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Effects of stimulus size, eccentricity, luminance, and attention on pupillary light response examined by concentric stimulus

Xiaofei Hu[a,*], Rumi Hisakata[a], Hirohiko Kaneko[a]

[a] Department of Information and Communications Engineering, School of Engineering, Tokyo Institute of Technology, 4259-G2-3 Nagatsuta-Cho, Midori-Ku, Yokohama 226-8502, Japan

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ABSTRACT

Previous studies show that the amplitude of pupillary light response (PLR) depends on the corneal flux density (CFD), which is the product of stimulus area by luminance. However, the contribution of CFD has been investigated only when the stimulus was centered on the fovea, whereas perceived luminance to pupillary response would reduce with stimulus eccentricity. Additionally, it has been shown recently that attentional state modulates pupillary response. In this study, we aimed to clarify the complete mechanisms of PLR by manipulating the stimulus size, eccentricity, luminance, and the participants' attentional states. We focused on four indices to examine PLR, that is, pupillary latency (PL), maximum constriction velocity (MCV), maximum constriction (MC), and mean pupil change (MPC). Results showed that PL was a function of CFD, whereas MCV, MC, and MPC were functions of both CFD and stimulus eccentricity. Furthermore, the magnitude of effect due to stimulus eccentricity for MCV and MC was different from that for MPC. These results provided new evidence that the different processing systems in PLR existed.

1. Introduction

Pupillary light response (PLR) is a physiological phenomenon that depicts a pupil size change elicited by the light presented to the eyes (Loewenfeld & Lowenstein, 1993; Ellis, 1981). Many researchers have thoroughly investigated the factors affecting pupillary response. It has been shown that if the corneal flux density (CFD), which is the product of stimulus area by luminance, is constant, the steady pupil size is also constant (Stanley & Davies, 1995; Atchison et al., 2011; Park & McAnany, 2015; Joyce, Feigl, & Zele, 2016). Moreover, Watson and Yellott (2012) proposed a unified formula to estimate the pupil size. Despite the excellent work they did, they also acknowledged their limitation. Their formula could only be used when the stimulus was centered on the fovea. Indeed, Crawford (1936) found that the pupil size became large as the stimulus eccentricity from fovea increased even though CFD was constant. Therefore, we aimed to remedy this limitation by considering stimulus eccentricity in this study.

Recently, a series of studies indicate that attention can also modulate pupillary response (Binda, Pereverzeva, & Murray, 2013; Binda, Pereverzeva, & Murray, 2014; Binda et al., 2017; Daniels, Nichols, Seifert, & Hock, 2012; DiCriscio, Hu, & Troiani, 2018; Hu, Hisakata, & Kaneko, 2019; Binda & Murray, 2015; Mathôt, Van Der Linden, Grainger, & Vitu, 2013; Tkacz-Domb & Yeshurun, 2018). Binda et al. (2013), Binda et al. (2014), Binda et al. (2017) and Tkacz-Domb and Yeshurun (2018) found that attending to a bright stimulus could elicit a smaller pupil compared to attending to a dark stimulus. Daniels et al. (2012) found that the alternation between narrow and broad attention could elicit different pupil sizes. DiCriscio et al. (2018) found that selective attention to global and local parts of a Navon stimulus could elicit different pupil constriction. Hu et al. (2019) found that attention to a stimulus with high spatial frequency component reduced the pupil size. Therefore, we also regarded the attention as one of the factors for pupillary response in this study.

We considered there were two primary problems with designing an experiment by using a peripheral stimulus. First, the hemispheric asymmetry exists for many visual tasks (Hugdahl & Westerhausen, 2010). For example, a left visual field had an advantage in a bilateral rapid serial visual presentation paradigm, wherein the identification rate for the target stream presented in the left visual field was better than that presented in the right visual field (Holländer, Corballis, & Hamm, 2005). There was also a lower visual field advantage for many types of stimuli (Previc, 1990; Levine & McAnany, 2005). One possible interpretation of the asymmetry was the biased allocation of attention to some visual fields (Holländer et al., 2005). Since attention could enhance PLR (Binda et al., 2013; Binda & Murray, 2015), the biased attention allocation might affect the pupil size. Second, when we record

* Corresponding author.
E-mail address: hu.x.aa@m.titech.ac.jp (X. Hu).

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the pupillary response, there may be a recording error accompanied by a varying gaze position, which is called the pupil-foreshortening error (Gagl, Hawelka, & Hutzler, 2011; Mathur, Gehrmann, & Atchison, 2013; Brisson et al., 2013; Hayes & Petrov, 2016). It depicts a shrinkage of pupil image as much as 10% when gaze position changes. Gaze position biased to the specific position of the stimulus may elicit the unexpected recording error. Therefore, we used a concentric stimulus pattern in this study to overcome these possible problems.

The goal of this study was to examine the effects of stimulus size, eccentricity, luminance, and participants' attentional states on PLR and develop a model to portray the data adequately. We conducted three experiments in this study. In Experiment 1, the radius (size) and eccentricity of stimulus disks varied, whereas luminance was constant. This experiment was for verifying the dependence of stimulus size and eccentricity on PLR reported in the previous studies (Loewenfeld & Lowenstein, 1993; Ellis, 1981; Stanley & Davies, 1995; Atchison et al., 2011; Park & McAnany, 2015; Joyce et al., 2016; Watson & Yellott, 2012; Crawford, 1936; Yahia et al., 2018). In Experiments 2 and 3, a concentric stimulus pattern with eight inner and eight outer disks was used to consider the effect of attention. The radius and eccentricity of outer disks varied in Experiment 2, and the luminance of both inner and outer disks varied in Experiment 3. Finally, we developed functions to estimate the contribution of each factor to quantitatively explain PLR.

It has been shown that PLR comprises both a transient and sustained components, leading to as much as 14 indices to demonstrate the characteristics of pupillary response (Young, Han, & Wu, 1993; Young & Kennish, 1993; Barbur, 2004; Hall & Chilcott, 2018; Link et al., 2006). In this study, we chose the four most important indices. First, we used pupillary latency, which is defined as the duration between the onset of pupil constriction and the onset of stimulus presentation and is essential to estimate the underlying mechanism of pupillary response in the visual system (Barbur, Wolf, & Lennie, 1998; Gamlin, Zhang, Harlow, & Barbur, 1998). Second, we used maximum constriction velocity, which is said to be useful in diagnosing retinal pathologies (Chibel et al., 2016; Ortube et al., 2013; Yahia et al., 2018; Wang et al., 2016). Third, we used maximum constriction, which is the smallest pupil size and directly reflects the PLR (Loewenfeld & Lowenstein, 1993; Ellis, 1981; Yahia et al., 2018). Finally, we used mean pupil change, which is the average value after recovering from the initial constriction and reflects the sustained component of PLR (Young et al., 1993; Young & Kennish, 1993).

2. General methods

2.1. Participants and apparatus

Five males (age range: 23–27 years) with corrected-to-normal visual acuity participated in this study. Informed consent was obtained from each of them. The protocol was approved by Tokyo Institute of Technology Ethics Committee.

An infrared video-based eye tracker with a spatial resolution of 0.1% of diameter, when tested with a 5 mm artificial pupil (EyeLink 2000, SR Research, 500 Hz sampling rate), was used to record participants' eye movements and pupillary responses. Visual stimuli were presented on a cathode-ray tube monitor (Sony GDM-F500R, 1280 × 1024 pixels, 60 Hz refresh rate). The monitor was placed at 57 cm in front of the participants, and a chin rest was set to prevent their head movements. The participants had a numeric keypad and were asked to press a key based on the instruction.

