  $\lambda$ , in descending order. The flankers were presented at high contrast adjusted to be highly visible for every patient.

### 2.6.2. Procedure

A single image with the stimulus was presented for 160 ms. The subjects, seated 1.5 m from the screen, wearing their best optical correction, with the non-amblyopic eye occluded, were required to report the position of the upper target patch relative to the lower (left or right displacement). A visible fixation circle indicated the location of the target between presentations. The subjects activated the presentation of each stimulus display at their own pace by pressing a mouse button that initiated the stimulus presentation after 500 ms. They were informed of a wrong answer by auditory feedback after each presentation. Trials were grouped in blocks, each consisting of 50 trials, on average, across which the flankers’ distance was kept constant. We used a 3:1 staircase procedure over the displacement of the upper patch (three correct responses to reduce, one mistake to increase) to determine the alignment threshold based on the average of the last six reversals in a sequence of eight. Two blocks without flankers at the beginning and at the end of a session were used to determine the unflanked alignment threshold and their average for normalizing alignment thresholds within a session (subtracting log units) in order to obtain threshold elevation measures. Each patient was tested in 3–4 sessions, with each session covering the whole range of flankers’ distance. As a measure for crowding in Gabor alignment, we took the threshold elevation at a 10- $\lambda$  flanker distance, which was selected in order to capture the effect of crowding with a minimal number of “ceiling” cases. In those cases in which threshold could not be measured due to the flankers being too close, a fixed value of factor

20 (1.3 log units) was taken as a “ceiling value” for the threshold elevation measure. The control subjects were tested only on the unflanked conditions and on a 10- $\lambda$  flanker distance, repeated 2–3 times.

## 2.7. Data analysis

We compared group averages of the different acuity and crowding measures across amblyopia types as well as computed multiple correlations between the different acuity and crowding measures across subjects. For each correlation, we computed the probability ( $p$ -value) for the null hypothesis (zero correlation). Although our tests for the inter-relations between the different crowding and acuity measures were based on specific hypotheses rather than on an arbitrary search for significant correlations, we analyzed the False Discovery Rate (FDR) (Genovese, Lazar, & Nichols, 2002) of all uncorrected  $p$ -values for these correlations to obtain a corrected threshold significance value, i.e. a  $p$ -value for significance equivalent to 0.05 without correction. The conservative non-parametric version of the FDR yielded in our case a 0.007 significance threshold (factor 7 over 0.05), while assuming independence or positive dependence it yielded 0.03 (factor < 2), as compared to a factor 40 of a full Bonferroni correction.

## 3. Results

### 3.1. Temporal crowding in rapid serial presentations (RSVP-VA)

Results for the temporal crowding experiment appear in Fig. 2a and b. This experiment is an attempt to translate the spatial crowding effect to the temporal domain by measuring comparable LogMAR acuity measures under uncrowded (target isolated in a slow temporal sequence) as well as crowded (target surrounded in time in a fast temporal sequence) conditions. The temporal crowding effect itself (RSVP-VA elevation) was taken to be the difference between the two logarithmic measures. Similar to the spatial crowding effect, the strabismic patients had a relatively high temporal crowding effect (0.22 LogMAR U), significantly more ( $p < .003$ ) than the anisometropic patients, who had almost none, as shown in Fig. 2a. In comparison, a control group of normal observers ( $N = 10$ ), with monocular viewing, had a small crowding effect of 0.08 log units, significantly less than the strabismic group ( $p < .03$ ), but not significantly different from the anisometropic group ( $p = .13$ ).

We also investigated the relationship between RSVP-VA and the optotype VA using correlation analysis for the amblyopic subjects (shown in Fig. 2b). The RSVP-VA for the crowded (fast, SOA = 200 ms) condition was found to be highly correlated with the optotype VA, ( $R^2 = 0.85$ ), with a high correlation also found within groups:  $R^2 = 0.87$  for strabs,  $R^2 = 0.57$  for aniso (data not shown), showing that the correlation is not based on the distinction between the groups shown in Fig. 2a. In comparison, the correlation of the slow (400 ms) “uncrowded” RSVP-VA was found to be lower ( $R^2 = 0.56$  compared with  $R^2 = 0.85$ ,  $p = .06$ ).

