Spatial attention increases the pupillary response to light changes

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We measured pupil size in adult human subjects while we manipulated both the luminance of the visual scene and the location of attention. We found that, with central fixation maintained, pupillary constrictions and dilations evoked by peripheral luminance increments and decrements are larger when spatial attention is covertly (i.e., with no eye movements) directed to the stimulus region versus when it is directed to the opposite hemifield. Irrespective of the size of the attended region (focused at the center of the stimulus or spread within and outside the stimulus), the attentional enhancement is large: more than 20% of the response to stimuli in the unattended hemifield. This indicates that a sizable portion of this simple ocular behavior—often considered a subcortical "reflex"—in fact depends on cortical processing. Together, these features indicate that pupillometry is not only an index of retinal and brainstem function, but also an objective measure of complex constructs such as attention and its effects on sensory processing.

Introduction

One of the most thoroughly investigated questions in psychophysics is whether and how attention enhances the effective intensity of a sensory stimulus. Two main approaches have been taken. One approach, exemplified by Posner's paradigm (Posner, 1980), indirectly estimates the effects of attention by measuring performance in tasks that depend on stimulus intensity; however, a long chain of processes leads from stimulus detection to task execution (including decision making), and it is difficult to determine which of these stages is primarily affected by attention (Eckstein, Peterson, Pham, & Droll, 2009; Carrasco, 2011).

Another approach attempts to directly estimate whether attention increases the strength of sensations, such as apparent contrast or brightness (Carrasco, Ling, & Read, 2004; Tse, 2005; but see Prinzmetal, Nwachuku, Bodanski, Blumenfeld, & Shimizu, 1997); however, it is difficult to exclude that variations of appearance judgments are due to changes in response criterion (Schneider & Komlos, 2008). We aimed to overcome some of these concerns by measuring the effects of attention on one of the simplest responses to visual stimulation: the pupillary light response, or the pupillary constrictions and dilations evoked by increases and decreases of luminance (Loewenfeld, 1993). We reasoned that if attention increases the efficacy of a luminance stimulus at generating sensations, it might also increase the behavioral responses to such stimulus and, in particular, the pupillary response it evokes. Because the latter is involuntary, differences between responses to attended and unattended stimuli cannot be explained by changes in criterion or decision strategies.

The pupillary light response has long been considered a reflex mediated by subcortical circuits (Loewenfeld, 1993; Gamlin & Clarke, 1995). This stands in contrast with other, typically smaller pupillary responses, which clearly depend on cortical processing: dilations with cognitive effort, with attentional load and perceptual decisions (Hess & Polt, 1960; Kahneman & Beatty, 1966; Einhauser, Stout, Koch, & Carter, 2008; Hupe, Lamirel, & Lorenceau, 2009; Nassar et al., 2012; Wierda, van Rijn, Taatgen, & Martens, 2012), or constrictions with accommodation ("near response"; Marg & Morgan, 1949; Phillips, Winn, & Gilmartin, 1992; Bharadwaj, Wang, & Candy, 2011) and visual transients ("onset response"; J. L. Barbur, Harlow, & Sahraie, 1992; Young, Han, & Wu, 1993; Sahraie & Barbur, 1997). All of these secondary responses of the

Background (cd/m^2)	Stimulus (cd/m^2)			Experiments (*n* subjects)
0.9	24.9	61.0	109.0	Exp. 1, 2, 3 (*n* = 6)
5.7	28.8	63.4	109.5	Exp. 1 (*n* = 4)
11.9	33.7	66.5	110.1	Exp. 1 (*n* = 4)
60.3			110.1	Exp. 1 (*n* = 4)
110.1	0.6			Exp. 1 (*n* = 5)

Table 1. Parameters of stimulation.

pupil are generally independent of the response to light and probably mediated by distinct pathways (Zhang, Clarke, & Gamlin, 1996; Wilhelm, Wilhelm, Moro, & Barbur, 2002).

However, there is evidence to implicate cortical processing even in the simple pupillary light response. Patients with lesions of the visual cortex tend to have reduced pupillary light responses (J. Barbur, 2004). In sighted subjects, pupillary light responses are reduced during interocular or saccadic suppression (Lorber, Zuber, & Stark, 1965; Richards, 1966). Moreover, we recently showed that, with no change in stimulus luminance, attending to a brighter versus a darker region of an image is sufficient to elicit a pupil size change (Binda, Pereverzeva, & Murray, 2013a; see also Mathôt, van der Linden, Grainger, & Vitu, 2013). Here we test the relationship between this effect of attention and the pupillary light response by measuring how shifting spatial attention to a region where a luminance change occurs affects the evoked pupillary responses. If attention increases the pupillary response to luminance changes, then pupil diameter could be used as a tool to measure the attentional enhancement of sensory signals. In our second experiment, we apply this approach to testing one of the most basic properties of attentional enhancement: whether it is affected by the spatial distribution of attention, focused versus divided, as several prominent models predict (Treisman & Gelade, 1980; Eriksen & St James, 1986; Sperling & Dosher, 1986; Reynolds & Heeger, 2009).

Methods

Subjects and apparatus

A total of six naïve subjects (three females, age range: 21–24 years, mean: 22.67) with normal (four subjects) or corrected-to-normal vision (two subjects with corrected myopia and refractive errors smaller than 2.5 in both eyes) gave informed consent to participate in the experiments, which were approved by the University of Washington Human Subjects Institutional Review Board and in line with the Declaration of Helsinki. The same six subjects participated in Experiments 1, 2, and 3, but not all subjects completed all the conditions of Experiment 1 (see details in Table 1). Data were acquired over multiple sessions in different days, each lasting approximately 45 min (including the initial instructions and calibration procedures and the breaks that participants were encouraged to take between blocks of trials).