The experiments were conducted in a dark room. The background of monitor was black throughout all experiments even for the inter-trial interval. The chroma meter CL-200A (Konica Minolta, the lower limit is 0.1 lux) was used to measure the illumination at the position of participants' eye during the experiment period. The lowest illumination was 0 lux (lower than 0.1 lux) when stimulus was not presented, and the highest illumination was 3.3 lux when the brightest stimulus was presented. Before each experiment, participants were asked to adapt to the darkness for 1 min. The chroma meter CS-100A (Konica Minolta, the lower limit is 0.01 cd/m^2) was used to measure the luminance and chromaticity of stimulus. The luminance of black background is 0.07 cd/m^2 and that of the brightest white stimulus is 73.1 cd/m^2. The chromaticity of white stimulus is (0.355,0.410).

2.2. Preprocessing of raw pupil data

The procedure of pupil data analysis was similar to that used in Hu et al., 2019's study. First, if the deviation of either the horizontal or vertical eye position during the stimulus presentation was more than 1°from the fixation position, the trial data were excluded from the analysis. Second, the baseline of pupillary response in each trial was defined as the average value during 100 ms prior to the stimulus onset. If the baseline deviated more than 2.5 standard deviations from the average baseline in the whole experimental block for each participant, the trial data were also excluded from the analysis. This manipulation was to select trials with a similar state of participants' arousal (de Gee, Knapen, & Donner, 2014; Murphy, Vandekerckhove, & Nieuwenhuis, 2014; Urai, Braun, & Donner, 2017; Wang et al., 2018). Third, if there was a blink, it was reconstructed by using a cubic Hermite spline interpolation. Subsequently, the raw pupil data were normalized by subtracting the baseline and then dividing it by the baseline, leading to a negative percentage value representing the constriction rate in relation to the baseline (Mathôt, Fabius, Van Heusden, & Van der Stigchel, 2018). Finally, the pupillary response was smoothed by using a Savitzky-Golay filter (order 2, window length 100 ms) (Bergamin & Kardon, 2003).

2.3. Extraction of PLR indices

To analyze the pupillary response quantitatively, we used four indices of PLR. An example of a pupillary response is presented in Fig. 1. The pupil diameter, velocity, and acceleration of a pupillary response are illustrated from top to bottom. The vertical black chain lines indicate specific timings. Time 1 (T1) indicates the onset of stimulus. Time 2 (T2) indicates the timing of maximum constriction acceleration. Pupillary latency (PL), which is defined as the onset of pupil constriction in reaction to the onset of stimulus, is calculated by the difference between T1 and T2 (Bergamin & Kardon, 2003; Canver et al., 2014). Time 3 (T3) indicates the timing of maximum constriction velocity, and the velocity at T3 is regarded as maximum constriction velocity (MCV). Time 4 (T4) indicates the timing of the smallest pupil size, and the pupil size at T4 is regarded as maximum constriction (MC). Time 5 (T5) indicates the offset of the stimulus. Mean pupil change (MPC), which reflects the sustained component of the pupillary response (Young et al., 1993; Young & Kennish, 1993), is calculated by averaging pupil size over 1 s prior to T5. For simplicity, abbreviations were used in the following texts.

3. Experiment 1: The effects of stimulus size and eccentricity on PLR

Previous studies have shown that the pupil size becomes large as the stimulus size decreases or stimulus eccentricity increases when stimulus luminance is constant (Stanley & Davies, 1995; Atchison et al., 2011; Park & McAnany, 2015; Joyce et al., 2016; Watson & Yellott, 2012; Crawford, 1936; Yahia et al., 2018). In this experiment, we systematically investigated the effects of stimulus size and eccentricity on PLR by using four indices mentioned in Section 2.3. The stimulus radius (size) and eccentricity varied in separate blocks.

3.1. Stimulus and procedure

The stimulus comprised eight bright disks (73.1 cd/m^2); the disks

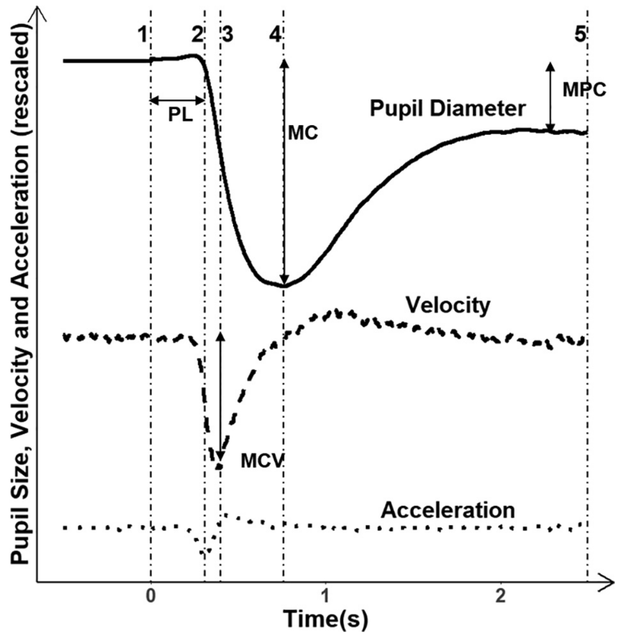

Fig. 1. An illustration of pupillary response indices used in this study. The solid line indicates the pupil diameter in relation to time. The dashed line indicates the velocity of pupillary response, and the dotted line indicates the acceleration of pupillary response. All curves are rescaled to fit in this figure. Five vertical chain lines represent the following specific timings: time 1 (T1) – stimulus onset, time 2 (T2) – maximum constriction acceleration, time 3 (T3) – maximum constriction velocity, time 4 (T4) – maximum constriction, time 5 (T5) – stimulus offset. Four indices were extracted: pupillary latency (PL), maximum constriction velocity (MCV), maximum constriction (MC), and mean pupil change (MPC). Refer to the text for more details.

were located around fixation dot at regular intervals. We manipulated the radius (size) and eccentricity of the disks. Two examples of stimulus are depicted in Fig. 2. The eccentricity of each disk was defined as the visual angle subtended by the center of the disk and fixation dot. Experiment 1 comprised two blocks. In Experiment 1a, the radius of disks varied (0.5°, 0.82°, 1.12°, 1.36°and 2.5°), whereas the eccentricity of disks was fixed at 10°. In Experiment 1b, the eccentricity of disks varied (2°, 5°, 7.5°, and 13°), whereas the radius of disks was fixed at 0.5°. The radius and luminance of fixation dot was 0.05°and 3.4 cd/m^2, respectively. The stimulus was presented against a dark background (0.07 cd/m^2).

On each trial, the fixation dot was presented for 1.5 s. The participants were instructed to fix the fixation dot throughout each trial. Subsequently, a randomly chosen stimulus was presented for 2.5 s. Pupil diameter and eye movement were recorded until the disappearance of the stimulus. The participants could take rest and blink after stimulus offset. After they pressed a button, a new trial began. Twenty trials were conducted for each stimulus, leading to a total of 100 trials (20 trials × 5 radiuses) in Experiment 1a and 80 trials (20 trials × 4 eccentricities) in Experiment 1b. To reduce the burden on the participants, the two experiments were conducted on separate days. It lasted approximately 10 and 8 min for each experiment, respectively.

3.2. Results

A total of 1.5% and 3.5% of the trials in Experiment 1a and 1b, respectively, were excluded from the analysis because of the criteria mentioned in Section 2.2. The results are illustrated in Fig. 3. Fig. 3A–D show the results for Experiment 1a (manipulating the radius) and Fig. 3E–H show the results for Experiment 1b (manipulating the eccentricity). The results of PL, MCV, MC, and MPC are plotted from top to bottom, respectively.

As shown in Fig. 3A–D (the results for Experiment 1a), PL decreased as the radius of disks increased, and the amplitudes (absolute values) of MCV, MC, and MPC increased as the radius of disks increased. As shown in Fig. 3E–H (the results for Experiment 1b), PL remained almost unchanged as the eccentricity of disks increased, whereas the amplitudes (absolute values) of MCV, MC, and MPC decreased as the eccentricity increased.

