Contextual Modulation of Attentional Control Mechanisms:
A Pupillometry Study

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Table of Contents

Abstract

An important dimension of cognitive control is the adaptive regulation of the balance between focused and flexible attention in response to task-utility. Recent studies have suggested that the locus-coeruleus norepinephrine system may play an important role on this function, and that pupil diameter may correlate closely with control state and associated changes in behavior. To investigate this, we measured pupillary changes in eighteen participants while performing a visual search task during a threatening- and a neutral context. We predicted that increases in baseline pupil diameter would be associated with decreases in task utility and longer reaction times, whereas reduced baseline pupil diameter would be associated with faster reaction times. Findings from this experiment were consistent with these predictions, suggesting that pupillometry may be useful as an index of both attentional state, and indirectly, locus coeruleus function.

Introduction

Affective states can influence the way we interpret and react to external events and objects. Behavioral performance depends on attending to important objects in our environment rather than irrelevant objects. Recent findings have demonstrated that current affective states modulate the way in which we allocate attention (Vermeulen, 2010), which in turn might change our behavior. Earlier work by Aston-Jones and colleagues (Aston-Jones, Rajkowski & Cohen, 1999) suggested that the locus coeruleus-norepinephrine (LC-NE) system may play an important role in regulating the balance between focused versus flexible attention. More recently, it has been suggested that pupil diameter can be used as an index of LC-NE function in humans. This work examines the influence of threat on orienting of attention. This is done by measuring pupil size, which is suggested to be correlated with the state of the LC-NE system.

Negative Affect and Attention Modulation

Visual selective attention enables us to focus our attention on objects and events that are of most relevance according to our immediate goals (Hopfinger, Buonocore & Mangun, 2000). The ability to respond selectively to certain aspects of the environment, and filter out others that are irrelevant or disruptive to the current behavioral plan, is at the heart of the capacity for goal-driven control of behavior (Aston-Jones et al., 1999). Current models of visual selective attention describe it as a system influenced by both endogenously (voluntary) and exogenously (reflexive) processes (Corbetta, Patel & Shulman, 2008). Endogenous orienting of attention refers to attention that is said to be under control of the intentions of the observer. This type of orienting can be illustrated by the Posner task (Posner, 1980), were the observers direct their attention at will to a particular location in space. While endogenous orienting is considered to be voluntary, exogenous orienting occurs in a passive and automatic way. According to the biased competition model of visual selective attention (Desimone & Duncan, 1995), when two or more objects occur simultaneously in a visual scene, these objects compete over our limited attentional resources, in order to be selected for further processing. This competition may be biased by mental representations concerning features and properties of the object or event that promote the currently most adaptive behavior. Adaptive behavior also requires that we respond to information that is outside the current focus of attention, such as when a target appears at an unexpected location. Reorienting can be defined as the complex set of adjustments of the attention focus, in response to novel or

unexpected targets (Posner, 1980). Reorienting to new objects may occur reflexively, and the salience of an object is strongly influenced by its behavioral relevance (Posner & Petersen, 1990).

Specifically, threatening or potentially dangerous stimuli receives a high priority in the human attentional system (Cisler & Koster, 2009; Öhman, Soares, Juth, Lindström & Esteves, 2012). The presence of threat-related information leads to enhanced processing of this information at the early stage of visual selection (Birk, Dennis, Shin & Urry, 2011). For instance, when searching for a face that is the odd-one-out in a visual search task, the time to detect the target will be shorter if the target is an angry face among neutral faces compared to if the target is a neutral face among happy faces (Cisler & Koster, 2009). Similarly, a vast amount of evidence for attentional bias towards threatening or fearful stimuli has come from studies using the emotional Stroop task. These results typically show that the Stroop effect, or the time it takes to report the color of the ink of a written word, is significantly larger if the word has negative emotional value compared to if the words are neutral (Bishop, 2007; Cisler & Koster, 2009).