Subjects viewed a 35 × 28 cm CRT monitor binocularly from a distance of 81 cm (the monitor was calibrated, had a minimum luminance of 0.6 cd/m^2 and was driven at 85 Hz); a chin rest was used to stabilize head position. The experimental room had no illumination other than the display screen. Displays were generated in Matlab (Mathworks) using the Psychophysics Toolbox (Brainard, 1997; Pelli, 1997). Subjects were asked to refrain from blinking at all times except during the intertrial interval (defined below) and to maintain their gaze on a fixation mark.

Pupil diameter and 2-D eye position were measured monocularly with a video-based eye tracker (ASL Eyetrack 6, with a remote sensor mounted below the monitor screen). A standard nine-point calibration was run at the beginning of each session.

Stimuli and task

In all experiments, the display consisted of a single disk, 7° in diameter, presented in the left or right hemifield at 8° eccentricity (Figure 1A, C, and D). The disk appeared 2 s after trial onset, lasted 6 s, and was followed by an intertrial interval of 2 s (yielding a 10 s trial duration, Figure 1B). Except in control Experiment 3, a line cue (0.5° long, 0.1° thick) extending left or right from the central fixation mark was presented at trial onset and lasted 8 s (i.e., it appeared 2 s before the luminance disk and was extinguished simultaneously with it; see top and middle curves in Figure 1B). This instructed subjects to attend to either hemifield. It is of crucial importance to note that subjects covertly shifted their attention to the left/right, but their eye position was required to be constant at all times, centered on the fixation point. Disk and attention side were varied pseudorandomly across trials.

The disk stimulus appeared against a homogenous dim background (luminance 0.9 cd/m^2); the luminance of the disk was varied from trial to trial, taking three possible values: 24.9, 60.9, or 109 cd/m^2. Upon presentation of the disk, a pupillary light response is expected, its size depending on the luminance of both the disk and its background (J. Barbur, 2004). For Experiment 1, we took advantage of this to extend the range of measured pupillary responses and tested additional combinations of disk and background luminance (see Table 1).
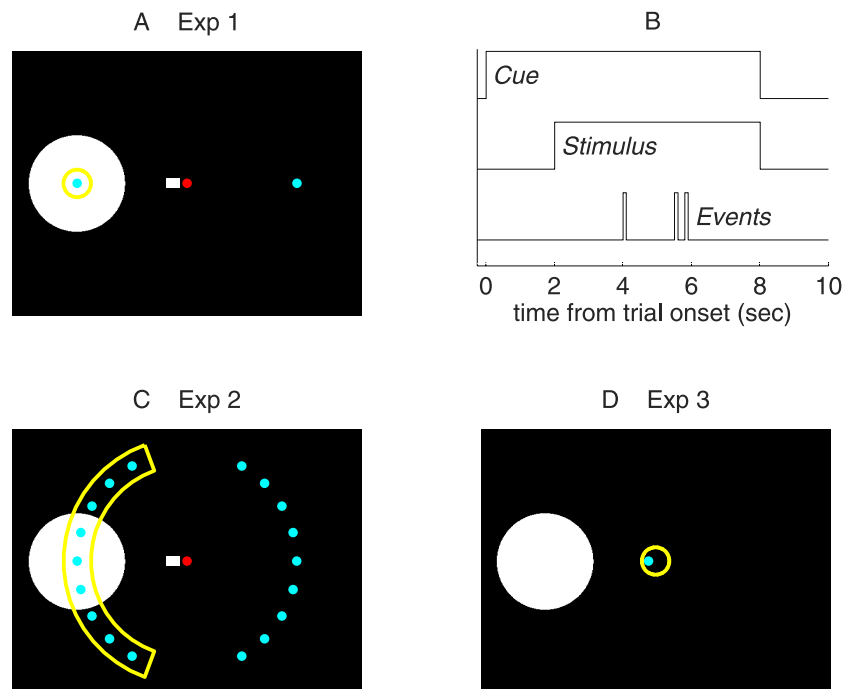
Figure 1. Spatial arrangement and time course of stimulation. (A, C, D) Approximately in-scale representation of the display in Experiments 1, 2, and 3. A disk of homogeneous luminance (here, brighter than the background) was presented in the left or right hemifield. Subjects maintained fixation on a dot at the center of the screen and reported color changes of the cyan dot(s) located in the cued region (yellow area, not part of the actual display). (B) Time course of presentations, marking onset/offset of the cue and the disk stimulus and showing a representative distribution of color-change times (between one and three changes occurred at random times between 2 and 8 s from trial onset). In Experiments 1 and 2, the number of changes and their timing varied independently in the two hemifields.

In Experiment 3, no line cue was presented; subjects were instructed to maintain attention on the fixation mark, which was displaced left/right by 0.5° at trial onset and returned to screen center at stimulus offset, thereby inducing a displacement of gaze position toward either hemifield. Disk and fixation displacement side varied pseudorandomly across trials.

In order to control the direction and focus of attention, we asked subjects to perform a task on target stimuli (small dots) that we manipulated independently of the disk. In Experiment 1, there was a small dot in each hemifield: one at the center of the disk and one at a symmetrical location in the opposite hemifield. In Experiment 2, a nine-dot semicircular array was presented in each hemifield with all dots displayed at the same eccentricity (8°), some within and some outside the disk (see Figure 1C). In Experiment 3, there were no peripheral dots, and the fixation point served as target. The task was designed as a simple-feature detection task. Subjects attended to an individual feature, the color of the small dot(s), and detected its brief (100 ms long) changes (at a single location or across multiple locations in the cued hemifield). However, in order to ensure that attention remained focused at the cued location throughout the extended course of the disk presentation (6 s), we chose to

present multiple color changes in each trial (separated by random intervals, constrained to be at least 200 ms long to ensure perceptual segregation of consecutive changes), thereby adding a counting component to the simple detection task. Specifically, subjects counted, and reported during the intertrial interval using the computer keyboard, the number (1 to 3) of color changes in the cued hemifield, ignoring color changes in the opposite hemifield (in Experiment 3, subjects counted the number of color changes of the fixation dot). In all cases, the target dot(s) remained visible across a session and changed from cyan to greenish with the percentage of blue light staircased to maintain performance at about 70% correct. Specifically, the staircase procedure adjusted the percentage of blue light based on the participant's response on the previous trial, decreasing it by 1% in case of a correct response and increasing it by 2% following an incorrect response. Note that we analyzed pupil size from both trials with correct responses and incorrect responses.

