The impact of luminance on tonic and phasic pupillary responses to sustained cognitive load

Vsevolod Peysakhovich [a,*], François Vachon [b], Frédéric Dehais [a]

[a] ISAE-SUPAERO, Université de Toulouse, Toulouse, France
[b] Ecole de Psychology, Université Laval, Québec, Canada

A B S T R A C T

Pupillary reactions independent of light conditions have been linked to cognition for a long time. However, the light conditions can impact the cognitive pupillary reaction. Previous studies underlined the impact of luminance on pupillary reaction, but it is still unclear how luminance modulates the sustained and transient components of pupillary reaction – tonic pupil diameter and phasic pupil response. In the present study, we investigated the impact of the luminance on these two components under sustained cognitive load. Fourteen participants performed a novel working memory task combining mathematical computations with a classic n-back task. We studied both tonic pupil diameter and phasic pupil response under low (1-back) and high (2-back) working memory load and two luminance levels (gray and white). We found that the impact of working memory load on the tonic pupil diameter was modulated by the level of luminance, the increase in tonic pupil diameter with the load being larger under lower luminance. In contrast, the smaller phasic pupil response found under high load remained unaffected by luminance. These results showed that luminance impacts the cognitive pupillary reaction – tonic pupil diameter (phasic pupil response) being modulated under sustained (respectively, transient) cognitive load. These findings also support the relationship between the locus-coeruleus system, presumably functioning in two firing modes – tonic and phasic – and the pupil diameter. We suggest that the tonic pupil diameter tracks the tonic activity of the locus-coeruleus while phasic pupil response reflects its phasic activity. Besides, the designed novel cognitive paradigm allows the simultaneous manipulation of sustained and transient components of the cognitive load and is useful for dissociating the effects on the tonic pupil diameter and phasic pupil response.

Keywords:
Pupillary reaction
Tonic pupil diameter
Phasic pupil response
Sustained cognitive load
N-back task
Luminance condition

1. Introduction

Pupillary reactions independent of luminance have been linked to cognition since the early sixties (e.g. Hess and Polt, 1964; Kahneman and Beatty, 1966). The pupillary reaction can be divided into two components: tonic pupil diameter and phasic pupil response (Beatty, 1982b). Tonic pupil diameter reflects a sustained component of the pupillary response and is expressed as an absolute pupil diameter. Often, tonic pupil diameter is also used as basal pupillary diameter. In turn, phasic pupil response refers to a transient component of the pupillary response and is expressed as dilation relative to some basal pupil diameter. While the typical order of magnitude of the tonic pupil diameter is 1 mm, that of phasic pupil response is 0.1 mm. Many authors stated that the magnitude of phasic pupil response to a given task was independent of tonic pupil diameter (Beatty, 1982a, p.284; Bradshaw, 1969; Kahneman and Beatty, 1967). Thus, given the presumption of the independence of these two pupillary components, Beatty (1982a) concluded that it is possible to compare the phasic pupil responses issued from various set-ups and reported by different laboratories. Notably, in the review, he presented a table of quantitative comparison of qualitatively different cognitive tasks (memory, language, reasoning and perception). The table confronted the results obtained by different researchers and permitted to see that, for example, the storage in memory of four words makes the pupil dilate more than that of a multiplicand, which is roughly equivalent to retaining in memory two digits. According to the corresponding pupillary reactions, it also put an easy multiplication problem higher (phasic pupil response about 0.1 mm larger) than a hard auditory discrimination task. However, one may call in question such ordering assuming that multiplication of two digits is sometimes easier than detection of a deviant sound. Such task classification, using the magnitude of phasic pupil response as a marker of difficulty, would prevail but on one condition; if tonic pupil diameter does not impact phasic pupil response. Suppose, indeed, that tonic pupil diameter varies as a function of the experimental setup at one hand, and phasic pupil response depends on tonic pupil diameter at another. In this case, in order to compare results issued from different experimental setups one should first make sure that the conditions were the same or at least similar. The investigation of these questions is of an

* Corresponding author at: ISAE, DCAS, 10 Avenue E. Belin, 31055 Toulouse Cedex 4, France.
E-mail address: vsevolod.peysakhovich@isae.fr (V. Peysakhovich).

importance when using pupil reaction as a marker of stress or workload in ecological conditions where such factors as light are difficult to control. Because if there exists a strong relationship between tonic pupil diameter and phasic pupil response, the transportability of laboratory results into real life conditions for applications such as human factors in aviation needs a whole reflection apart.

The dependence of the extent of a physiological reaction to an event on the pre-stimulation basal level was named "law of initial value" in the fifties (Lacey, 1956; Wilder, 1967). Lacey (1956) postulated that a high autonomic excitation before a stimulus would affect the reactivity and diminish the response but did not refer to the pupil, talking rather about skin resistance, heart rate, blood pressure, muscle potentials, etc. Recently, a few mentions of this law appeared in pupillometric studies (Gilzenrat et al., 2010; Höfle et al., 2008; Van Gerven et al., 2004). Formulated in terms of tonic and phasic components of pupillary response, the law of initial value would postulate that a large tonic pupil diameter would imply a smaller phasic pupil response. On the other hand, Sokolov in his work on orienting response (1963) also distinguished tonic and phasic components. In particular, his model (including pupil dilation response) incorporated a response amplifier associated with general arousal (tonic state) which amplifies the phasic response. Thus, according to Sokolovian work, large tonic pupil diameter would imply a larger phasic pupil response. Afterwords, Jin (1992) reviewed experimental data and proposed that the law of initial value should be revisited as follows: "The higher the initial value, the greater the organism's following reactivity, although a tendency to reversed responses may occur when the initial value reaches its upper extremity." Therefore, Jin proposed to consider the law of initial value as a restriction of pupillary dynamic range, i.e. when the pupil is already large, it cannot dilate further. Thus, the direction of the law is still questionable.