### 3.2. Spatial crowding in static Tumbling-E patterns (EVA)

Results for the Tumbling-E visual acuity experiment appear in Fig. 2c and d. In Fig. 2c, we show that the

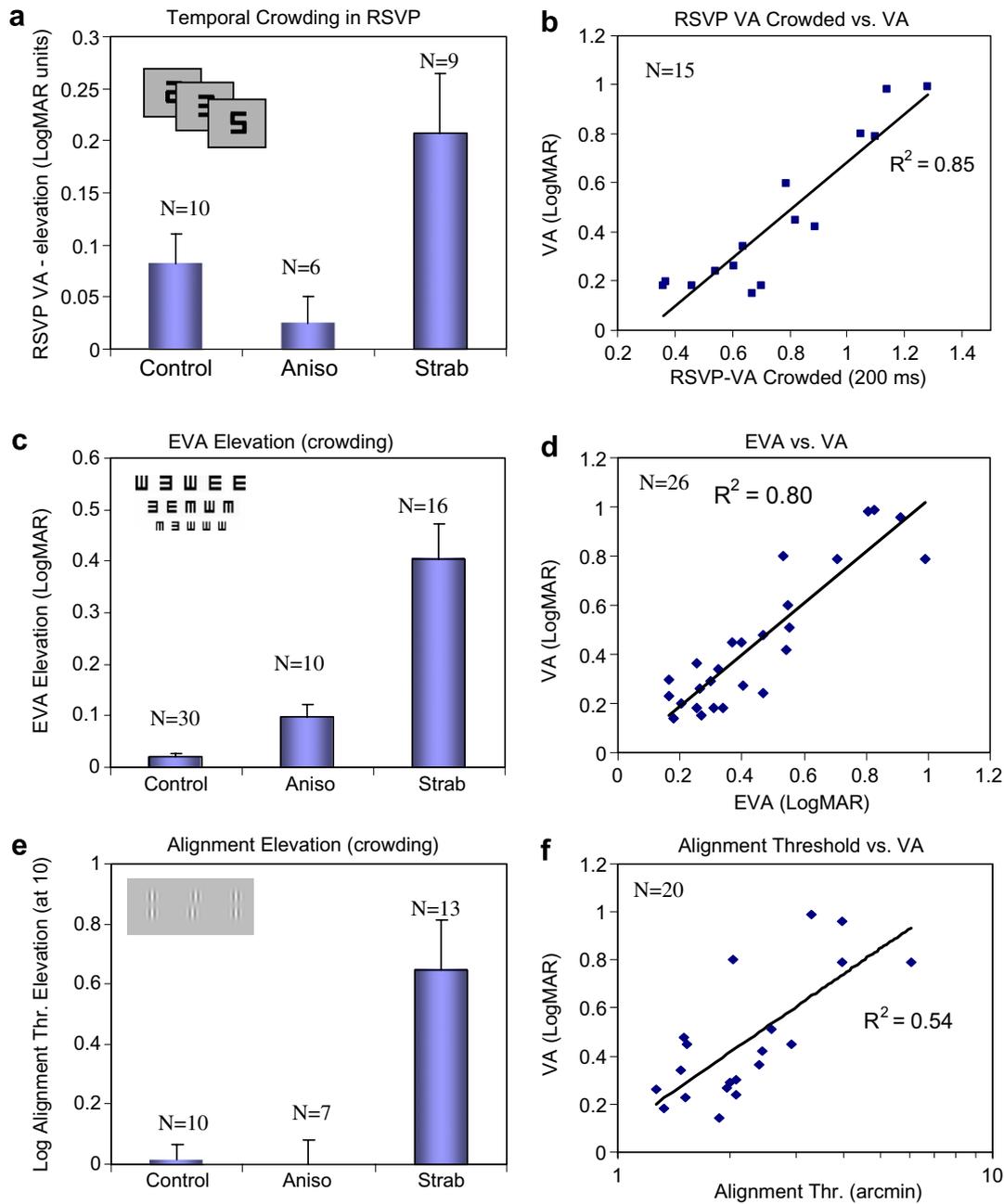


Fig. 2. Comparable results for the three different crowding experiments. The left column shows the group averages of the crowding effects, whereas the right column shows correlation plots between the different acuity measures and the optotype acuity (VA). The three rows correspond to the three different experiments (RSVP-VA, EVA, and Alignment,). Note the larger crowding effect of the strabismic amblyopes in all cases (left column) and the significant correlation of all measures with the optotype VA (right column).

strabismic amblyopes exhibited a large difference between the acuity measured for an isolated pattern and that measured when the pattern was surrounded by other E patterns. This difference, which we term EVA elevation, was 0.4log units for the whole strabismic group (0.32 for strabimics with VA < 0.7, not shown) and 0.1log units for the anisometropic group (significant difference in both cases,  $p < .02$ ). In comparison, the controls ( $N = 30$ ) showed almost no EVA elevation. These results are similar to those reported previously (Bonneh et al., 2004a). To

validate the EVA measure, we also correlated the average EVA of the amblyopes under crowded and uncrowded conditions with the optotype visual acuity (VA), which showed a high correlation ( $R^2 = 0.8$ ,  $p < .00005$  and Fig. 2d).