The exact instructions given to the participants follow (the part specific for each experiment, and the part common to all experiments).

Experiment 1: "The screen will show three small dots: one at the center and one on either side of it. Always keep your eyes on the central dot, the 'fixation

point'. The left and right dot will briefly change their color, with changes on each side occurring independently from the other, between 1 and 3 times in a trial. At trial start, a line will extend out from the fixation point, pointing left or right; your task is to covertly monitor the dot on the same side as the line and take notice of the number of times the monitored dot changes color (you'll see them out of the corner of your eye, because the center of your gaze must remain on the fixation point at all times). As soon as the line cue disappears,…"

Experiment 2: "The screen will show a small dot at the center and several dots on the left and right side. Always keep your eyes on the central dot, the 'fixation point'. Some of the left and right dots will briefly change their color, with changes on each side occurring independently from the other, between 1 and 3 times in a trial. At trial start, a line will extend out from the fixation point, pointing left or right; your task is to covertly monitor the dots on the same side as the line and take notice of the number of times any dot on the monitored side changes color (you'll see them out of the corner of your eye, because the center of your gaze must remain on the fixation point at all times). As soon as the line cue disappears,…"

Experiment 3: "The screen will show a small dot at the center, the 'fixation point'. At trial start, this will jump slightly to the right or to the left. Always keep your eyes on the fixation point, following its displacements. The color of the dot will change briefly between 1 and 3 times in a trial, and your task is to take notice of the number of these color changes. As soon as the fixation point jumps back to the screen center,…"

Common to all experiments: "…you may report the number of color changes by pressing the corresponding figure on the keyboard (a two-second interval is allowed, after which a new trial will start). Trials will come in blocks of 10, lasting approximately 2 minutes, and there will be time to rest between blocks. Please refrain from blinking during a block; if you have to, please do so in the pause between trials (when you are using the keyboard). During part of the time, a large bright/dark disk will be visible; this is not relevant to your task."

Data analyses

Eye position and pupil diameter were measured at 120 Hz (pupil diameter was measured with a resolution of 0.05 mm); individual samples in which eye position took unrealistic values (locations outside the screen monitor, mostly due to blinks) were treated as signal losses.

Horizontal eye position samples were preprocessed as follows: The average gaze position in the first 50 ms of each trial was subtracted from samples acquired across the full trial. For Experiments 1 and 2, trials were excluded if any gaze deviation sample acquired during the stimulus presentation window (2–8 s into the trial) was larger than 2° (6 ± 2% for Experiment 1 and 11 ± 3% for Experiment 2). We did not exclude trials in which blinks occurred (visual inspection of the traces, however, indicates that blinks were rare and anyway concentrated in the intertrial interval, indicating that subjects complied with the instructions).

Pupil size samples were preprocessed as follows: The average pupil diameter in the 500 ms preceding the disk presentation in each trial was subtracted from samples acquired across the duration of the same trial; the resulting pupil change time courses were binned in steps of 50 ms. For each subject, the mean pupil change and the peak pupil change in the stimulus presentation window (2–8 s into each trial) were averaged across valid trials (at least 30 per condition) and taken as indices of the pupillary response.

A secondary approach to compute pupillary responses adopted Principal Component Analysis (PCA, following Young & Kennish, 1993). Time courses from individual trials (bin width: 50 ms) were entered into PCA, after excluding trials with missing values (no sample available in one or more of the 50 ms bins between 1 and 8 s from trial onset; this led to consider 75 ± 3% of the trials included in the main analysis). PCA was performed separately for each subject, pooling trials across conditions (attend to the disk hemifield or to the opposite hemifield) and experiments (1, 2, and 3); the first eigenvector of the covariance matrix defines the (first) PC (the waveforms in Figure 3A). The projection of the individual time courses to the PC (the inner product of the pupil time course and the component waveform) yields the component scores, which were averaged across trials for each condition and experiment.

Although all analyses were based on the individual subjects' results, we also computed grand averages across subjects: of the three indices used to quantify pupillary responses (average response, peak response, and first PC score) and of the pupil-change time courses (Figures 2A and 4A).