The tonic pupil diameter has numerous sources of variation (Tryon, 1975). For instance, it is modulated by general organism's arousal, sustained cognitive load, or light conditions, both ambient illumination and focal luminance. When tonic pupil diameter is modulated by vigilance state, an inverse relationship between tonic and phasic pupil diameters was found by Gilzenrat et al. (2010) in an auditory oddball task. The authors discussed this finding with regard to the law of initial value but considered it as exclusively mechanical. Therefore, the authors verified if the inverse relationship between tonic pupil diameter and phasic pupil response held true when tonic pupil diameter was modulated by light conditions and proved it false in that case. This finding was afterward confirmed by Murphy et al. (2011) also in an auditory oddball task and, more recently, by de Gee et al. (2014) in a perceptual decision-making paradigm and Knapen et al. (2016) in an auditory vigilance task. Steiner and Barry (2011), on the other hand, in their study on orienting reflex, found that vigilance state modulated tonic pupil diameter but not phasic pupil response. As for cognitive tasks implying working memory, Steinhauer et al. (2004) found that the phasic pupil diameter was modulated by ambient illuminance when engaged in sustained processing. More recently, Peysakhovich et al. (2015) found that the phasic pupil diameter was modulated by the screen luminance in a short-term memory task. Most recently, Pfleging et al. (2016) also studied pupillary response, manipulating illuminance and luminance during a cognitive task. However, the authors used a one-factor-at-a-time method that does not enable the investigation of the illuminance-luminance interaction and reported exclusively the absolute pupil diameter values making impossible to compare tonic and phasic pupil responses. Altogether, to be able to compare pupil reactions issued from different studies that maintain different light conditions, and to transport the laboratory results into real-life applications, it is important to investigate further the relationship between the tonic and phasic components of the pupillary response and the factors that modulate these components. The pupillometry literature still has not given a clear answer to these questions, and a further investigation is needed. To the best of our knowledge, no studies investigated the impact of luminance on the tonic and phasic components of the pupillary response during sustained cognitive load.

Therefore, in the present study, we manipulated the sustained cognitive load and the screen luminance. To explore both tonic and phasic pupil response and so that both components would reflect cognitive processing, we used the Toulouse N-back Task – a novel working-memory task that couples n-back task with mathematical problems solving. This paradigm has the particularity to combine sustained memory load during a block and transient stimulus processing during each trial. We did not manipulate the transient load, and the stimulus processing was equal for all conditions. The objective of the study was to investigate the impact of luminance on the tonic and phasic pupil response during various levels of sustained cognitive load. We assessed the following questions: a) How does the luminance impact both tonic and phasic pupillary components under different sustained cognitive load conditions? b) What is the relationship between tonic and phasic pupil response during sustained cognitive load?

2. Materials and methods

2.1. Subjects

The subjects were 14 healthy volunteers (4 females, 2 left-handed, age 26.6 ± 5.0, educational level 15.9 ± 2.4), students and staff of ISAE-SUPAERO (French Aerospace Engineering School). All reported normal auditory acuity and normal or corrected-to-normal vision, had no history of neurological diseases and were free of the regular use of medication. The subjects slept 7.1 ± 1.1 h the night before the experiment and 8 out of 14 took coffee at least 2 h before the start of the experiment. All participants gave their written informed consent in accordance with local ethical board requirements before the experiment.

2.2. Experimental design and procedure

The experiment was conducted in a dimly lit sound-attenuated room with one indirect light source behind the participants' back. The ambient illuminance was about 10 lx at the site of participants' eyes. Participants were seated at a viewing distance of approximately 65 cm from the 22-in. LCD monitor (1680 × 1250 pixels screen resolution) with a refresh rate of 60 Hz. Stimulus display and behavioral data acquisition were conducted using Psychophysiological Toolbox V3 for Matlab.

Participants performed the Toulouse N-back Task (Mandrick et al., 2016; Causse et al., 2017) – an N-back task coupled with mathematical calculation – where participants have to solve a simple mathematical formula to perform the n-back task on the result of arithmetic operations. Mathematical operations were either additions or subtractions, of which all summands were a multiple of 5 (e.g., 65 + 10, 50–25 etc.). Two levels of working memory load were produced with 1-back and 2-back tasks. Two levels of luminance were produced by changing the screen background from block to block that was either gray (~11 cd/m^2) or white (~28 cd/m^2). As illustrated in Fig. 1, each block began with the announcement of the working memory load ("1-BACK" or "2-BACK"; 1.76° × 7.88° in the center of a screen) for 15 s. It allowed participants to calm down between blocks but primarily served as an accommodation period to the display luminosity. Each block was comprised of 25 trials that began with the presentation of a mathematical problem (1.76° × 6.15° in the center of a display) for 3000 ms, followed by a 1000-ms blank screen. Participants had to resolve the current problem and then to match the result with the previous (1-back) or with the result of the problem two presentations earlier in the sequence (2-back). Subjects were instructed to respond as quickly and accurately as possible for each trial. They had to answer via a response Cedrus Pad placed under their right and left index fingers and containing a green "yes" key and a red "no" key. Participants were told to press "no" key