### 3.3. Spatial crowding in Gabor alignment

Results for the Gabor alignment experiment appear in Fig. 2e and f, and in Fig. 3. For the strabismic groups, alignment thresholds decreased monotonically with

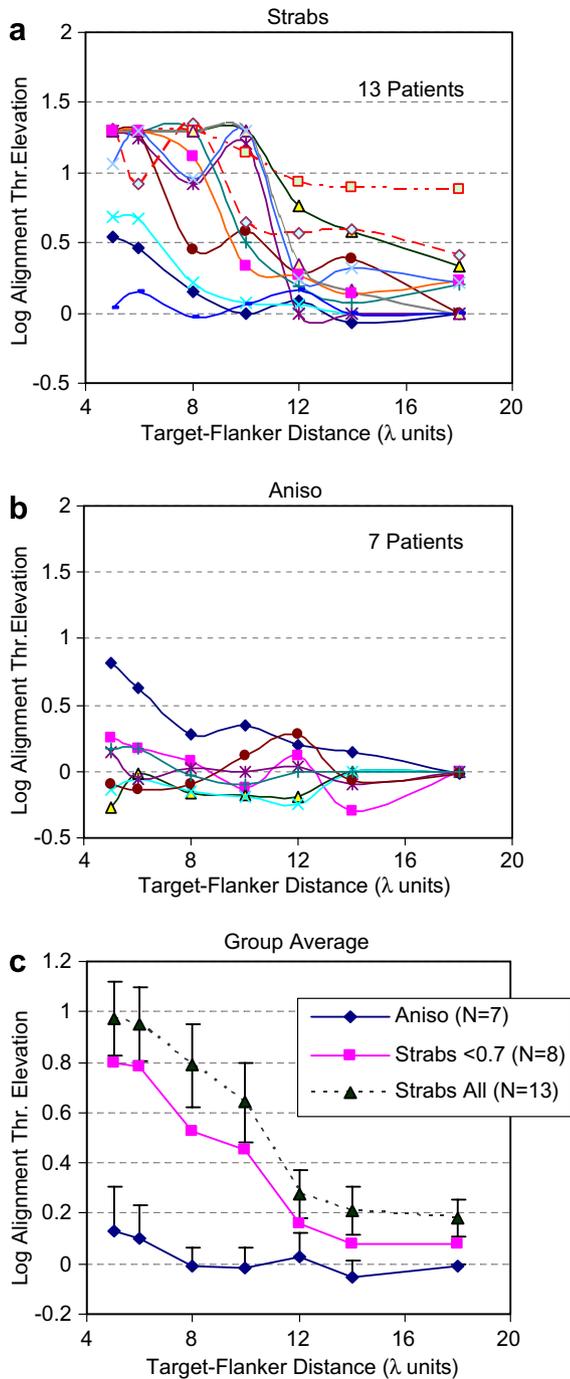


Fig. 3. Detailed results for the spatial crowding in the Gabor alignment experiment. The figures show the Gabor-alignment “crowding” curves depicting the log of alignment threshold elevation relative to the unflanked condition for different flanker distances. Individual results for 7 anisometric (a) and 13 strabismic (b) observers are shown as well as group averages (c). The severe amblyopia patients ( $VA > 0.7$ ) are shown in shades of red, while the others in shades of blue. Note that the anisometric group alignment threshold was only slightly affected by the flankers, whereas the strabismic groups were strongly affected at short flanker distances. (For interpretation of color mentioned in this figure the reader is referred to the web version of the article.)

flankers’ distances up to 12 wave-lengths ( $\lambda$ ) (Fig. 3c), but the flankers had a significant effect even at a 18- $\lambda$  distance for the strabismic patients with severe amblyopia