Results

Attention modulates the pupillary responses to light increments and decrements

While maintaining fixation at the center of a homogeneous screen, participants covertly (i.e., without eye movements) shifted their attention to the left or right hemifield according to a central cue that appeared
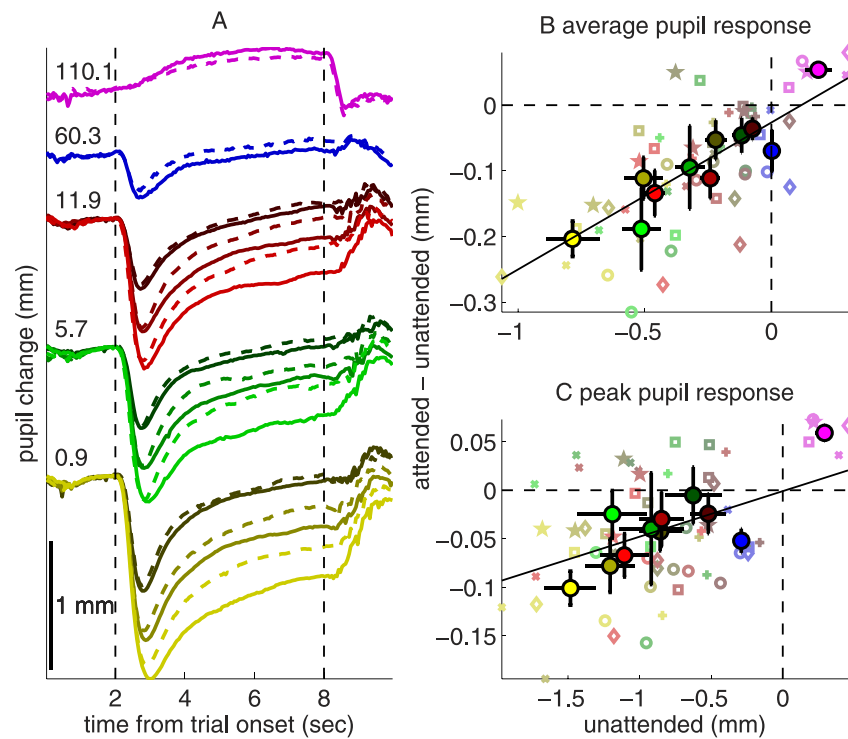
Figure 2. Pupil responses in Experiment 1. (A) Pupil time courses from Experiment 1, averaged across subjects, separately for trials in which the disk appeared in the attended hemifield (continuous lines) or in the opposite hemifield (dashed lines). Vertical lines mark the onset and offset of the disk; traces for different background luminance levels are displaced vertically (text insets give the luminance of the background in cd/m^2). By definition, pupil change is 0 in the 0.5 s preceding disk offset; see Figure 5 for the raw values of pupil diameter in this interval. Note that pupil size often failed to return to baseline before the end of a trial, which coincided with the beginning of the next one. However, the randomized order in which we presented trials from different experimental conditions ensures that these carryover effects do not confound the results (and that they cannot explain the reported effect of attention). (B, C) Effect of attention on the average (B) and peak (C) pupil responses over the disk presentation interval, plotted against responses to disks in the unattended hemifield. Small colored symbols show values for the individual participants— same color coding as in (A), different symbols for each participant; please see legend in Figure 5A—and black-outlined symbols with error bars show means and standard errors across participants. Continuous lines are the best-fit linear function; dashed lines show the functions x = 0 (no pupillary response to unattended stimuli) and y = 0 (no effect of attention).

at trial onset. Crucially, fixation accuracy was checked and trials with gaze deviations larger than 2° were discarded (see Methods). Two seconds after the cue presentation, a local luminance increment or decrement

(a peripheral bright or dark disk) was presented in either hemifield. In two experiments (detailed below), the task was to count the number of brief color changes of small peripheral dots, and the difficulty of detecting
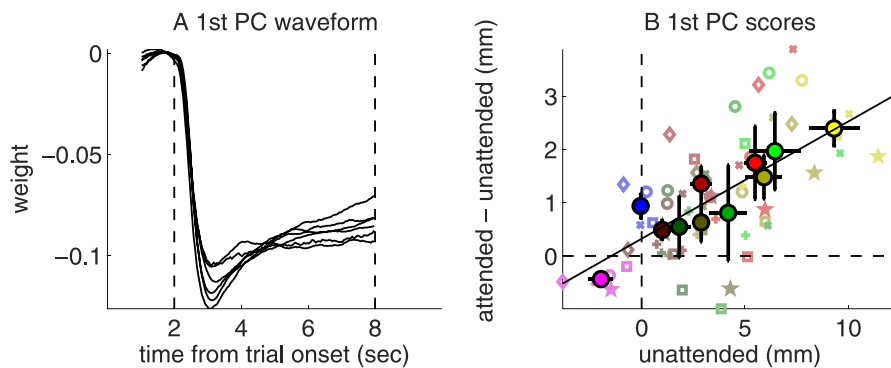