A one-way repeated analysis of variance (ANOVA) was performed separately for each index in each experiment. In Experiment 1a (Fig. 3A–D), the radius of disks was regarded as within-subject factor. The main effect of radius was significant for PL ($F(4, 16) = 17.10, p < .001$), MCV ($F(4, 16) = 32.92, p < .001$), MC ($F(4, 16) = 361.20, p < .001$), and MPC ($F(4, 16) = 145.24, p < .001$). In Experiment 1b (Fig. 3E–H), the eccentricity of disks was regarded as within-subject factor. The main effect of eccentricity was significant for MCV ($F(3, 12) = 18.01, p < .001$), MC ($F(3, 12) = 26.26, p < .001$), and MPC ($F(3, 12) = 9.87, p = .002$), whereas not for PL ($p = .279$).

The effect of radius (size) on PL, MCV, MC, and MPC and that of eccentricity on MCV, MC, and MPC were clearly shown in our results. However, the difference in the attentional state that could be elicited by different radius and eccentricity were completely ignored in this experiment. To examine whether the attentional state affected pupillary response in the present stimulus configuration, we controlled the participants' attentional states in the next experiment.

4. Experiment 2: The effects of stimulus size, eccentricity, and attention on PLR

We examined the effects of stimulus size and eccentricity on PLR in Experiment 1. However, the effect of the difference in attentional state accompanied by different radius and eccentricity of disks was ignored. DiCriscio et al. (2018) have shown that even the sustained MPC was not affected by different attentional states, the transient MC was. Here, a concentric stimulus configuration was used. The participants' attentional states were controlled by a cue presented with the stimulus. As in Experiment 1, the radius and eccentricity of disks varied in separate blocks.

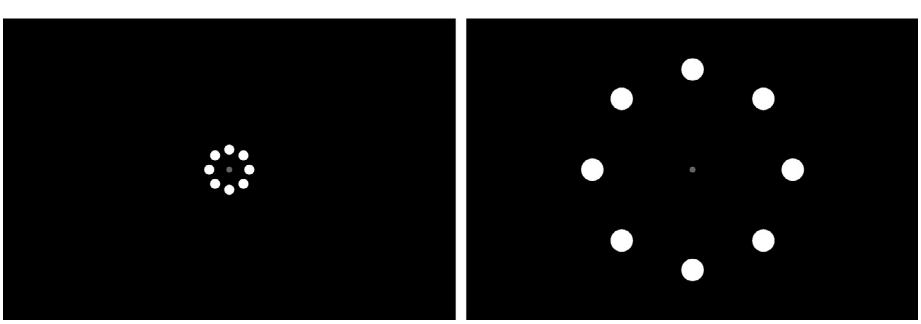

Fig. 2. Two examples of stimulus in Experiment 1. The radius and eccentricity of disks in the left stimulus was 0.5°and 2°, respectively. Those in the right stimulus were 1.12°and 10°, respectively. A fixation dot was shown at the center of the annulus stimulus. The radius of the fixation dot was rescaled. Refer to the text for more details.

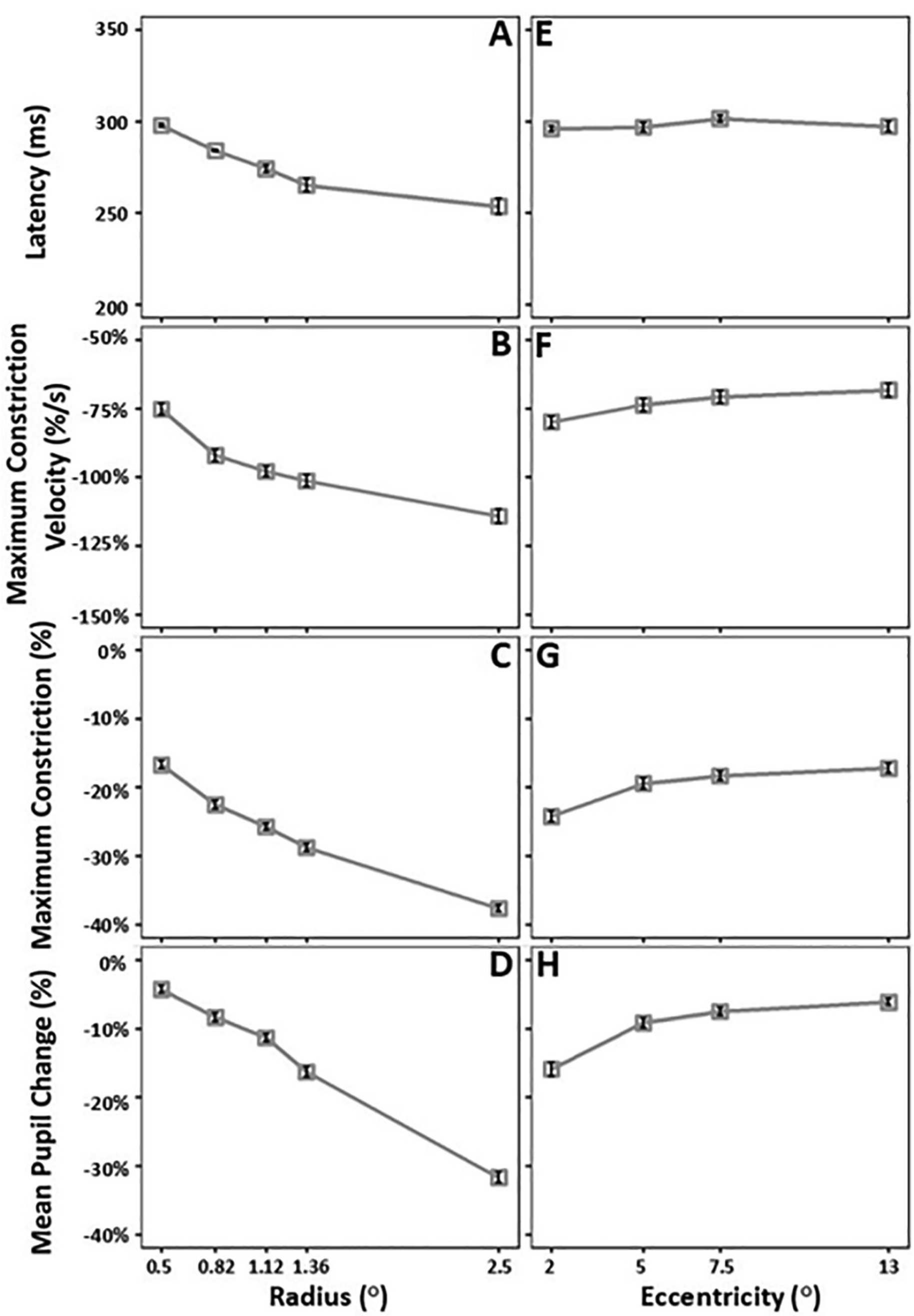

Fig. 3. The results for Experiment 1a (radius) and 1b (eccentricity). Panels A–D are the results for Experiment 1a, which investigated the effect of stimulus radius (size), and panels E–H are the results for Experiment 1b, which investigated the effect of stimulus eccentricity. PL, MCV, MC, and MPC are plotted from top to bottom, respectively. The abscissa indicates the radius and eccentricity of disks for Experiments 1a and 1b, respectively. The ordinate indicates the value of each index. They have different units and scales with PL in millisecond (ms), MCV in the proportion of change per second (%/s), and MC and MPC in the proportion of change (%). The black error bars represent the standard error of the means across five participants.