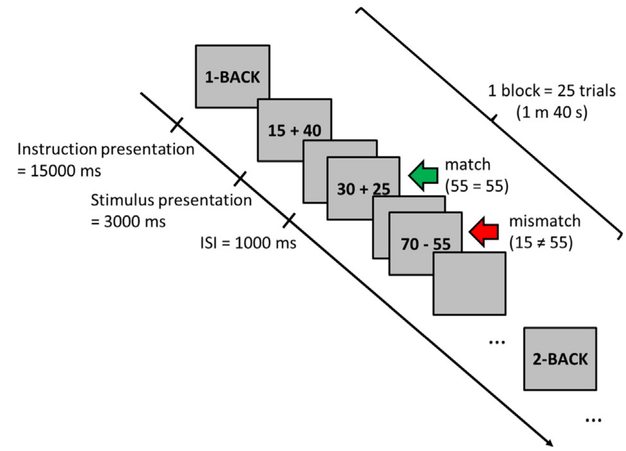

Fig. 1. Illustration of the Toulouse N-back Task paradigm.

for the first trial in the 1-back task and the first two trials in the 2-back task. Each block contained 8 matches.

Before the main experiment, to familiarize themselves with the Toulouse N-back Task, participants performed two blocks of each load level with both gray and white backgrounds containing 10 practice trials. The practice phase contained a feedback for each trial indicating whether the response was correct or not. Then participants completed 12 blocks (3 blocks for each of 4 conditions) with a short pause after each four blocks. The experiment lasted for a total of about 30 min.

2.3. Pupillary recording and processing

Participants' gaze position and pupil diameter were recorded at 120 Hz with a remote SMI RED eye-tracker (SensoMotoric Instruments GmbH, Germany). This device allows tracking the pupil diameter with precision despite the absence of a chinrest and small head movements. At the beginning of the experiment and after each four blocks, a 5-point calibration was validated with four additional fixation points, until a precision of gaze position was inferior to 1°.

The data analyses were performed using Matlab R2014b (Mathworks, USA). The data losses (including eye blinks) were replaced using linear interpolation. To minimize the eyelid closure effect in the neighborhood of blinks (considered as such if the data loss exceeded 30 ms), 12 adjoined samples (100 ms) from each side of a blink were replaced as well. Then the data were smoothed using a "two-pass" 9-point filter. Trials were segregated according to experimental conditions and averaged point-by-point, giving a pupillary per condition per participant. A trial was validated for the statistical analyses if 1) all the gaze points during the trial and the baseline were within 400 × 400 pixels square in the screen center, and 2) there were at least 50% of trial data without any original blink or data loss. With these criteria, a mean of 52 ± 18 trials per condition (out of 75) was available for the statistical analyses. A two-way ANOVA showed that a number of valid trials were condition-independent ($ps \geq 0.28$). For statistical analyses, the mean value between 1 and 3 s post-stimulus was used as the tonic pupil diameter. For the phasic pupil response, a maximum value within the same interval was used, after subtraction of a baseline defined as a median of 500 ms pre-stimulus.

2.4. Statistical analyses

Statistical analyses were performed using Statistica 10 (StatSoft, USA) software. Descriptive data were presented as a mean ± standard error. The significance level for all statistical tests was set at 0.01. Four two-way repeated-measures ANOVA were performed on mean reaction time (RT), accuracy rate, tonic pupil diameter, and pupil phasic response with working memory load (1-back vs. 2-back) and luminance (gray vs. white) as the two within-subject factors. Tukey's Honestly Significant Difference (HSD) was used for posthoc testing. Partial eta-squared (partial η^2) was reported to demonstrate the effect size in ANOVA tests when the effect was significant.

3. Results

3.1. Behavioral performance

The behavioral performance measures are presented in Fig. 2. The main effect of working memory load on accuracy was significant, $F(1, 13) = 19.2$, $p < 0.001$, partial $\eta^2 = 0.60$, participants performing better at the 1-back task compared with the 2-back task. There were neither luminance, $F(1, 13) = 1.2$, $p = 0.28$, nor interaction effect on accuracy, $F(1, 13) = 0.1$, $p = 0.83$.

The main effect of working memory load on RT was also significant, $F(1, 13) = 48.8$, $p < 0.001$, partial $\eta^2 = 0.79$, participants being faster to answer in the 1-back task than in the 2-back task. There were neither a luminance, $F(1, 13) = 0.7$, $p = 0.41$, nor an interaction effect on RT, $F(1, 13) = 1.1$, $p = 0.33$.

3.2. Tonic pupil diameter

The measures of tonic pupil diameter are presented in Fig. 3A. The main effect of working memory load on the tonic pupil diameter was significant, $F(1, 13) = 64.0$, $p < 0.001$, partial $\eta^2 = 0.84$, corresponding to larger pupils under high working memory load. The main effect of luminance was also significant, $F(1, 13) = 122.7$, $p < 0.001$, partial $\eta^2 = 0.90$, corresponding to larger pupils under dimmer (gray) condition. In addition, there was a significant interaction between working memory load and luminance, $F(1, 13) = 38.8$, $p < 0.001$, partial $\eta^2 = 0.75$. The posthoc analysis of the interaction showed that the differences between the 1-back and the 2-back tasks were larger under the gray background condition (HSD < 0.001) compared to the white background condition (HSD = 0.002). This interaction effect was present for all the participants (see Fig. S1 in Supplementary Material).