Figure 3. PCA of Experiment 1. (A) Waveforms of the first PCs plotted separately for each participant. (B) Effect of attention on the first PC scores for the individual participants (small colored symbols) and averaged (black-outlined symbols) with best-fit linear function. Same conventions as in Figure 2B.
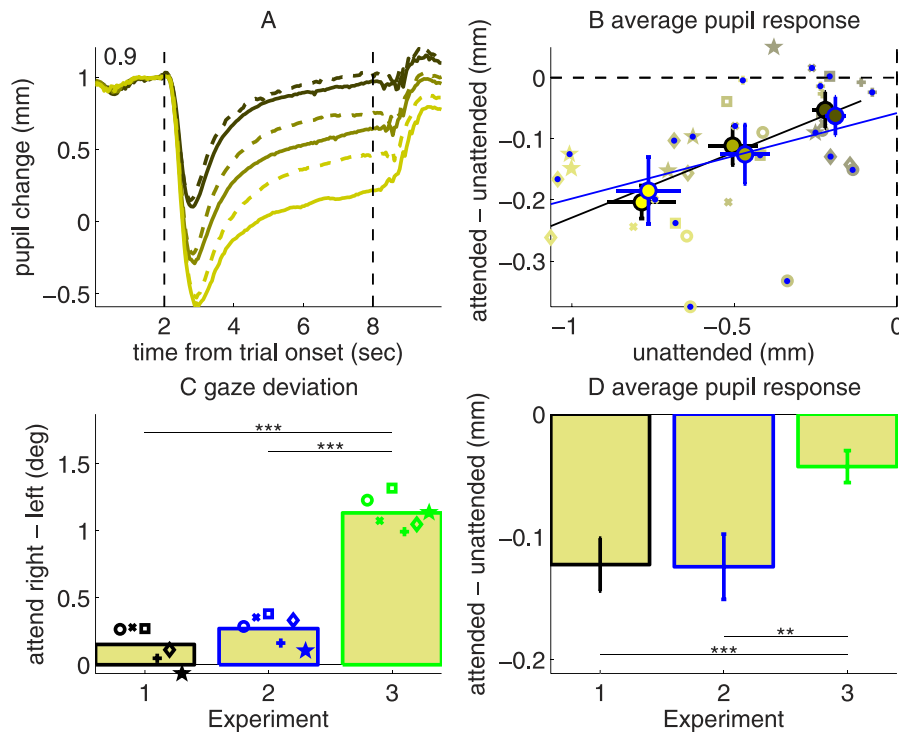
Figure 4. Pupil responses in Experiment 2 and comparison across Experiments 1 through 3. (A) pupil time courses from Experiment 2 when the disk appeared in the attended or unattended hemifield (continuous or dashed lines). Same format as in Figure 2A; background luminance (cd/m^2) in the upper left corner. (B) Effect of attention on the pupil responses averaged over the stimulus presentation window versus responses to disks in the unattended hemifield: data from Experiment 1 (black, selectively for the 0.9 cd/m^2 background luminance condition) and from Experiment 2 (blue) and respective best-fit linear functions. (C, D) Horizontal gaze deviation (C) and effect of attention (D) averaged across subjects; in (C), individual subject data are also shown. Error bars shown in (B) and (D) are standard errors across subjects. Asterisks give the results of paired t tests comparing values across experiments (***p < 0.001; **p < 0.01).

changes in the same hemifield as the disk and in the opposite hemifield was matched; average performance in the two cases was 67 ± 1% and 67 ± 2%, respectively, in Experiment 1 (not significantly different, paired t test, t: 0.0023, df: 56, p > 0.1) and 73 ± 2% and 70 ± 2% in Experiment 2 (not significantly different, paired t test, t: −1.2733, df: 17, p > 0.1).

Pupillary behavior was measured by computing the change of pupil diameter relative to the mean in the 0.5 s preceding stimulus presentation in each trial, separately for trials in which the disk appeared in the attended hemifield and the opposite hemifield. Irrespective of the direction of attention, the presentation of the disk is expected to elicit a pupil change of variable size, depending on its luminance relative to the background (in Experiment 1, we varied both parameters to extend the range of observed response). However, we find that attention enhances the pupil response across all combinations of disk and background luminance. This may be qualitatively appreciated in Figure 2A (continuous vs. dashed lines), showing averages across all participants. We quantified

this effect with two independent analyses of the individual subject results (Figures 2B, C and 3).

In the first and most straightforward approach, we computed pupillary responses to the luminance disk by either averaging pupil size over the disk presentation interval (2–8 s into each trial: "average response") or taking the maximum pupil constriction/dilation following the presentation of luminance increments/decrements ("peak response") separately for trials in which the disk appeared in the attended and unattended hemifield. Figure 2B and C plots the difference between the two attention conditions (i.e., the attentional modulation) for the average and peak response, respectively, against the responses to disks in the unattended hemifield. Attentional modulation values are significantly different from 0 for both pupillary dilations evoked by luminance decrements (magenta symbols; t test for average responses, t: 5.93, df: 4, p = 0.004; for peak responses, t: 8.43, df: 4, p = 0.001) and pupillary constrictions evoked by luminance increments (color codes as in Figure 2A; t test for average responses, t: −8.96, df: 51, p < 0.001; for peak responses, t: −6.24, df: 51, p < 0.001). This means that,

given a stimulus that causes a pupillary dilation or constriction, attending to the stimulus area increases this response.

Moreover, attentional modulation values are proportional to responses to disks in the unattended hemifield (R^2: 0.49 for average responses and R^2: 0.18 for peak responses, both significant at $p \leq 0.001$), and the best-fit linear models have slopes of 0.22 (95% confidence interval [CI]: 0.16–0.29) and 0.05 (95% CI: 0.02–0.07) for average and peak responses, respectively. This means that the effect of attention in pupil size observed here is not a constant added on top of the light response. Rather, Figure 2 shows that the effect of attention is larger when the light response is large and smaller when the light response is small, i.e., it is multiplicatively related to the size of the pupillary light response, amounting to 22% and 5% of the average and peak response to unattended stimuli.

Note that, in our previous study (Binda et al., 2013a) we only observed attentional enhancement of pupillary constriction, not dilation, whereas here we find an effect on both constriction and dilation; this discrepancy may be explained by the weaker luminance decrement used previously (the background–disk difference was 49 cd/m^2 and 109 cd/m^2 here). Given the multiplicative nature of the attentional modulation, weaker stimulation predicts a smaller and possibly undetectable attentional modulation.

While peak and time averages are commonly used parameters of pupillary responses, we chose to also consider an alternative analysis approach: PCA. The aim of this approach is to take into account the complexity of pupil time courses, which is expected given the numerous factors affecting pupil size besides light (see Introduction). For example, consider how pupils dilate over the disk presentation time in spite of luminance remaining exactly constant (Figure 2A). This behavior may in part be ascribed to the physiology of the pupillary light response; a slow return to baseline or "pupillary escape" often occurs in the face of constant stimulation, especially for weak light stimuli (Loewenfeld, 1993). However, the cognitive-related dilation (e.g., Kahneman & Beatty, 1966) associated with the progressively increasing effort required by our counting task may be an equally important component (similar for all luminance increments and decrements).