4.1. Stimulus and procedure

The stimulus comprised eight bright inner disks and eight bright outer disks (73.1 cd/m^2). Stimuli used in Experiment 2 are depicted in Fig. 4. Experiment 2 comprised two blocks. The top panel shows the three stimuli used in Experiment 2a, where the radius of outer disks varied (0.5°, 1.12°, and 2.5°) and the eccentricity was fixed at 10°. The bottom panel shows the three stimuli used in Experiment 2b, where the eccentricity of outer disks varied (5°, 7.5°, and 13°) and the radius was fixed at 1.12°. The radius of outer disks was set to 1.12°because we found that the MC and MPC with the disks whose radiuses were 0.5°and eccentricities were 2°were comparable with those with the disks whose radiuses were 1.12°and eccentricities were 10°(Fig. 3). By this manipulation, we aimed to eliminate the effect of stimulus size per se. The radius and eccentricity of inner disks were separately fixed at 0.5°and 2°in both experiments. The radius and luminance of fixation dot was 0.05°and 3.4 cd/m^2, respectively. A thin circular ring (a pixel width) of which the radius and luminance corresponded with the eccentricity and luminance of the inner or outer disks was presented. It was used as the cue to instruct the participants to narrow or broaden attention. The stimulus was presented against a dark background (0.07 cd/m^2).

On each trial, the fixation dot was presented for 1.5 s. The participants were instructed to fix the fixation dot throughout each trial. Subsequently, a randomly chosen stimulus was presented for 2.5 s. A circular ring (the width was one pixel) was also presented as cue at the same location of either inner or outer disks. Note that, the cue was simultaneously presented with the stimulus onset. The preceding cue was not used because the pupil baseline was different if participants knew how to deploy their attention in advance (DiCriscio et al., 2018). During the stimulus presentation, the circular ring flashed with a random duration (0.5–2 s). The participants were instructed to look at the fixation dot throughout each trial and respond to how many times the ring had flashed, that is, one, two, or three, right after the stimulus presentation. This task was to maintain participants' attention on the

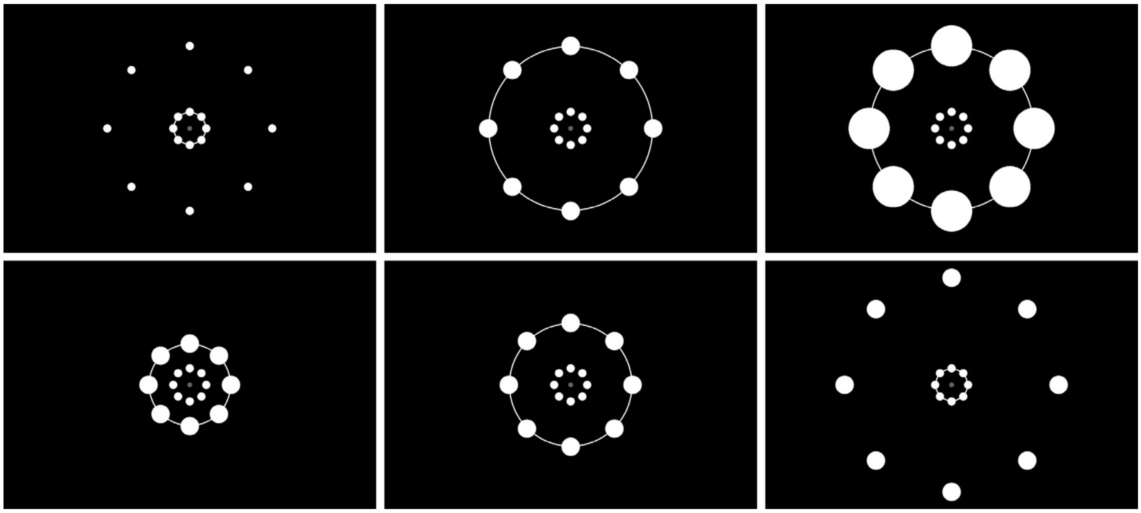

Fig. 4. The stimuli used in Experiment 2. The top and bottom panels depict the stimuli used in Experiments 2a and 2b, respectively. The radius of outer disks varied in Experiment 2a, and the eccentricity of outer disks varied in Experiment 2b. A circular ring was drawn through all eight inner or outer disks. A fixation dot was shown at the center of the concentric stimulus. The width of the circular ring and radius of the fixation dot were rescaled. See the text for more details.

corresponding inner or outer disks. Pupil diameter and eye movement were recorded until the disappearance of all stimuli. The participants could take rest and blink after stimulus offset. After they pressed a button, a new trial began. To reduce the burden on the participants, the two experiments were conducted on separate days. Twenty trials were conducted for each stimulus and attentional state (inner or outer disks), leading to a total of 120 trials (20 trials $\times$ 3 stimuli $\times$ 2 attentional states) in Experiments 2a and 2b, respectively. Each experiment lasted approximately 13 min.

4.2. Results

The average percentage of the participants' correct responses for the counting task was 95.9% and 97.3% for Experiments 2a and 2b, respectively. After discarding the incorrect trials, a total of 2.0% and 2.8% of the remaining correct trials were also excluded from the analysis for Experiments 2a and 2b, respectively, because of the criteria mentioned in Section 2.2. The results are illustrated in Fig. 5. Fig. 5A–D show the results for Experiment 2a (manipulating the outer disks radius) and Fig. 5E–H show the results for Experiment 2b (manipulating the outer disks eccentricity). The results of PL, MCV, MC, and MPC are plotted from top to bottom, respectively. The solid lines show the results when inner disks were attended (narrow attention), and the dashed lines show the results when outer disks were attended (broad attention).

As shown in Fig. 5A–D (the results for Experiment 2a), PL decreased as the radius of disks increased, and the amplitudes (absolute values) of MCV, MC, and MPC increased as the radius of outer disks increased. As shown in Fig. 5E–H (the results for Experiment 2b), PL remained almost unchanged as the eccentricity of outer disks increased, whereas the amplitudes (absolute values) of MCV, MC, and MPC decreased as the eccentricity increased. Furthermore, there was no difference when different attentional states, inner or outer disks, were deployed for all indices.

A paired two-tailed t-test was performed for pupil baseline for two experiments. We found that there were no significant difference between two attentional states in Experiment 2a (p = .566) and in Experiment 2b (p = .396). Then, a two-way repeated ANOVA was performed separately for each index in each experiment. In Experiment 2a (Fig. 5A–D), the radius of outer disks and the attentional state were regarded as within-subject factors. The main effect of radius of outer disks was significant for PL ($F(2, 8) = 8.07$, $p = .012$), MCV ($F(2, 8) = 17.35$, $p = .001$), MC ($F(2, 8) = 102.90$, $p < .001$), and MPC ($F(2, 8) = 140.70$, $p < .001$). However, there was no significant main effect of attentional state ($p > .200$, for all indices), nor the interaction between the radius of outer disks and attentional state ($p > .400$, for all indices). The lack of interaction effect suggested that although the radiuses of inner and outer disks were different, it would not affect our results. In Experiment 2b (Fig. 5E–H), the eccentricity of outer disks and the attentional state were regarded as within-subject factors. The main effect of eccentricity of outer disks was significant for MCV ($F(2, 8) = 6.91$, $p = .018$), MC ($F(2, 8) = 15.79$, $p = .002$) and MPC ($F(2, 8) = 18.64$, $p = .001$), whereas not for PL ($p = .687$). There was no significant main effect of attentional state ($p > .300$, for all indices), nor the interaction between the eccentricity of outer disks and attentional state ($p > .200$, for all indices). The lack of interaction effect suggested that although the eccentricities of inner and outer disks were different, it would not affect our results.

We found that the attentional state did not affect PLR. It was consistent with Daniels et al. (2012)'s study, which indicated that the difference in area of sustained attention, narrow or broad, did not affect pupil size, whereas inconsistent with DiCriscio et al. (2018)'s study, which indicated that the difference in area of sustained attention affected pupil size. The obvious discrepancy might be caused by the timing when the cue was presented. The cue was presented with stimulus onset in both Daniels et al. (2012)'s and our studies, whereas it was presented before the experimental block in DiCriscio et al. (2018)'s study. As a result, the pupil baselines were the same for narrow and broad attention in the present study, whereas different in DiCriscio et al. (2018)'s study. Since pupil baseline is usually linked to participants' arousal state (de Gee et al., 2014; Murphy et al., 2014; Urai et al., 2017; Wang et al., 2018), we argue that the difference in the arousal states might cause the discrepancy.