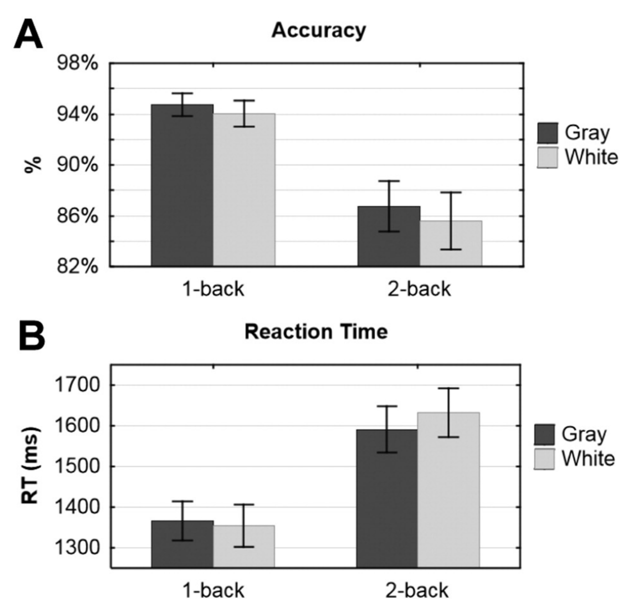

Fig. 2. Mean accuracy (A) and RT (B) for low (1-back) and high (2-back) working memory load in the gray and white background conditions. Error bars denote the standard error of the mean.

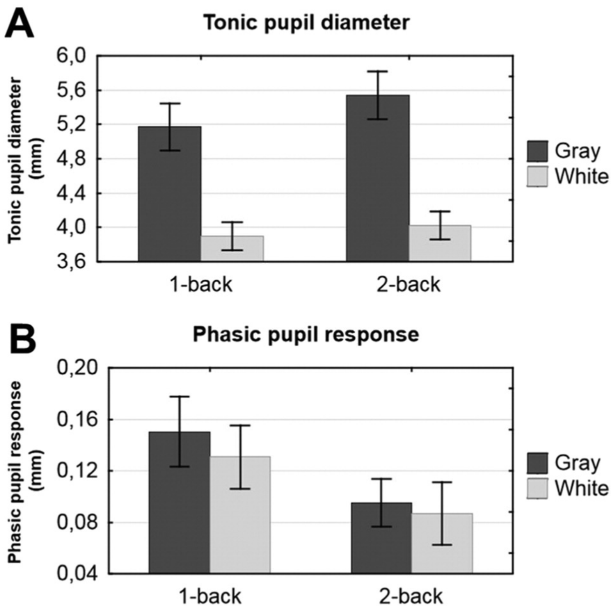

Fig. 3. Mean tonic pupil diameter (A) and phasic pupil response (B) for low (1-back) and high (2-back) working memory load in the gray and white background conditions. Error bars denote the standard error of the mean.

3.3. Phasic pupil response

The measures of phasic pupil response are presented in Fig. 3B. The phasic pupil response is represented in Fig. 4. The main effect of working memory load on phasic pupil response was significant, $F(1, 13) = 9.7$, $p < 0.01$, partial $\eta^2 = 0.43$. The phasic pupil response was larger for the 1-back task compared with the 2-back task. There was neither a luminance, $F(1, 13) = 0.8$, $p = 0.38$, nor an interaction effect, $F(1, 13) = 0.2$, $p = 0.67$. The main effect of working memory load on phasic pupil response was individually present for 11 subjects out of 14.

4. Discussion

The goal of this study was to examine the impact of luminance on sustained and transient components of cognitive pupillary response – tonic pupil diameter and phasic pupil response – during sustained cognitive load. To that end, we designed a novel paradigm – Toulouse N-back Task – that allows a simultaneous study of both sustained and transient components of cognitive pupillary response. This working-memory task couples classic n-back task with mathematical problem-solving. The task induces sustained cognitive load, maintained during the whole block. The mathematical operations, on the other hand, need to be resolved punctually for each trial and are of equal difficulty for both 2-back and 1-back conditions. We obtained pupillary data for low and high working memory load conditions (1-back and 2-back respectively), the screen background being gray or white, modifying thus its luminance. We aimed to investigate the impact of the luminance on both tonic and phasic components under different sustained cognitive load and the relationship between these two components.

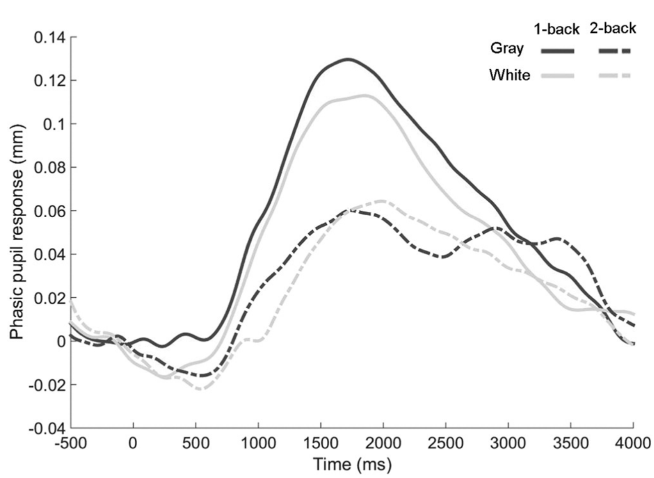

Fig. 4. Mean phasic pupil response for the low (1-back; solid lines) and high (2-back; dashed lines) working memory load in the gray and white background conditions.