Following Young and Kennish (1993), we used PCA to decompose the time courses into simpler waveforms; we limit our analysis to the first PC, for which coefficients are large (84% on average) and waveforms are remarkably consistent across subjects (Figure 3A). This is well suited to describe a major component of the pupillary light response: largely sustained over the stimulus presentation time (except for a small "escape," see above) with magnitude dependent on the relative luminance of the disk and the background (multiple

linear regression of the first PC scores against the logarithm of stimulus and background luminance: R^2: 0.80, df: 52, F: 70.9, $p < 0.001$; coefficients: log-luminance of the disk: 10.8, log-luminance of the background: 5.3, interaction: −4.9, intercept: −12.7, all significantly different from 0 at $p < 0.05$). Although the first PC has these simple features, the other PCs have complex dynamics, likely reflecting the combination of complex pupil behaviors (e.g., transient light response, cognitive and accommodative related responses). Knowing how these behaviors interact with each other is exceedingly complex; however, we assume that they (considered as a whole with no attempt at associating any of them with any of the PCs) combine linearly with the sustained light-dependent response described by the first PC. This, limited, linearity assumption is at the basis of our PCA approach. Violations certainly exist, e.g., when the light response drives the pupil close to its mechanical limits. However, these should have minimal impact under the present experimental conditions (for example, Figure 5A shows that we work at about the midpoint of the pupil mechanical range).

Thus, PCA allows for isolating a sustained pupillary light response from more complex pupil behaviors; we test how attention affects it. Figure 3B plots the difference between the first PC scores for attended versus unattended disks against the first PC scores for unattended disks. The distribution of values is well fit by a linear function (R^2: 0.42, $p < 0.001$), with slope 0.22 (95% CI: 0.15–0.29). These results closely parallel the analyses on the average pupil responses (Figure 2B), supporting our conclusion that attention affects the sustained pupillary light response and increases it by more than 20%.

The effect of attention does not depend on the spatial extent of the attended region

In Experiment 1, attention was focused on a small spatial area; the task was to count the number of color changes of a small dot presented at the center of the disk or in the opposite hemifield. In Experiment 2, we asked subjects to divide their attention over a larger spatial area, extending well beyond the disk (Figure 1C). Like in Experiment 1, pupil time courses are affected by attention (Figure 4A). The effect of attention increases monotonically with the response to unattended stimuli in a similar way in both experiments (Figure 4B) although the linear regression is a better model for the results of Experiment 1 (R^2: 0.49) than Experiment 2 (R^2: 0.13).

Likewise, the effect of attention on the average pupil response (Figure 4D, left and middle bar) is statistically indistinguishable across experiments (mean difference: 0.0017 mm; paired t test, t: −0.07, df: 17, $p > 0.1$), in
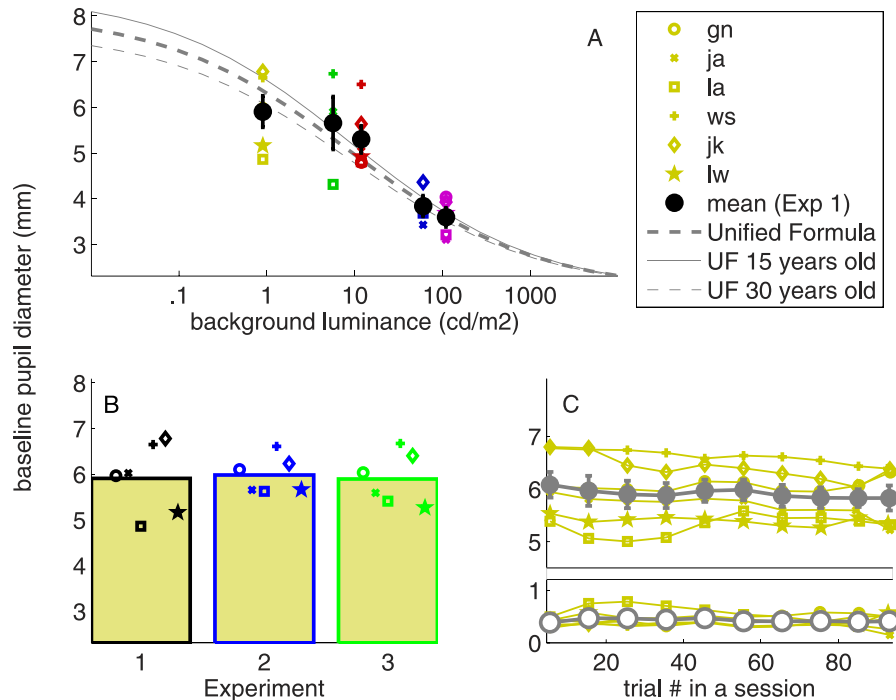
Figure 5. Baseline pupil diameter, i.e., pupil measurements in the 0.5 s preceding the onset of the luminance disk when subjects were exposed to the uniform background only. (A) Baseline pupil diameter from Experiment 1, plotted as a function of the log-luminance of the background. Individual subjects are plotted as open symbols (same color coding as in Figure 2), and solid black symbols give the average across subjects. Curves are the predictions of the unified formula for area of the luminance field = 506 deg² (our screen area), number of stimulated eyes = 2 (viewing was binocular), and three participant ages in years = 22.6 (average in our sample, thick dashed line), 15, and 30 (thin lines). (B) Baseline pupil diameter across experiments (for Experiment 1, considering only sessions with 0.9 cd/m² background luminance, i.e., the same as in the other experiments); symbols report values for individual subjects (with a slight x-axis offset to improve visibility), and bars give the average. (C) Baseline pupil diameter as function of trial number (averaged across experiments) for the individual participants (symbols as in A, B), and averaged (solid gray symbols); data points below the y-axis break show the variability (standard deviation) of baseline pupil size across sessions and its average across participants (hollow gray symbols). Error bars in (A) and (C) are standard errors across subjects.

both cases being significantly different from 0 (one-sample *t* tests: for Experiment 1, *t*: 5.84, *df*: 17, *p* < 0.001; for Experiment 2, *t*: 4.81, *df*: 17, *p* < 0.001).