The effects of stimulus size and eccentricity were reexamined when participants' attentional states were manipulated. Consequently, we found no effect of attentional state and reproduced the results of Experiment 1. We found that MCV, MC, and MPC varied with stimulus size and eccentricity, while PL varied with stimulus size but independent of stimulus eccentricity.

There was still one limitation as regards the experimental design, that is, the luminance of inner and outer disks was the same in Experiments 1 and 2. For the completeness of experimental design, we differed the luminance of inner and outer disks and examined the effects of luminance and attention on pupillary response using the same stimulus configuration in the next experiment.

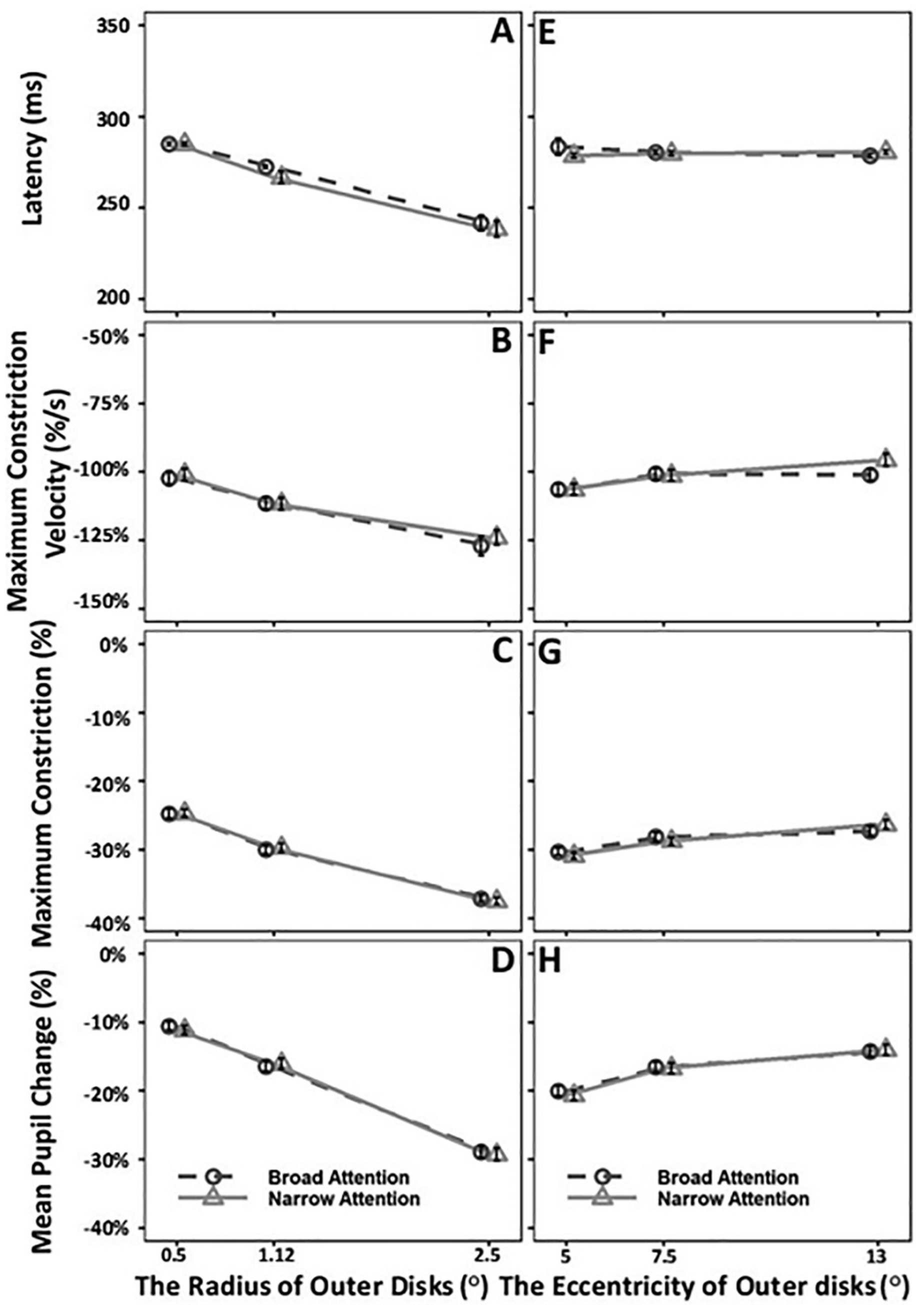

Fig. 5. The results for Experiment 2a (radius of outer disks) and 2b (eccentricity of outer disks). Panels A–D are the results for Experiment 2a, which investigated the effects of stimulus radius (size) and attentional state, and panels E–H are the results for Experiment 2b, which investigated the effects of stimulus eccentricity and attentional state. PL, MCV, MC, and MPC are plotted from top to bottom, respectively. The abscissa indicates the radius and eccentricity of outer disks for Experiments 2a and 2b, respectively. The ordinate indicates the value of each index; they have different units and scales with PL in millisecond (ms), MCV in the proportion of change per second (%/s), and MC and MPC in the proportion of change (%). The open triangle symbol and solid light gray line show the data when participants attended to inner disks (narrow attention), and the open round symbol and dark gray dashed line show the data when participants attended to outer disks (broad attention). The black error bars represent the standard error of the means across five participants.

5. Experiment 3: The effects of stimulus luminance and attention on PLR

It has been shown that attending to a bright stimulus could elicit a smaller pupil compared to attending to a dark stimulus (Binda et al., 2013; Binda et al., 2014; Binda et al., 2017; Tkacz-Domb & Yeshurun, 2018). In Experiment 3, we aimed to study the effects of stimulus luminance and attention on PL, MCV, MC, and MPC using the same stimulus configuration as in Experiment 2. Since only bright and dark disks that had high contrast between them could elicit different MPC significantly (Binda et al., 2013), we chose two extreme conditions, that is, the inner disks were much darker than outer disks, and vice versa.

5.1. Stimulus and procedure

The stimulus comprised eight inner disks and eight outer disks. Stimuli used in this experiment are depicted in Fig. 6. The radius and eccentricity of outer disks were 1.12°and 10°, respectively. The radius and eccentricity of inner disks were 0.5°and 2°, respectively. The radius of the fixation dot was 0.05°. There were two stimulus configurations. In one configuration, as shown in the left of Fig. 6, the luminance of outer disks was 73.1 cd/m^2, and that of inner disks was 7.3 cd/m^2. In another configuration, as shown in the right of Fig. 6, the luminance of outer disks was 7.3 cd/m^2 and that of inner disks was 73.1 cd/m^2. The luminance of the fixation dot was 3.4 cd/m^2. A thin circular ring (a pixel width) of which the radius and luminance corresponded with the eccentricity and luminance of the inner or outer disks was presented. It was used as the cue to instruct participants to narrow or broaden attention. The stimulus was presented against a dark background (0.07 cd/m^2).

The procedure of each trial was the same as in Experiment 2. The two stimulus configurations were randomized in this experiment, leading to a total of 80 trials (20 trials × 2 stimulus configurations × 2 attentional states). It lasted approximately 8 min.

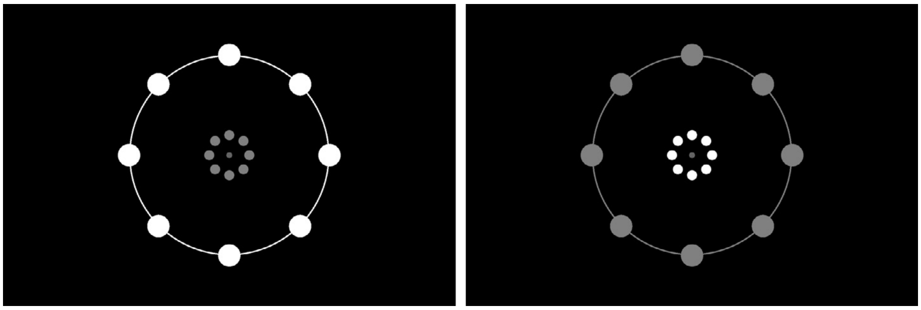

Fig. 6. The two stimulus configurations used in Experiment 3. The left panel represents the configuration when inner disks were darker than outer disks. The right panel represents the configuration when inner disks were brighter than outer disks. A circular ring was drawn through all eight inner or outer disks. A fixation dot was shown at the center of the concentric stimulus. The width of the circular ring and radius of the fixation dot were rescaled. See the text for more details.