( $VA > 0.7$ ) (more than 0.3log units above the unflanked alignment threshold). In comparison, very little threshold elevation was found for the anisometric group and their alignment thresholds were largely invariant to the flanker distance in the range measured (5- $\lambda$  and above). We took the alignment threshold elevation at 10- $\lambda$  relative to the unflanked threshold as a measure for crowding and the group averages of this measure are depicted in Fig. 2e, showing a huge difference (a factor of 10) between the strabismic and anisometric patients. This difference is also evident in the individual plots for the two groups (Fig. 3a and b). Note the single exceptional anisometric patient with a relatively large crowding effect, and the single exceptional strabismic patient with no crowding. Note also that several of the strabismic patients could not perform the task at short flanker distances where misaligned patches were displaced beyond the flankers or close to them, consequently producing a ceiling effect. The threshold elevation measured with these ceiling effects was arbitrarily set to a factor of 20 (1.3log units). However, note that for the 10- $\lambda$  flanker’s distance, which we took as a measure for crowding, only two patients were at ceiling level. In comparison, the control subjects ( $N = 10$ ) who were tested only on the unflanked and 10- $\lambda$  flanked conditions, showed insignificant crowding (Fig. 2e). We also checked the consistency of our unflanked alignment threshold measure by correlating it with the optotype VA for all patients. The results (Fig. 2f) show a significant correlation ( $R^2 = 0.54$ ,  $p < .0005$ ), similar to a previous study (Levi & Klein, 1982b). A similar correlation was obtained for the flanked condition (see Table 2 and below).

### 3.4. The inter-relations between the different acuity and crowding measures

The overall pattern of results can be appreciated by inspecting Fig. 2 and Table 2. The left panels of Fig. 2a, c and d show that for all three paradigms, there were significant crowding effects for the strabismic amblyopes and very little crowding for the anisometric amblyopes. In comparison, low crowding was measured for the control groups in all three paradigms (Fig. 2a, c and e, left columns). Table 2 shows the correlation values (expressed as  $R^2$ ) and  $p$ -values for the null hypothesis of all different combinations of acuity measures. The false discovery rate (FDR) analysis we performed on the uncorrected  $p$ -values (see Section 2) yielded a significance threshold of 0.007 (factor 7 of the common 0.05 threshold). First, we note that all measures were significantly correlated with the optotype VA (Table 2, upper line), with a tendency for the crowded conditions to be better (but not significantly different) correlated with the VA rather than the uncrowded conditions (with one exception of the alignment task). The crowding effects (elevations) were in general less correlated with the VA than the uncrowded or crowded measures, e.g., the correlations with the VA of EVA elevation ( $R^2 = 0.26$ ) and EVA crowded ( $R^2 = 0.7$ ). There was a tendency for the

Table 2

Correlation summary of all different pair-wise correlations between the different measures of visual acuity, divided into crowded, uncrowded, and crowding effect categories

$R^2$ / $p$ -value		Uncrowded			Crowded			Crowding Effect		
		EVA	RSVP	Align.	EVA	RSVP	Align.	EVA	RSVP	Align.
VA		<b>0.61</b> 0.0005	<b>0.56</b> 0.001	<b>0.53</b> 0.0005	<b>0.7</b> 0.0005	<b>0.85</b> 0.0005	<b>0.48</b> 0.0008	<b>0.26</b> 0.007	<b>0.48</b> 0.004	<b>0.43</b> 0.002
Uncrowded	EVA		<b>0.79</b> 0.0005	<b>0.39</b> 0.003	0.38 0.0007	0.6 0.0007	0.15 0.09	<b>0.01</b> 0.7	<b>0.04</b> 0.5	<b>0.1</b> 0.2
	RSVP			<b>0.31</b> 0.1	0.4 0.01	<b>0.75</b> 0.0005	<b>0.17</b> 0.3	<b>0.08</b> 0.3	0.03 0.5	<b>0.1</b> 0.4
	Align.				0.57 0.0005	0.52 0.03	<b>0.59</b> 0.0005	<b>0.25</b> 0.02	<b>0.28</b> 0.1	0.45 0.001
Crowded	EVA					<b>0.74</b> 0.0005	<b>0.76</b> 0.0005	0.7 0.0005	<b>0.55</b> 0.002	<b>0.72</b> 0.0005
	RSVP						<b>0.57</b> 0.02	<b>0.42</b> 0.009	0.42 0.009	<b>0.45</b> 0.05
	Align.							<b>0.67</b> 0.0005	<b>0.72</b> 0.004	0.96 0.0005
Crowding Effect	EVA								<b>0.71</b> 0.0005	<b>0.7</b> 0.0005
	RSVP									<b>0.7</b> 0.005