The behavioral results showed that the 2-back condition was more difficult compared to the 1-back condition. Participants were less accurate and took more time to give an answer in the 2-back condition. As expected, the screen luminance did not affect behavioral performances. The analysis of the tonic pupil diameter showed that it was modulated by both working memory load, being greater under high working memory load condition, and luminance, being larger under the dimmer condition. We also found a significant interaction, the difference between two working memory load conditions being larger under the gray luminance condition. In turn, the analysis of the phasic pupil response showed that it was modulated exclusively by working memory load but not luminance. The following discussion is divided into two parts – first, we discuss the impact of the luminance on the two components of cognitive pupillary response; second, we reflect upon the relationship between the phasic pupil response and tonic pupil diameter. Also, before discussing the results of the experiment, a few words are worth being said about the study limitations. The first limitation concerns the population. The relatively small number of participants appears to be sufficient, given the size effects values and the presence of effects individually subject by subject (see further discussion). Further, we did not forbid caffeine intake before the experiment, and more than half of participants took coffee that might alter the pupillary behavior (Wilhelm et al., 2014). However, given the within-subject design, we believe that the caffeine did not significantly influence our results in any way. The second limitation concerns the 2×2 experimental design and the number of factor levels. As mentioned in the introduction, the pupil size range might be the problem in pupillary studies, and therefore we chose the two intermediate levels of luminance as used in our previous study (Peysakhovich et al., 2015). We believe that our results are valid because their direction "more dilation under dimmer background" in the case of a range problem would be rather "less dilation under dimmer background." Therefore, we used a robust 2×2 design to keep the time-on-task reasonable. However, it would be interesting in further studies to explore more levels of luminance to verify the validity of our results. Note that the inverse relationship between the tonic pupil diameter and phasic pupil response (see below), consistent with our findings and using the same cognitive task and three levels of working memory load, was recently published by Mandrick et al. (2016).

4.1. Impact of luminance on tonic and phasic pupil responses

As showed in the analysis of tonic pupil diameter – the pupils were larger in the 2-back condition than in the 1-back condition, and larger under lower luminance condition. Both main effects are well-established and known from the literature (e.g. Brouwer et al., 2014; Winn et al., 1994). Most interestingly, there was an interaction between the two factors. The difference between 1-back and 2-back conditions was larger under lower luminance. Moreover, this group effect was individually present for all the participants. Phasic pupil response was, in turn, found to be modulated by the working memory load only, neither luminance nor interaction of the two factors being found. Phasic pupil response was smaller in the 2-back condition compared to the 1-back condition, the effect being individually present in 11 out of 14 participants.

Because the used paradigm elicits sustained cognitive load, tonic pupil diameter is of particular interest because it reflects the sustained component of the pupillary response. The mathematical computations being of the same difficulty across working memory load condition, the transient load is roughly the same. Therefore, the modulation of the phasic pupil response by working memory load condition is a consequence of the relationship between tonic pupil diameter and phasic pupil response that is further discussed in the following subsection.

To the best of the authors' knowledge, this study was the first to report the impact of luminance on the cognitive pupillary response to sustained cognitive load. Previously, Steinhauer et al. (2004) studied the impact of the ambient illuminance on the pupillary response to sustained load. Nevertheless, they did not separate pupillary recordings into tonic and phasic responses but rather studies the 5-s period before the task and the difference of an average of 60-s response and the baseline period. Such a methodological issue does not allow comparison between our findings with their results. At the other hand, Peysakhovich et al. (2015) recently reported their findings on impacts of the luminance on the cognitive pupillary response to transient cognitive load (in a short-term memory task). They found that the luminance modulated the phasic pupil response for a given amount of working memory load the response was larger under dimmer luminance. Our results complete their findings, and we can summarize the impact of the luminance on tonic pupil diameter and phasic pupil response in the following way. The luminance impacts the cognitive pupillary reaction with the response to the same stimulus being larger under lower luminance condition. In the sustained cognitive load paradigms, the changes of tonic pupil diameter are affected; in turn, in the transient cognitive load paradigms, it is the phasic pupil response which is modulated by the luminance.

Peysakhovich et al. (2015) speculated that the differences in their findings with the results of Steinhauer et al. (2004) were due to the nature of the cognitive task: sustained versus transient. However, the present paper showed that even in response to sustained cognitive load, the pupillary response is greater under dimmer luminance. Given the recent findings by Benedetto et al. (2014) that the pupil diameter is more impacted by screen luminance rather than the ambient illuminance, it would be interesting though to perform an experiment containing both sustained and transient cognitive load varying both screen luminance and ambient illuminance to investigate the interaction between these factors further.

The present study also shows the importance of dissociating tonic pupil diameter and phasic pupil response. This proposition is supported by the theories about working memory functioning and the existence of the two mechanisms of activation – sustained and transient (Cohen et al., 1997; Reynolds et al., 2009). As the results showed, depending on the sustained versus transient nature of the cognitive task, the luminance modulates the corresponding component of the pupillary response. Note also that the designed Toulouse N-back Task allows the simultaneous manipulation of the sustained and the transient cognitive load, which is useful for the future studies of the relationship of these two pupillary components.