5.2. Results

The average percentage of the participants' correct responses for the counting task was 97.9%. After discarding the incorrect trials, a total of 5.3% of the remaining correct trials were also excluded from the analysis because of the criteria mentioned in Section 2.2. The results are illustrated in Fig. 7. Fig. 7A–D show the results of PL, MCV, MC, and MPC, respectively. The light gray bars show the results when brighter disks were attended, and the dark gray bars show the results when darker disks were attended.

As shown in Fig. 7A–C, there was no difference for PL, MCV, and MC when different attentional states were deployed. Furthermore, there was no difference between two attentional states for MPC when inner disks were darker than outer disks (on the left side of Fig. 7D). However, as shown on the right side of Fig. 7D, the amplitude (absolute value) of MPC was larger when brighter inner disks were attended compared to when darker outer disks were attended.

Although the two stimulus configurations were presented in one block, they were totally different stimuli. Hence, we analyzed the results separately. A paired two-tailed t-test was performed for pupil baseline of each stimulus configuration. We found that there were no significant difference between two attentional states when inner disks were darker than outer disks ($p = .560$) and when inner disks were brighter than outer disks ($p = .261$). Then, a paired two-tailed t-test was performed for each index of each stimulus configuration. As shown on the left side of Fig. 7 (inner disks were darker than outer disks), PL, MCV, MC, and MPC were not significantly different between attending to darker inner disks and attending to brighter outer disks ($p > .300$, for all indices). As shown on the right side of Fig. 7 (inner disks were brighter than outer disks), the amplitude of MPC was significantly larger when attending to brighter inner disks compared to when attending to darker outer disks ($t = -5.26$, $p = .006$), whereas PL, MCV, and MC showed no significant difference between two attentional states ($p > .300$, for three indices). Attention modulated MPC differently from other three transient indices, which was consistent with the study of Hu et al. (2019). They argued that the attentional modulation was different at each point in the time course of pupillary response. In our study, the cue was presented with stimulus onset. It has been shown that it takes 100–120 ms to deploy exogenous attention and 300 ms to deployed endogenous attention (Carrasco, 2011). Therefore, it is possible to assume that attention was not fully deployed to the cued location during the initial period of PLR, wherein PL, MCV, and MC were measured.

6. Estimating the contribution of each factor to explain PLR

In this section, we formulated the relationship between stimulus factors and pupillary response (PLR). We fitted four functions for pupillary latency (PL), maximum constricition velocity (MCV), maximum constriction (MC), and mean pupil change (MPC) separately. From Experiments 1 and 2, we found that PL decreased as the stimulus radius (size) increased and was independent of stimulus eccentricity (Figs. 3 and 5). Additionally, PL decreased as the stimulus luminance increased, as shown in the previous studies (Ellis, 1981; Bitsios, Prettyman, & Szabadi, 1996; Myers & Stark, 1993; Gavriysky, 1991; Feinberg & Podolak, 1965). From these observations, we assumed that PL is a function of only corneal flux density (CFD), that is, the production of stimulus area by luminance. Regarding MCV, MC, and MPC, we found that their amplitudes (absolute values) increased as the stimulus radius increased and decreased as the stimulus eccentricity increased when the luminance was constant (Figs. 3 and 5). From these observations, we assumed that MCV, MC, and MPC are the functions of CFD with a modification of stimulus eccentricity. Although we manipulated the attentional states in Experiments 2 and 3, the attentional modulation was only found on MPC in Experiment 3 (on the right side of Fig. 7D). None of the other experiments reached significant effect of attentional modulation. Furthermore, the magnitude of attentional effect was about 2.5% change on MPC (on the right side of Fig. 7D). The magnitude of attentional effect on pupil size change has been reported to be about 3% or 0.01 mm, which is much smaller than the effect of luminance on PLR (Loewenfeld & Lowenstein, 1993; Ellis, 1981; Binda et al., 2013; Binda et al., 2014; Binda et al., 2017; Mathôt, 2018; Sperandio, Bond, & Binda, 2018; Tkacz-Domb & Yeshurun, 2018). Therefore, we will ignore the effect of attention and use the average values between the two attentional states in Experiments 2 and 3 to fit our four functions.

Here, we proposed the following functions to depict the four indices of PLR. The power model of the function was determined based on the formula for CFD reported by Stanley and Davies (1995).

$$PL = a^* \left(\sum_{i=1}^{N} \pi^* R_i^2 * L_i \right)^b + c \tag{1}$$

$$MCV, MC, orMPC = a^* \left(\sum_{i=1}^{N} \frac{\pi^* R_i^2 * L_i}{1 + E_i^c} \right)^b \tag{2}$$

Where "E" is the eccentricity of each disk in degree, "R" is the radius of each disk in degree, "L" is the luminance of each disk in cd/m^2, "N" is the number of disks, and "a," "b," and "c" are the parameters for the function. For PL, it does not contain "E" because it was independent of stimulus eccentricity (see the results in Section 3.2 and 4.2). Since PL would have the largest value with the smallest CFD and it decreased with increasing the CFD, we put the intercept "c" in the Eq. (1). For MCV, MC, and MPC, since there were no changes of the pupil if there was no stimulus, we excluded the intercept for Eq. (2).

We conducted a non-linear regression for each index of PLR. The final parameters we got are illustrated in the Eq. (3)–(6). For PL (Eq. (3)), the power of CFD (that is, "b") was marginally significant ($p = .056$) and the intercept (that is, "c") was significant ($p < .001$). The intercept value, 335 ms with a standard error of 28 ms, which was comparable to the largest PL obtained in this study (Fig. 3E, 302 ms) and was smaller than the largest PL found in Myers and Stark (1993)'s study (400 ms). For MCV, MC, and MPC (Eq. (4)), the exponents of stimulus eccentricity (that is, "c") and the powers of CFD (that is, "b") were all significant (all $p < .010$).