Gaze shifts in the direction of the attended region do not explain pupil size differences

When attention is focused on a peripheral location, eye position tends to be biased in the direction of attention in spite of specific instructions to maintain gaze on the central fixation point. Indeed, during the stimulus presentation window of both Experiments 1 and 2, we find a small but significant gaze displacement in the direction of the attended hemifield, relative to the prestimulus interval (Figure 4C; Experiment 1, mean: 0.15°; one-sample *t* test, *t*: 3.84, *df*: 17, *p* < 0.01; Experiment 2, mean: 0.26°; one-sample *t* test, *t*: 9.56, *df*: 17, *p* < 0.001). Because the sensitivity of pupillary responses scales with eccentricity, it is important to demonstrate that these gaze deviations cannot explain

the effect of attention. We directly addressed this issue in control Experiment 3. Subjects were asked to ignore both the left and right hemifields and to keep their attention focused on the fixation point (to count the number of its color changes with average performance: 63 ± 1%). The fixation point was displaced left or right by 0.5°, producing gaze deviations (sustained over the disk presentation window) toward or away from the luminance disk. Induced gaze deviations were much larger than those observed in Experiments 1 and 2 (Figure 3C; mean difference Experiments 1 through 3: −0.98°; paired *t* test, *t*: −21.58, *df*: 17, *p* < 0.001; mean difference Experiments 2 and 3: −0.86°; paired *t* test, *t*: −23.84, *df*: 17, *p* < 0.001). However, the modulation of the pupil response (the difference between the average pupil response when gaze deviated toward vs. away from the disk) was smaller than the effect of attention measured in Experiments 1 and 2 (Figure 4D; mean difference Experiments 1 through 3: 0.08°; paired *t* test, *t*: 4.44, *df*: 17, *p* < 0.001; mean difference Experiments 2 and 3: 0.08°; paired *t* test, *t*: 3.34, *df*: 17, *p* < 0.01).

This implies that the small deviations of gaze toward the attended location in Experiments 1 and 2 cannot explain the effect of attention on pupil responses (given that even larger gaze deviations, if not accompanied by focused attention to the disk vs. away from it, do not produce such pupil size changes).

Pupil diameter as a function of luminance

Although our primary aim was to quantify the pupil size changes in response to changes in light level (and their attentional modulation), the design of Experiment 1 also allowed us to study the dependence of steady-state pupil diameter as a function of illumination level, which we report for completeness. Figure 5 plots the baseline pupil diameter (in the 0.5 s preceding the presentation of the disk) against the log-luminance of the background, which remained constant across all trials of a given session. Averages across subjects are well modeled by a sigmoidal curve that takes into account luminance, binocularity, and subject age, such as the unified formula developed by Watson and Yellott (2012). However, at the individual subject level, the variability is larger than expected from age differences (thin curves show predictions for an age range much larger than in our sample), and this is especially evident at low luminance (as noted in previous reports, reviewed in Watson & Yellott, 2012). However, interindividual differences are fairly consistent across our three experiments (performed on separate days, Figure 5B) and over the approximately 100 trials composing each session (Figure 5C). Also note that there is no trend toward increased pupil size (top of Figure 5C) or pupil-size variance (hollow symbols at the bottom of Figure 5C) at the end of a session, both of which would have been expected had participants experienced fatigue (known to correlate with pupil dilation and increased pupil variability or "unrest"; Loewenfeld, 1993).

Discussion

We find that pupillary responses to light increments and decrements are enhanced by attention, implying that pupil size depends on a (light change) × (location of attention) interaction. It is well known that luminance is not the only determinant of pupil size and that there are cortically mediated influences (see next paragraph); however, these appear to be independent from the pupillary response to luminance (Zhang et al., 1996; Wilhelm et al., 2002). In contrast, we show here an effect of attention that interacts with light, increasing the magnitude of the sustained pupillary

constriction/dilation evoked by a luminance change. This phenomenon is consistent with our prior work (Binda et al., 2013a; Binda, Pereverzeva, & Murray, 2014) and clearly distinct from, though not incompatible with, the well-known cognitive-related pupil dilations (see below).

We demonstrate the effect of attention with multiple analysis approaches: using different indices to define pupil responses (time averages over the stimulus window and the peak constriction/dilation) or applying PCA to the pupil traces and analyzing the first component, which we found to be well suited to describe a sustained component of the pupillary response to light, isolating it from more complex pupillary behaviors.

This effect of attention cannot be an artifact of eye position biases as shown in Experiment 3. Other known cortical modulations of pupil size cannot explain it either. The pattern of retinal stimulation was largely independent of the direction of attention, implying the same visual transients and the same "onset response" (e.g., J. L. Barbur et al., 1992) across attention conditions. Pupil constrictions with accommodation ("near response"; Bharadwaj et al., 2011) and pupil dilations with cognitive effort (e.g., Kahneman & Beatty, 1966) should be approximately constant in all trials, given that the task forced subjects to maintain the stimulus plane in sharp focus, and the effort required by the behavioral task was strictly matched across conditions. Conditions were pseudorandomly alternated across trials, ruling out explanations based on trial-order effects, for example, fatigue and the resulting pupil unrest/dilation (Loewenfeld, 1993), which were anyway not evident in our data set. More generally, the phenomenon we report here is radically different from the previously reported effects of attention on pupil size when pupils dilate when more attention is paid to a given task, compared to a less demanding condition (Laeng, Sirois, & Gredeback, 2012). Here, we do not compare two conditions, one entailing a task that requires more cognitive effort than the other. Rather, we compare two conditions in which the same task is performed, requiring the same "amount of attention," and we show a pupil size difference depending on *where* attention is focused (on the luminance stimulus or elsewhere).