Correlation Sample Numbers

N	EVA	RSVP-VA	Alignment
RSVP-VA	*	15	9
EVA	26	15	20
Alignment	*	*	20

In each cell, the  $R^2$  value appears above the corresponding  $p$ -value. A color code is used for the important correlation types, among which red is used for the correlation between the crowding effect and the uncrowded acuities and blue for the correlation between the different crowding effects (corresponding to the columns of Fig. 4). The significance level threshold was determined to be 0.007 using false discovery rate (FDR) analysis for multiple correlations (factor 7 of the standard 0.05 level, see Section 2). The small, lower table summarizes the sample size of the different correlations, corresponding to the group overlap across experiments, since not all patients completed all experiments.

correlations between the different crowded conditions (Table 2, green) to be higher than the correlations between uncrowded and crowded conditions (Table 2, gray). For example, the uncrowded EVA and RSVP were not significantly correlated with the crowded Alignment (0.15 and 0.17, respectively), but the crowded EVA and RSVP were highly correlated to it (0.76 and 0.57, respectively). This is consistent with the idea that the uncrowded tasks do not capture the whole amblyopic deficit.

The important point of the current study is in the comparison between the correlations across subjects of the different crowding measures (Table 2, blue) and the correlations between the crowding measures and the uncrowded measures (Table 2, red). Some of these correlations (all three crowding-to-crowding correlations and three out of nine of the crowding-to-uncrowded conditions) are detailed in Fig. 4. The crowding measures were taken as

the elevation in acuity thresholds in crowded relative to uncrowded acuities, with elevation computed in log units. For the temporal crowding condition, this means the difference between the acuities in the fast (200 ms, “crowded”) condition and the slow (400 ms “uncrowded”) condition. The overall pattern of the results is that the crowding effect was poorly (insignificantly) correlated with the acuity measured for isolated (uncrowded) patterns, as seen in the examples in Fig. 4b, d and f, with the Alignment task being somewhat exceptional (see below). On the other hand, all 3 correlations between the different crowding effects were very significant ( $p < .005$ ,  $R^2$  around 0.7). A key finding is the correlation between the temporal and spatial crowding effects in Figs. 4a and c. This correlation does not reflect a simple clustering effect of the strabismic and anisometric groups, since a high correlation was also found within the strabismic group ( $R^2 = 0.66$  as compared to  $R^2 = 0.71$  of