It is also worth noting that the modulation of tonic pupil diameter and phasic pupil response are probably linked to the cognitive aspects of the tasks. Thus, in studies by Bradshaw (1969) and Gilzenrat et al. (2010, Experiment 1B), the authors used the reaction time task and auditory oddball discrimination tasks but did not report any significant differences under different light conditions. That may indicate that the effects of luminance are stronger when performing a more demanding cognitive task such as the Toulouse N-back Task.

Additionally, the fact that under a constant transient load the phasic pupil response was not modulated can have an interesting application to design a luminance-independent measure of cognitive load. Indeed, given an existing relationship of phasic pupil response and tonic pupil diameter (see section below) and the luminance-independent phasic response, it would be possible to induce the level of the load by measuring the pupil response to some probe of a constant load (for instance, an auditory probe).

4.2. Relationship of phasic pupil response and tonic pupil diameter

The analysis of the peak dilation showed that the phasic pupil response was smaller for the 2-back condition compared to the 1-back condition. The luminance had no influence on the phasic pupil response. The same pattern of smaller phasic pupil response for the 2-back condition held true for both luminance conditions. Comparing these results with the findings on tonic pupil diameter, we conclude that a greater load on memory evokes larger tonic pupil diameter and is associated with the smaller phasic response. The absence of any luminance impact on phasic pupil response demonstrates that the relationship between large tonic pupil diameter and smaller phasic pupil response is not an issue of pupillary dynamic range but cognitively driven. These findings bring new light on the law of initial value (in its physiological and not mechanical interpretation) concerning the pupil diameter (see Van Gerven et al., 2004). It shows that the law of "greater baseline – smaller reactivity" stands true contrary to the Jin's interpretation (1992). Note also that the smaller reactivity is not an issue of disengagement from the task, the accuracy rates for the high working memory load condition being elevated (around 86%).

These are the first results of such a pattern of larger tonic pupil diameter corresponding to lower phasic pupil response in a cognitive task inducing working memory load (see also Mandrick et al. (2016) where we simultaneously obtained similar patterns using the Toulouse N-back Task). Earlier, such relationship was found in auditory vigilance paradigms (Gilzenrat et al., 2010, Knapen et al., 2016, Murphy et al., 2011) and a perceptual decision-making task (de Gee et al., 2014). But while in these studies, the tonic pupil diameter was modulated by arousal and vigilance of participants, in the present paper, tonic pupil diameter was modulated by working memory load. These findings are in line with theories about the relationship between pupil size and locus-coeruleus norepinephrine (LC-NE) system. Locus-coeruleus is a small brainstem nucleus that provides the majority of norepinephrine to the brain (Aston-Jones and Waterhouse, 2016; Samuels and Szabadi, 2008). The LC-NE system was found to be closely related to the pupil diameter, first in primates (Rajkowski et al., 1993), then in humans (Murphy et al., 2014). Recent reviews by Joshi et al. (2016) and Costa and Rudebeck (2016) discussed the complex relationship between pupil size and LC-NE system and the direct and indirect evidence supporting this relationship. In particular, Joshi et al. (2016) found that the relationship is not specific to the LC-NE and the correlations are also present in the inferior and superior colliculi and anterior and posterior cingulate cortices. These brain regions being interconnected with the LC, the results nevertheless suggest that the pupil diameter reflects LC-mediated coordination of neuronal activity. Although the pupil diameter is often interpreted as a biomarker of LC activity, the exact neural substrates linking cognitive state and pupil changes remain unclear. Thus, the recent results of Wang and Munoz (2015) and Lehmann and Corneil (2016) on primates suggested the existence, in addition to LC-mediated arousal circuits, of a parallel pathway from the frontal cortex to pupil diameter through the superior colliculus (SC). This SC pathway should assume primacy for pupil orienting response such as in auditory vigilance paradigms used in previous studies establishing the inverse relationship between tonic pupil diameter and phasic pupil response. Given that in our experiment, the working memory load was highly involved, we suppose that the dominant pathway responsible for pupil changes in our case was LC-mediated arousal circuit. Hence, together with our results published in Mandrick et al. (2016), to our best knowledge, this is the first report of an inverse tonic-phasic relationship in a paradigm using working memory load. Furthermore, the findings of the present study are, in particular, supported by the theory of two existing modes of LC-NE firing. The LC-NE system supposedly functions according to a continuum of states between tonic firing mode and phasic firing mode (Aston-Jones and Cohen, 2005; Aston-Jones et al., 1999). High tonic firing mode is associated with high overall arousal. Phasic firing mode allows for selective responses to a particular target. The relationship supposedly resembles an inverted-U shape. A moderate level of tonic activity is needed to be aroused enough to perform the task, but an excess of such activity should be harmful to the performance because the phasic firing would be drowned in the tonic arousal. Such understanding of the LC-NE functioning also supports the hypothesis of a greater tonic pupil diameter implying smaller phasic pupil response. Together with previous findings in attentional and perceptual tasks, our results using a cognitive paradigm, give another strong evidence of the relationship between LC-NE and pupil size and, in particular, the association between tonic pupil diameter and tonic LC firing mode and phasic pupil response and phasic LC firing mode.