Pupillary light responses (i.e., size changes that may span the full range of the pupil, 2–8 mm) cause small but measurable improvements of visual sensitivity: light detection, acuity, depth of field (Campbell & Gregory, 1960; Loewenfeld, 1993). One may speculate that the attentional influence on pupil size serves the same purpose: adjusting pupil size so to improve vision at the luminance of behaviorally relevant stimuli. However, it should be noted that the effect size of attentional pupil

modulations is on the order of 10ths of millimeters, significantly smaller than the pupil size changes for which visual improvements have been documented (e.g., Campbell & Gregory, 1960). Yet no matter how subtle their impact on vision is, these pupil modulations might be symptomatic of a general phenomenon—the ubiquity of attentional modulations on sensory processing—and thereby serve as a quantitative, sensitive method for studying it.

Our second experiment exemplifies this approach, using pupil size measurements to ask whether the effect of attention is affected by its spatial distribution: focused on the stimulus or divided across space. Several models predict that divided attention should be associated with a cost (Treisman & Gelade, 1980; Eriksen & St James, 1986; Sperling & Dosher, 1986). Most assume that a larger cost should apply to tasks requiring the allocation of a fixed amount of resources (e.g., discrimination of feature conjunctions) compared to tasks that can be solved in parallel across multiple stimuli (e.g., simple feature detection). Here we employed a task that required the detection of a simple feature (color changes) and manipulated the spatial spread of attention (i.e., increasing spatial uncertainty as in Herrmann, Montaser-Kouhsari, Carrasco, & Heeger, 2010); the results support the above models, showing similar effects of divided versus focused attention.

Our experimental paradigm allowed us to characterize the effect of attention further by measuring its impact on (a portion of) the luminance-response curve of the pupil. Luminance changes of variable intensity evoked pupillary responses of variable size; the difference between responses to attended versus unattended stimuli is an approximately constant proportion of the response to the unattended stimuli. These observations are better explained by a model in which attention enhances the response gain of the pupillary response, which predicts proportionality between the effect of attention and the response to unattended stimuli, than by a contrast gain enhancement model, which predicts an inverted U-shaped relationship instead (Boynton, 2009; Lee & Maunsell, 2009; Reynolds & Heeger, 2009). The recent "normalization model of attention" (Lee & Maunsell, 2009; Reynolds & Heeger, 2009) predicts that the effect of attention on the response function should be affected by the spatial spread of its focus; it should shift from response gain to contrast gain enhancement when the attended area is enlarged relative to the stimulus area (as shown empirically in Herrmann et al., 2010; Ni, Ray, & Maunsell, 2012). Contrary to this prediction, our results for focused and spatially spread attention are both best described by a response gain enhancement model. There are several possible accounts of this inconsistency. On the one hand,

available evidence on the physiology of the pupillary light response system is not sufficient to guarantee that this response can be satisfactorily described by the divisive normalization principle (Carandini & Heeger, 2012), which forms the basis of this model. On the other hand, it must be noted that our stimulus range is limited (luminance changes are small compared to those commonly found in natural conditions) and may afford limited power to discriminate between the two models.

This methodological limitation may also be considered before generalizing our observations. The pupillary response to light and dark has long been associated with subcortical processing—a retino-pretectal-oculomotor parasympathetic pathway for pupillary constrictions and a hypotalamo-sympathetic pathway for dilations (Loewenfeld, 1993; Gamlin & Clarke, 1995). Our observations indicate that a prominent component (more than 20%) of these pupillary responses depends on cortical processing (which controls the distribution of attention) with no insights into the neural circuitry involved, the results being equally compatible with sympathetic and parasympathetic modulations. Given the small range of stimulus–background luminance levels that we explored, we cannot exclude that responses to more intense light stimuli would show a smaller effect of attention. In fact, there is evidence to suggest that responses to more intense light have a smaller contribution of cortical versus subcortical signals. For example, patients with visual cortical lesions have impaired pupillary responses to weak stimuli but preserved responses to more intense light (J. Barbur, 2004). Moreover, signals from melanopsin-containing ganglion cells, which participate in pupillary light responses, are preferentially driven by very intense light (Lucas et al., 2003; Gamlin et al., 2007; Guler et al., 2008) and give minor (if any) contribution to cortical visual processing (Lucas, 2013).

In spite of these limitations, our results clearly agree with previous reports that indicate changes of pupil size are affected by the "internal state" of the subject: the planning of eye movements (saccadic suppression, Lorber et al., 1965; Zuber, Stark, & Lorber, 1966), binocular competition (interocular suppression, Richards, 1966), the subject's interpretation of the context of the luminance stimulus (Binda, Pereverzeva, & Murray, 2013b; Naber & Nakayama, 2013) and perceived or imaginary brightness (Laeng & Endestad, 2012; Laeng & Sulutvedt, 2014). By showing that "what is attended" and light level interact to determine pupil size, our findings imply that pupillometry provides an index of attentional modulations. We suggest that its features (such as sensitivity, objectivity, and a relative independence of task/

decision strategies) should make it a particularly useful tool for the study of the effects of attention on sensory responses (e.g., testing different models of attentional enhancement or comparing the effects of different "forms" of attention) and to monitor the control of attention, e.g., to track the focus of attention across hemifields or over a finer spatial scale (Pereverzeva, Binda, & Murray, 2013) and across colocalized features (Binda et al., 2014).

Keywords: pupillary light response, attention, attentional enhancement

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