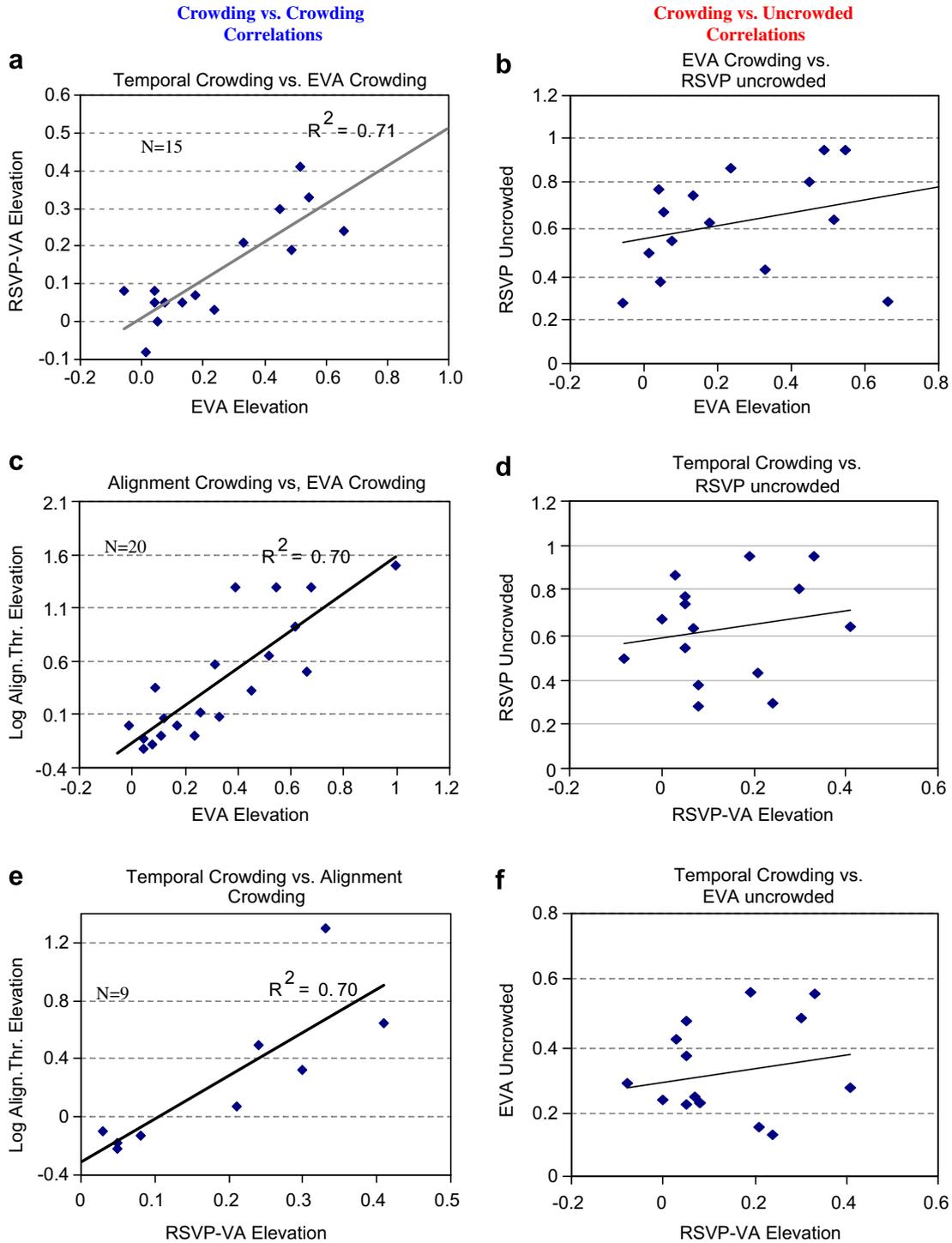


Fig. 4. The relationship between the different spatial and temporal crowding measures. The left column shows all three possible pair-wise correlations, with a high correlation found in all cases ( $R^2 = 0.7$ ). In comparison, the right column shows three of the nine possible correlations between the crowding effect and the uncrowded acuity. These correlations were insignificant (shown) or low. See Table 2 for the corresponding  $R^2$  and  $p$ -values marked with the corresponding color titles of the current figure columns (blue for left, red for right). (For interpretation of color mentioned in this figure the reader is referred to the web version of the article.)

all patients in Fig. 4a, not shown), whereas the anisometric group did not show any correlation ( $R^2 = 0.03$ ).

Overall, the alignment task was somewhat different from the other tasks in its correlation pattern. The uncrowded alignment, unlike the other uncrowded

conditions, was significantly correlated with two of the three crowding effects (EVA and alignment crowding, Table 2, red part, bottom line and the corresponding  $p$ -values). This suggests that uncrowded alignment, unlike the other uncrowded measures, captures part of the

deficit, and perhaps the crowding effect itself, in the form of “self crowding”. However, note that the crowded alignment had a higher correlation with the crowding effects than the uncrowded alignment, with significant or approaching significance of the correlation differences. We noted that in comparing the RSVP crowding with the Gabor alignment crowding effect we correlated a relative measure between two possibly crowded conditions (slow and fast) with a measure relative to a completely isolated stimulus (unflanked Gabor alignment). Some justification is provided by the correlation of the slow RSVP condition with the uncrowded measure of EVA ( $R^2 = 0.79$ , Table 2), but we also tested an alternative alignment crowding measure obtained from the difference between the alignment threshold at a  $8\text{-}\lambda$  distance and at a  $14\text{-}\lambda$  distance. This measure yielded a lower but still significant correlation, compared with Fig. 4c ( $R^2 = 0.52$ ).

In order to verify that the correlations were not significantly altered by the lack of full participation of all subjects in all tasks, we checked that all three crowding-to-crowding correlations remained high and significant even within the small group ( $N = 9$ ) that performed all three tasks, and this was indeed the case ( $R^2 \sim 0.7$  in all three cases). Another reservation relates to the correlation between the crowding effect and the crowded and uncrowded acuities. In cases where this was done within task (e.g. EVA elevation correlated with EVA uncrowded), the correlation could have been underestimated, due to the correlated errors shared by the compared variables. This underestimation is likely to be relatively small since it depends on the variability of the crowded and uncrowded acuity measurements across subjects (typically large, in the range of  $0.4 \log$  units, see Fig. 4 and Table 1) as compared to the variability of the measurements within each subject (typically  $<0.05 \log$  units in normal observers). However, it is possible that all or part of the six within-task correlations of the crowding effects (on the diagonals in Table 2, in non-bold font) were significantly underestimated and this fact should be taken into account in the interpretation.