5. Conclusion

In the present study, we showed that the screen luminance has an impact on the cognitive pupillary reaction. It is an important issue, together with the impact of ambient illuminance, when performing pupillometric experiments in ecological conditions, and also when comparing results issued from different laboratories or setups. We dissociated tonic pupil diameter and phasic pupil response and showed that depending on the nature of the cognitive load – sustained or transient – the corresponding component of the pupillary response would be impacted. We can postulate that the same amount of cognitive load under dimmer luminance condition would elicit larger tonic pupil diameter in a sustained load paradigm and larger phasic pupil response in a transient load paradigm.

Furthermore, we found a smaller phasic pupil response for a larger tonic pupil diameter. This finding supports the relationship between the LC-NE system, presumably functioning in two firing modes – tonic and phasic – and the pupil diameter. We suggested that the tonic pupil diameter tracks the tonic activity of the LC-NE system while phasic pupil response reflects the phasic activity of the LC.

Finally, we designed a novel cognitive paradigm – Toulouse N-back Task – that allows the simultaneous manipulation of sustained and transient components of the cognitive load. Therefore, it allows the further investigation of the complex relationship between the tonic pupil diameter and phasic pupil response, and, especially, the interaction of screen luminance and ambient illumination.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ijpsycho.2016.12.003.

References

Aston-Jones, G., Cohen, J.D., 2005. An integrative theory of locus coeruleus-norepinephrine function: adaptive gain and optimal performance. Annu. Rev. Neurosci. 28: 403–450. http://dx.doi.org/10.1146/annurev.neuro.28.061604.135709.

Aston-Jones, G., Waterhouse, B., 2016. Locus coeruleus: from global projection system to adaptive regulation of behavior. Brain Res. http://dx.doi.org/10.1016/j.brainres.2016.03.001.

Aston-Jones, G., Rajkowski, J., Cohen, J., 1999. Role of locus coeruleus in attention and behavioral flexibility. Biol. Psychiatry 46 (9):1309–1320. http://dx.doi.org/10.1016/S0006-3223(99)00140-7.

Beatty, J., 1982a. Task-evoked pupillary responses, processing load, and the structure of processing resources. Psychol. Bull. 91 (2), 276.

Beatty, J., 1982b. Phasic not tonic pupillary responses vary with auditory vigilance performance. Psychophysiology 19 (2):167–172. http://dx.doi.org/10.1111/j.1469-8986.1982.tb02540.x.

Benedetto, S., Carbone, A., Drai-Zerbib, V., Pedrotti, M., Baccino, T., 2014. Effects of luminance and illuminance on visual fatigue and arousal during digital reading. Comput. Hum. Behav. 41:112–119. http://dx.doi.org/10.1016/j.chb.2014.09.023.

Bradshaw, J.L., 1969. Background light intensity and the pupillary response in a reaction time task. Psychon. Sci. 14 (6):271–272. http://dx.doi.org/10.3758/BF03329118.

Brouwer, A.M., Hogervorst, M.A., Holewijn, M., van Erp, J.B., 2014. Evidence for effects of task difficulty but not learning on neurophysiological variables associated with effort. Int. J. Psychophysiol. 93 (2):242–252. http://dx.doi.org/10.1016/j.ijpsycho.2014.05.004.

Causse, M., Peysakhovich, V., Mandrick, K., 2017. Eliciting Sustained Mental Effort Using the Toulouse N-Back Task: Prefrontal Cortex and Pupillary Responses. Advances in Neuroergonomics and Cognitive Engineering. Springer International Publishing: pp. 185–193 http://dx.doi.org/10.1007/978-3-319-41691-5_16.

Cohen, J.D., Perlstein, W.M., Braver, T.S., Nystrom, L.E., Noll, D.C., Jonides, J., Smith, E.E., 1997. Temporal dynamics of brain activation during a working memory task. Nature 386 (6625):604–608. http://dx.doi.org/10.1038/386604a0.

Costa, V.D., Rudebeck, P.H., 2016. More than meets the eye: the relationship between pupil size and locus coeruleus activity. Neuron 89 (1):8–10. http://dx.doi.org/10.1016/j.neuron.2015.12.031.

de Gee, J.W., Knapen, T., Donner, T.H., 2014. Decision-related pupil dilation reflects upcoming choice and individual bias. Proc. Natl. Acad. Sci. 111 (5):E618–E625. http://dx.doi.org/10.1073/pnas.131755711.

Gilzenrat, M.S., Nieuwenhuis, S., Jepma, M., Cohen, J.D., 2010. Pupil diameter tracks changes in control state predicted by the adaptive gain theory of locus coeruleus function. Cogn. Affect. Behav. Neurosci. 10 (2):252–269. http://dx.doi.org/10.3758/CABN.10.2.252.

Hess, E.H., Polt, J.M., 1964. Pupil size in relation to mental activity during simple problem-solving. Science 143 (3611), 1190–1192.

Höfle, M., Kenntner-Mabiala, R., Pauli, P., Alpers, G.W., 2008. You can see pain in the eye: pupillometry as an index of pain intensity under different luminance conditions. Int. J. Psychophysiol. 70 (3):171–175. http://dx.doi.org/10.1016/j.ijpsycho.2008.06.008.

Jin, P., 1992. Toward a reconceptualization of the law of initial value. Psychol. Bull. 111 (1), 176.

Joshi, S., Li, Y., Kalwani, R.M., Gold, J.I., 2016. Relationships between pupil diameter and neuronal activity in the locus coeruleus, colliculi, and cingulate cortex. Neuron 89 (1):221–234. http://dx.doi.org/10.1016/j.neuron.2015.11.028.