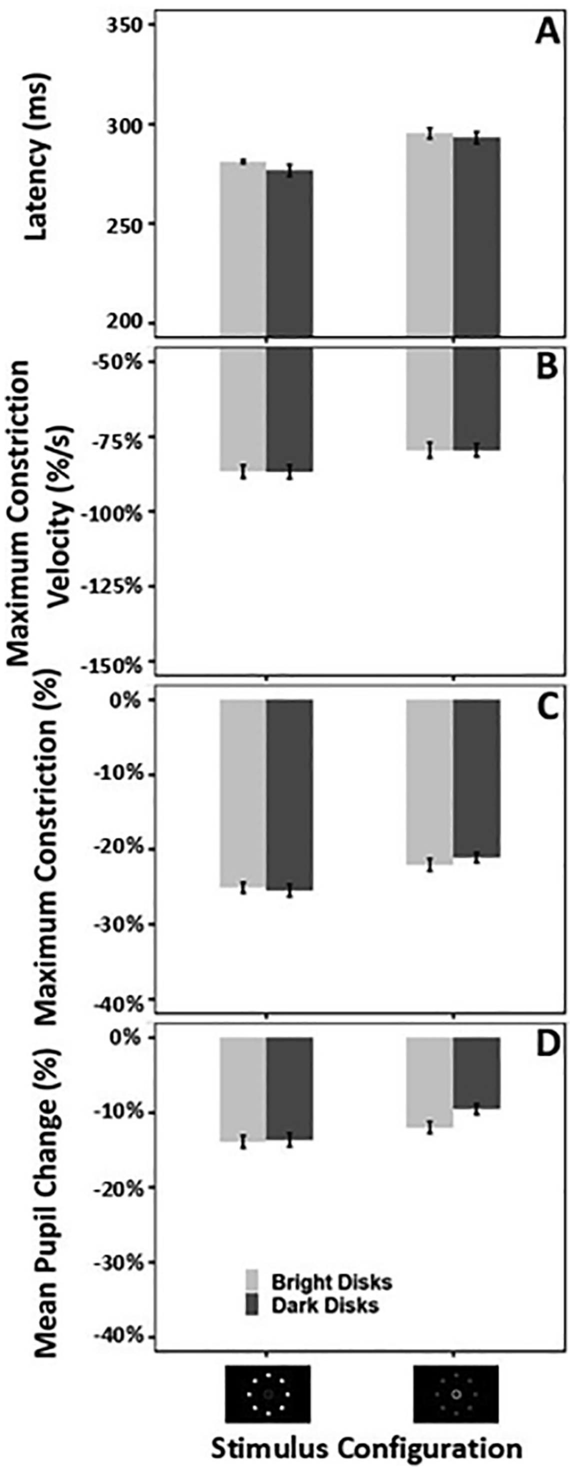

Fig. 7. The results for Experiment 3. Panels A–D show the results for PL, MCV, MC, and MPC, respectively. The abscissa indicates the two stimulus configurations. On the left side, the inner disks were darker than outer disks, and on the right, the inner disks were brighter than outer disks. The ordinate indicates the value of each parameter. They have different units and scales with PL in millisecond (ms), MCV in the proportion of change per second (%/s), MC and MPC in the proportion of change (%). The light gray bars show the data when participants attended to brighter disks, and the dark gray bars show the data when participants attended to darker disks. The black error bars represent the standard error of the means across five participants.

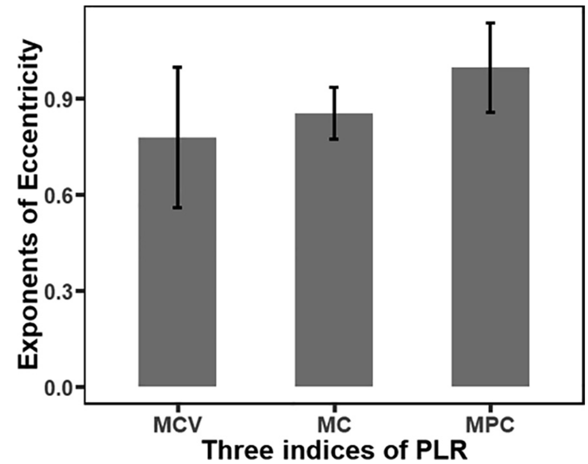

Fig. 8. The exponents of stimulus eccentricity for the three indices of PLR. The abscissa indicates MCV, MC, and MPC. The ordinate indicates the exponents of stimulus eccentricity. The black error bars represent the standard error of fitting results.

$$PL = -7.59 * \left(\sum_{i=1}^{N} \pi * R_i^2 * L_i\right)^{0.26} + 335 \tag{3}$$

$$MCV = -0.37 * \left(\sum_{i=1}^{N} \frac{\pi * R_i^2 * L_i}{1 + E_i^{0.78}}\right)^{0.16} \tag{4}$$

$$MC = -0.069 * \left(\sum_{i=1}^{N} \frac{\pi * R_i^2 * L_i}{1 + E_i^{0.85}}\right)^{0.23} \tag{5}$$

$$MPC = -0.0089 * \left(\sum_{i=1}^{N} \frac{\pi * R_i^2 * L_i}{1 + E_i^{0.99}}\right)^{0.50} \tag{6}$$

where "R" and "E" are in degree, "L" is in cd/m^2, "N" is in integer, PL is in ms, MCV is in %/s, and MC and MPC are in %. The R-squared are 93.4% for PL, 86.7% for MCV, 97.9% for MC, and 93.8% for MPC. These values indicate that the functions fit the data quite well.

Interestingly, the exponents of stimulus eccentricity varied for MCV, MC, and MPC. Fig. 8 shows the exponents and the corresponding standard errors for three indices. We found that the exponents of stimulus eccentricity for MCV and MC were comparable. This was consistent with those in the previous studies, wherein a high correlation between MCV and MC was reported (Ortube et al., 2013; Yahia et al., 2018; Bremner, 2012). Conversely, the exponents of stimulus eccentricity for MPC appeared to be different from those for MCV and MC, indicating that the function to process stimulus eccentricity was different between transient (MCV and MC) and sustained (MPC) components of PLR (Young et al., 1993; Young & Kennish, 1993; Barbur, 2004).

7. Discussion

We conducted a series of experiments to examine the effects of stimulus size, eccentricity, luminance, and attention on PLR. In Experiment 1, the stimulus radius (size) and eccentricity varied separately without considering the effect of attention on pupil size. In Experiment 2, similar experiments were conducted with considering the effect of attention by presenting inner and outer disks simultaneously. In Experiment 3, the effect of luminance and attention were examined. To quantitatively depict the function for PLR, we extracted the following four indices from PLR: pupillary latency (PL), maximum constriction velocity (MCV), maximum constriction (MC), and mean pupil change (MPC). A non-linear function was developed for each index, respectively. We found that PL could be described as a function of only corneal flux density (CFD), and MCV, MC, and MPC could be described as the functions of both CFD and stimulus eccentricity. Because the effect of attention on PLR found in this study was only 2.5% in Experiment 3 (on the right side of Fig. 7D), it was set aside in our function.

7.1. The function for PL

Irrespective of stimulus eccentricity and attention, we found that PL decreased as the stimulus size increased in Experiments 1 and 2. Combining the fact that PL decreased as the stimulus luminance increased (Ellis, 1981; Bitsios et al., 1996; Myers & Stark, 1993; Gavriysky, 1991; Feinberg & Podolak, 1965), we argued that it was the CFD that determined PL. The function is illustrated in Eq. (3).

PL (pupillary latency) is determined by CFD because–we suppose–PL is based on the response of the sensors at the initial level in the visual pathway. Previous studies indicated that PL was possibly based on the latency of retinal cells, latency of neurons in the midbrain, latency of the iris muscle, and latency of conduction along the pupillary reflex pathway (Ellis, 1981; Barbur et al., 1998; Gamlin et al., 1998; Myers & Stark, 1993; Bremner, 2012). It has been shown that the latency in the midbrain and that of the iris were fixed (Myers & Stark, 1993; Bremner, 2012; Mani & Schwartz, 2017). In addition, since the luminance was the only attribute along the pupillary reflex pathway in this study, the latency of conduction along the pupillary reflex pathway was constant. In contrast, the latency of retinal cells, cone, rod, and intrinsically photosensitive retinal ganglion cells (ipRGC) containing melanopsin is dependent on the stimulus luminance and size (Donner, 1989; Wolpert, Miall, Cumming, & Boniface, 1993; Williams & Lit, 1983; Kelbsch et al., 2019), indicating that CFD, which is the product of stimulus area by luminance, affects PL. Accordingly, PL could be depicted as a function of CFD.

The fact established in this study that PL was determined by CFD and independent of stimulus eccentricity seemed functionally significant. A similar phenomenon is the independence of stimulus eccentricity for saccadic latency (Kalesnykas & Hallett, 1994; Darrien, Herd, Starling, Rosenberg, & Morrison, 2001; Frost & Pöppel, 1976). The physiological mechanism underlying this invariant latency explained by Kalesnykas and Hallett (1994) and Dafoe, Armstrong, and Munoz (2007) was the faster axonal conduction velocity for peripheral ganglion cells compared to cells in the central retina. Moreover, since the first functional role of PLR is to prevent the retinal damage from intense light (Loewenfeld & Lowenstein, 1993), it is likely that the absolute light intensity modulates the latency and the perceived luminance is not essential for it. Therefore, it was quite possible to have invariant PL for stimuli with different eccentricities. However, we should consider that the maximum eccentricity we used in the present study was 13°, suggesting that the PLR system would be sensitive at least in near-peripheral vision, but latency might vary in far-peripheral vision.