#### 4. Discussion

We found that the strabismic amblyopes but not the anisometropic amblyopes or normal controls had a “temporal crowding” effect in the form of acuity reduction under conditions of fast vs. slow RSVP. Moreover, we found that the crowding effects in the spatial and temporal domain were correlated in the same patients. We previously reported evidence suggesting that the inability to isolate stimuli in space in crowded displays (spatial crowding) is a largely independent component of the characteristic amblyopic deficit (VA), which is typically found in strabismic amblyopia (Bonnef et al., 2004a). Here we extend this result to the temporal domain by showing that different measures of spatial and temporal crowding produce correlated effects, which are at the

same time largely independent of the acuity of an uncrowded pattern. These results are not at all straight-forward and cannot be explained as different manifestations of “poor vision” (see the discussion of “scaling” below). Instead, we discuss alternative explanations to the relation between the amount of distracter interference in space and time.

##### 4.1. Scale-shift and unsteady fixation are unlikely to account for crowding in amblyopia

The current results, in addition to recent accumulating evidence (Hess et al., 2001; Levi et al., 2002a), can be used to reject the popular “scale shift” account for crowding in amblyopia (Flom et al., 1963; Levi, Klein, & Aitsebaomo, 1985). According to this ‘linear scaling’ hypothesis, the amount of crowding should be proportional to the acuity for an isolated pattern because it is due to within-receptive-field integration of the first-stage filters, which are scaled according to the size of the target’s pattern. A related argument in the temporal domain is that people with low acuity were tested with larger patterns; hence, they used faster (lower spatial-frequency) channels and exhibited a less temporal crowding. Both arguments can be rejected because the amount of crowding we found in this as well as our previous study (Bonnef et al., 2004a) was not proportional to the acuity of a single isolated pattern, as can be seen from the low or insignificant correlations between the different crowding measures and the isolated acuities (Table 2 and Fig. 4d and f). This finding was most evident in some cases of strabismic amblyopes that we tested in which the acuity for a single pattern was normal but collapsed with the interference of flankers.

Another popular explanation for crowding in amblyopia is eccentric or unsteady fixation, which may cause observers to shift targets into the periphery where crowding is normally large (Levi, Hariharan, & Klein, 2002b), or to miss the correct target and respond to its neighbor (Regan, Giaschi, Kraft, & Kothe, 1992). Although unsteady fixation could produce crowding in some amblyopes, the current results are inconsistent with unsteady fixation as a general explanation for crowding, since two of the paradigms (the Gabor alignment and the RSVP-VA) were dynamic, involving brief presentations and targets that cannot be confused with their neighbors in space. Most importantly, the temporal crowding paradigm, which does not involve space, cannot be accounted for by assuming peripheral vision, and its correlation with the spatial crowding measures provides important, though indirect evidence against a major role of fixation problems in amblyopic crowding.

##### 4.2. The effect of amblyopia subtype on crowding

Our results show a marked difference between pure anisometropia and strabismic (or combined) amblyopia,

since the latter group had much more crowding, both spatial and temporal, as shown in Fig. 2 (see our previous study (Bonneh et al., 2004a) for more evidence supporting this distinction). In fact, the temporal crowding correlation is primarily based on the correlation within the strabismic group (Fig. 2f) as well as on the group difference between strabismus and anisometropia. Previous researchers have focused on a different property of strabismus in comparison to anisometropia, which appears to reflect abnormal local mechanisms. They found that whereas in anisometropia, grating-acuity (spatial-frequency cutoff), Vernier acuity, and optotype acuity (with multiple patterns) were correlated, strabismic subjects had a disproportional deficit in optotype and Vernier acuities, as compared with grating acuity (Levi & Klein, 1982a; Levi, Klein, & Yap, 1987; McKee et al., 2003). In a recent paper, McKee et al. (2003) found evidence for a different sub-division of amblyopia, according to the loss of binocularity, which in general parallels the anisometropia/strabismus classification, but not always. A lack of binocularity could be the result of a history of high exposure to unfused and dissimilar stimuli in both eyes (see our preliminary report of a lack of binocular rivalry with such an exposure, including in amblyopia (Bonneh, Polat, & Tsodyks, 2006)). This is likely to be the case in strabismus, but theoretically, could also happen in anisometropia if the vergence mechanism fails. In such a developmental history the actual center of fixation of the amblyopic eye with the highest retinal resolution is constantly displaced relative to the desired fixation with the highest density of visual information. This could result in a long integration field between these two locations and hence spatial crowding. If this long-range integration is mediated by signal propagation, then this could also explain temporal crowding as discussed below.