Kahneman, D., Beatty, J., 1966. Pupil diameter and load on memory. Science 154 (3756), 1583–1585.

Kahneman, D., Beatty, J., 1967. Pupillary responses in a pitch-discrimination task. Percept. Psychophys. 2 (3), 101–105.

Knapen, T., de Gee, J.W., Brascamp, J., Nuiten, S., Hoppenbrouwers, S., Theeuwes, J., 2016. Cognitive and ocular factors jointly determine pupil responses under Equiluminance. PLoS One 11 (5), e0155574. http://dx.doi.org/10.1371/journal.pone.0155574.

Lacey, J.I., 1956. The evaluation of autonomic responses: toward a general solution. Ann. N. Y. Acad. Sci. 67 (5), 125–163.

Lehmann, S.J., Corneil, B.D., 2016. Transient pupil dilation after Subsaccadic Microstimulation of primate frontal eye fields. J. Neurosci. 36 (13):3765–3776. http://dx.doi.org/10.1523/JNEUROSCI.4264-15.2016.

Mandrick, K., Peysakhovich, V., Rémy, F., Lepron, E., Causse, M., 2016. Neural and psychophysiological correlates of human performance under stress and high workload. Biol. Psychol. http://dx.doi.org/10.1016/j.biopsycho.2016.10.002.

Murphy, P.R., Robertson, I.H., Balsters, J.H., O'connell, R.G., 2011. Pupillometry and *P*3 index the locus coeruleus–noradrenergic arousal function in humans. Psychophysiology 48 (11):1532–1543. http://dx.doi.org/10.1111/j.1469-8986.2011.01226.x.

Murphy, P.R., O'Connell, R.G., O'Sullivan, M., Robertson, I.H., Balsters, J.H., 2014. Pupil diameter covaries with BOLD activity in human locus coeruleus. Hum. Brain Mapp. 35 (8):4140–4154. http://dx.doi.org/10.1002/hbm.22466.

Peysakhovich, V., Causse, M., Scannella, S., Dehais, F., 2015. Frequency analysis of a task-evoked pupillary response: luminance-independent measure of mental effort. Int. J. Psychophysiol. 97 (1), 30–37.

Pfleging, B., Fekety, D.K., Schmidt, A., Kun, A.L., 2016. A model relating pupil diameter to mental workload and lighting conditions. Proceedings of the 2016 CHI Conference on Human Factors in Computing Systems. ACM:pp. 5776–5788 http://dx.doi.org/10.1145/2858036.2858117.

Rajkowski, J., Kubiak, P., Aston-Jones, G., 1993. Correlations between Locus Coeruleus (LC) Neural Activity, Pupil Diameter and Behavior in Monkey Support a Role of LC in Attention. Society for Neuroscience Abstracts vol. 19, p. 974.

Reynolds, J.R., West, R., Braver, T., 2009. Distinct neural circuits support transient and sustained processes in prospective memory and working memory. Cereb. Cortex 19 (5):1208–1221. http://dx.doi.org/10.1093/cercor/bhn164.

Samuels, E.R., Szabadi, E., 2008. Functional neuroanatomy of the noradrenergic locus coeruleus: its roles in the regulation of arousal and autonomic function part I: principles of functional organisation. Curr. Neuropharmacol. 6 (3):235–253. http://dx.doi.org/10.2174/157015908785777229.

Sokolov, E.N., 1963. Perception and the Conditioned Reflex. Pergamon Press, London, UK.

Steiner, G.Z., Barry, R.J., 2011. Pupillary responses and event-related potentials as indices of the orienting reflex. Psychophysiology 48 (12), 1648–1655.

Steinhauer, S.R., Siegle, G.J., Condray, R., Pless, M., 2004. Sympathetic and parasympathetic innervation of pupillary dilation during sustained processing. Int. J. Psychophysiol. 52 (1):77–86. http://dx.doi.org/10.1016/j.ijpsycho.2003.12.005.

Tryon, W.W., 1975. Pupillometry: a survey of sources of variation. Psychophysiology 12 (1):90–93. http://dx.doi.org/10.1111/j.1469-8986.1975.tb03068.x.

Van Gerven, P.W., Paas, F., Van Merriënboer, J.J., Schmidt, H.G., 2004. Memory load and the cognitive pupillary response in aging. Psychophysiology 41 (2):167–174. http://dx.doi.org/10.1111/j.1469-8986.2003.00148.x.

Wang, C.A., Munoz, D.P., 2015. A circuit for pupil orienting responses: implications for cognitive modulation of pupil size. Curr. Opin. Neurobiol. 33:134–140. http://dx.doi.org/10.1016/j.conb.2015.03.018.

Wilder, J., 1967. Stimulus and Response: The Law of Initial Value. Wright, Bristol, England.

Wilhelm, B., Stuiber, G., Lüdtke, H., Wilhelm, H., 2014. The effect of caffeine on spontaneous pupillary oscillations. Ophthalmic Physiol. Opt. 34 (1):73–81. http://dx.doi.org/10.1111/opo.12094.

Winn, B., Whitaker, D., Elliott, D.B., Phillips, N.J., 1994. Factors affecting light-adapted pupil size in normal human subjects. Invest. Ophthalmol. Vis. Sci. 35 (3), 1132–1137.