7.2. The functions for MCV and MC

In Experiments 1a and 2a, we found that the amplitudes of MCV and MC increased as the stimulus radius increased. In agreement with previous studies (Daniels et al., 2012; Stanley & Davies, 1995; Atchison et al., 2011; Park & McAnany, 2015; Joyce et al., 2016; Watson & Yellott, 2012; Crawford, 1936), there were larger amplitudes of MCV and MC for larger CFD. However, in Experiments 1b and 2b, wherein CFD of the stimuli was constant, we found that the amplitudes of MCV and MC all decreased as the stimulus eccentricity increased. Therefore, we claimed that the dependency of CFD on MCV and MC was only valid when stimulus eccentricity was fixed. The functions are illustrated in Eqs. (4) and (5).

We argued that the dependence of eccentricity on MCV and MC could be explained by the decreased density of retinal ganglion cells as stimulus eccentricity from fovea increased (Curcio & Allen, 1990). Previous studies show that PLR is mediated by cone and rod in the retina whose signals are received by ganglion cells and ipRGC, which is a type of ganglion cells containing melanopsin (Loewenfeld & Lowenstein, 1993; Park & McAnany, 2015; Joyce et al., 2016; Privitera & Stark, 2006; Barrionuevo et al., 2014; Park et al., 2011; McDougal & Gamlin, 2011). Then, the ganglion cell axons project to the olivary pretectal nucleus, which connects with the Edinger-Westphal (EW) nucleus. The preganglionic parasympathetic neuron in the EW nucleus is activated to innervate the ciliary ganglion cells, which control the ciliary muscle to constrict the pupil (Loewenfeld & Lowenstein, 1993; Wang et al., 2016; Wang & Munoz, 2015; Peinkhofer, Knudsen, Moretti, & Kondziella, 2019; Szabadi, 2018). As the stimulus eccentricity increases, the density of ganglion cells and the corresponding projections become lower, which leads to weaker neural activity in the EW nucleus and then smaller amplitudes of MCV and MC.

Interestingly, the highly correlated relationship between MCV and MC found by the comparable exponents of stimulus eccentricity (Fig. 8) was also found for saccadic eye movement. The relationship between amplitude and velocity of saccades, which is called as the "main sequence relationship," represents a strategy to optimize the accuracy and speed trade-off (Harris & Wolpert, 2006; Bahill, Clark, & Stark, 1975). Although the role of such a relationship in pupillary response is still unknown, it can be served as a robust clinical tool to evaluate the parasympathetic nervous system activity (Chibel et al., 2016; Ortube et al., 2013; Yahia et al., 2018; Wang et al., 2016; Bremner, 2012).

7.3. The function for MPC

Similar to MCV and MC, we found that MPC was also a function of CFD and stimulus eccentricity. The function is illustrated in Eq. (6). The smaller density of ganglion cells could still explain the dependence of eccentricity on MPC in the periphery. However, the exponent of stimulus eccentricity for MPC was different from those for MCV and MC (Fig. 8), suggesting the existence of different processing systems in PLR. This was consistent with the findings of previous studies that MCV and MC are primarily controlled by the parasympathetic nervous system, whereas MPC is primarily controlled by the sympathetic nervous system (Wang et al., 2016; Wang & Munoz, 2015; Peinkhofer et al., 2019; Szabadi, 2018; Muppidi et al., 2013).

A compelling result found in this study was the asymmetry of attentional modulation on MPC (Fig. 7D). We found that attentional modulation on MPC existed only when the inner disks were brighter than the outer disks (Fig. 7D), although it has been shown that attending to a bright stimulus could elicit smaller pupil (that is, larger pupillary response) compared to attending to a dark stimulus for a set of bright and dark stimuli presented side by side (Binda et al., 2013; Binda et al., 2014; Binda et al., 2017; Tkacz-Domb & Yeshurun, 2018). The asymmetry of pupillary response to bright and dark stimuli was also found in Zavagno, Tommasi, and Laeng (2017)'s study. They found that pupil constrictions for central and peripheral glare stimuli were comparable, whereas pupil dilations between central and peripheral dark stimuli were significantly different from each other. They attributed the asymmetry to the different arousal effects elicited by attraction to the stimulus configurations. They argued that the effect of luminance on MPC might be counterbalanced or enhanced by the arousal effect on pupil size. In this study, narrow and broad attention were deployed. DiCriscio et al. (2018) reported pupil baseline became smaller when narrow attention was deployed relative to when broad attention was deployed. Although we did not measure arousal state in this study, many studies have used pupil size as an index of the arousal (larger pupil, indicating higher arousal) (de Gee et al., 2014; Murphy et al., 2014; Urai et al., 2017; Wang et al., 2018). Therefore, we believed that the arousal states would be different with narrow and broad attention. Consequently, when participants attended to the brighter outer disks (broad attention, indicating high arousal) in Experiment 3, the effects of arousal and luminance on pupil size were counterbalanced, leading to a non-significant size difference between two attentional states (on the left side of Fig. 7D). Conversely, when participants attended to the brighter inner disks (narrow attention, indicating low arousal), the effects of arousal and luminance on pupil size were enhanced by each other, leading to a smaller pupil (on the right side of Fig. 7D).

7.4. The different processing systems for pupillary response

We found the new behavioral evidence that different processing systems existed in pupillary response by comparing the exponents of stimulus eccentricity. Our results suggested that the transient and sustained components of pupillary response reflected the different properties of spatial integration in the near-peripheral vision. Additionally, other evidences were obtained in previous studies. For example, Young et al. (1993) and Young and Kennish (1993) found that MC saturated at higher luminance increments or contrasts, whereas MPC did not. They argued that MC and MPC reflected the activities of phasic and tonic cells separately. Furthermore, Kinner et al. (2017) found that the early and late parts of the pupillary response played different roles in the emotion process and reflected the cognitive emotion regulation effort and emotion regulation success, respectively.

Physiologically, different mechanisms underlie PL, MCV, MC, and MPC. PL is primarily controlled by the latency of retina, which belongs to the central nervous system (Ellis, 1981; Barbur et al., 1998; Gamlin et al., 1998; Myers & Stark, 1993; Bremner, 2012). MCV and MC are primarily controlled by the parasympathetic nervous system, and MPC is primarily controlled by the sympathetic nervous system (Wang et al., 2016; Wang & Munoz, 2015; Peinkhofer et al., 2019; Muppidi et al., 2013). Although not involved in this study, the re-dilation component of the pupillary response, which is between MC and MPC, is primarily controlled by the combination of the parasympathetic and sympathetic nervous systems (Wang et al., 2016; Wang & Munoz, 2015; Peinkhofer et al., 2019; Muppidi et al., 2013).

8. Conclusions

We examined the effects of stimulus size, eccentricity, luminance, and attention on pupillary light response (PLR) using four indices of the response. Pupillary latency (PL) was a function of corneal flux density (CFD) and was independent of stimulus eccentricity and participants' attentional states. Maximum constriction velocity (MCV), maximum constriction (MC), and mean pupil change (MPC) were the functions of CFD and stimulus eccentricity, although MCV and MC were equally affected by stimulus eccentricity, whereas MPC was affected differently by stimulus eccentricity. The effect of attention was only found on MPC when that of luminance was included. In addition, we developed a non-linear function for each index of PLR. The functions can successfully explain the characteristics of PLR at least for the stimuli used in the present study.

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CRediT authorship contribution statement

Xiaofei Hu: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing - original draft, Visualization. **Rumi Hisakata:** Conceptualization, Methodology, Writing - review & editing, Supervision. **Hirohiko Kaneko:** Conceptualization, Methodology, Resources, Writing - review & editing, Supervision, Project administration, Funding acquisition.

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