#### 4.3. Temporal crowding as a result of longer latencies in amblyopia

One way to account for poor performance with RSVP stimuli is by assuming a sluggish system with long latencies for transient responses. As summarized in the introduction, amblyopia is also associated with a temporal deficit in the form of increased latency of response for stimuli presented to the amblyopic eye (Ciuffreda et al., 1991; Davis et al., 2003; Hamasaki & Flynn, 1981; Loshin & Levi, 1983). This deficit has been previously explained in terms of a byproduct of the contrast-threshold deficit of the amblyopic eye (Ciuffreda et al., 1991). According to this explanation, if temporal crowding is due to longer response latencies, which are due to lower contrast sensitivities, then strabismic amblyopes, who were found to have more temporal crowding, should have lower contrast sensitivity. Currently, we do not have any direct way of measuring the latency of response in our amblyopic subjects, nor do we have a full set of comparable contrast sensitivity measures. However, in a previous study with a large sample (Polat et al., 2005) we found that the strabismic (and combined)

amblyopes had a contrast sensitivity comparable (not appreciably different) to the anisometropic amblyopes, while at the same time they had more lateral suppression (Polat et al., 2005) and spatial crowding (see Bonneh et al. (2004a) for the same group of subjects). This means that a contrast sensitivity deficit is unlikely to account for spatial crowding and since spatial and temporal crowding were found to be correlated in the current study, it is unlikely to explain temporal crowding as well. Moreover, a longer latency in amblyopia cannot explain the main finding that the temporal crowding was not correlated with acuity for an isolated pattern.

#### 4.4. Crowding as reflecting lower attentional resolution or pooling in space and time

In using RSVP stimuli, we tested the amblyopic visual system under conditions of temporal (forward and backward) masking. Some masking studies have shown that target detection is degraded by presentation of maskers shifted in time, usually up to an SOA of 100 ms (Breitmeyer, 1984; Polat & Sagi, 2006). Here the SOA was 200 and 400 ms and, in comparison to the control group, the results suggest that strabismic amblyopic vision is susceptible to the masking effect for prolonged target-mask time shifts. Note, however, that unlike a standard backward masking paradigm, the RSVP paradigm requires a two-step process: first, the target must be detected due to its smaller size, and then it has to be identified, while suppressing the masking effect of successive stimuli. Thus, extra time might be required for the two-step process and the RSVP task may be influenced by accumulating two-masking effects. In interpreting the RSVP process, we followed one interpretation of the attentional blink paradigm in which the first of the two targets in RSVP stimuli is assumed to trigger an attentional (top-down) inhibitory process required to suppress the masking effect of successive patterns and enable recognition (Keysers & Perrett, 2002; Kristjansson & Nakayama, 2002). According to this interpretation, our results reflect the strength of this attentional mechanism, i.e. the ability of the system to isolate successive stimuli in time. A recent preliminary finding of a prolonged attentional blink in amblyopia (Asper, 2003) supports this interpretation. It turns out that this ability to isolate stimuli in time affects visual acuity in a similar manner as the ability to isolate stimuli in space.

#### 4.5. Crowding as a result of excessive long-range signal propagation

One way in which time is related to space in the cortex is regarding the spatio-temporal properties of dynamic signal propagation (e.g., as reflected in “traveling waves” in V1 (Lee, Blake, & Heeger, 2005), see also Polat & Sagi (1994)). A visual system with longer integration periods will show extended range of lateral signal propagation causing distracter interference in space, as well as more

temporal interference between successive stimuli—hence, provide a link between spatial and temporal crowding. A recent study (Polat & Sagi, 2006) provides a clue to the mechanisms that underlie “slow integration” by pointing to a temporal difference between the excitatory and inhibitory lateral interactions in normal observers in response to transient stimuli: fast inhibition followed by slow and persisting excitation. The fast-reacting inhibitory processes may function to erase slowly decaying excitatory processes, allowing for new excitatory processes to develop. A “sluggish” more sustained inhibition in strabismic amblyopia could in principle explain and link longer response latencies with a larger extent of spatial crowding. According to this interpretation, the perceptual suppression observed in spatial crowding experiments is due to excessive excitatory propagation and not due to increased lateral inhibition. A similar but reversed argument can also apply: excessive excitatory propagation could alter a fast transient response into a slower, more sustained one, producing temporal crowding. Currently, there is no direct evidence to support this hypothesis, but preliminary results that we obtained with a few strabismic amblyopes indicate that the amount of abnormal perceptual suppression in a lateral masking contrast detection paradigm increases with duration, thus suggesting a link between space and time, which is consistent with the above explanation.

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