Studies have shown that this increased responsivity to threatening stimuli is more pronounced in people suffering from anxiety disorders than in the healthy population (Cisler & Koster, 2009; Fox, Russo, Bowles & Dutton, 2001; Notebaert, Crombez, De Houwer & Theewues, 2010). It is assumed that emotional states and anxiety in particular, may disrupt the balance between endogenous and exogenous attention. While endogenous attention supports the ability to focus on a specific task, exogenous attention broadens the attentional focus. Studies have demonstrated that people suffering from anxiety are more prone to exogenous orienting to both neutral and irrelevant distractors regardless of behavioral relevance compared to the healthy population (Vermeulen, 2010). As such, anxiety is held to increase the output from the threat evaluation mechanisms, biasing attentional competition in a threat-related direction, even when threat-related stimuli are absent (Bishop, 2007). For instance, a study by Moriya & Tanno (2009) used Posner's cost-benefit paradigm to investigate whether impaired endogenous attentional and enhanced exogenous attention for the processing of non-emotional stimuli were observed in individuals with social anxiety. Their results suggest that high social anxiety is associated with an enhanced exogenous attentional system, and that salient stimuli attract attention regardless of their emotionality (Moriya & Tanno, 2009). Eysenck, Derakshan, Santos & Calvo (2007) insisted that this impairment is a result of inefficient endogenous attentional control in anxious individuals. Accordingly, the attentional control theory (Eysenck et al., 2007) suggests that this impairment of goal-driven control in

3

anxious individuals increases the extent to which processing is influenced by the stimulus-driven attentional system. Studies have demonstrated a weakened recruitment of the prefrontal control mechanisms in individuals that score high on trait anxiety assessments (Bishop, 2007).

An important question is whether, and how, state anxiety affects attention to neutral stimuli in the non-clinical population. State anxiety can be defined as an aversive emotional and motivational state, occurring in threatening circumstances. State anxiety is determined by situational stress, and can be described as experiencing an event, object, or interpretation that is threatening an existing goal (Eysenck et al., 2007). To date, there are very few studies that discuss the attentional systems for non-emotional processing during state anxiety in the healthy population. It has long been documented that emotional and sensory events elicit a pupillary dilation (Privitera, Renninger, Carney, Klein & Aguilar, 2010).

Pupillometry

Pupillary responses in psychological research have been used for more than 50 years (Laeng, Sirois & Gredebäck, 2012). This research has now firmly established that change in ambient light is not the only influence on changes in pupil size (Hess & Polt, 1960; Laeng, Ørbo, Holmlund & Miozzo, 2011), and pupil size and dilation have been studied in relation to cognitive processing of visual information (Privitera et al., 2010). The size of the pupil is determined by two cooperative pathways that control the tone of the two smooth muscles (Laeng et al., 2012). The parasympathetic pathway is mediated by the Edinger-Westphal oculomotor complex and controls the sphincter, the circular muscle responsible for pupil constriction. The sympathetic pathway is mediated by the posterior hypothalamic nucleus innervates the radial dilator muscle of the iris (Privitera et al., 2010).

Pupil dilation has been interpreted as a general indicator of increased vigilance, arousal, and interest (Demos, Kelley, Ryan, Davis & Whalen, 2008). The increased dilation of the pupil in response to picture stimuli has also been shown to be determined by the motivational and/or emotional relevance to the observer (Laeng et al., 2012). Early results have demonstrated that the pupillary response is significantly larger when observers are presented pictures with sexually related content, compared to when neutral pictures are displayed. These findings are similar in both male and female observers (Laeng et al., 2012). Furthermore, only female observers show significant dilations to pictures of babies (Hess & Polt, 1960). Large pupillary dilations have also been demonstrated in response to threatening

stimuli, as well as detection of fearful or threatening cues in the human face (Demos et al., 2008).

Although the pupillary response has been studied mainly in terms of responding to emotionally significant and arousing stimuli, there is evidence indicating that the pupillary response offers more information about human cognition than previously thought (Laeng et al., 2012); the pupillary response also seems to express other fundamental cognitive mechanisms. For instance, the pupillary response may function as an index of the amount of load on the attentional processing capacity (Kahneman & Beatty, 1967; Kahneman, 1973). Similarly, Just and Carpenter (1993) suggested that the pupillary response can be used to indicate how intensely the processing system is operating. As such, studies have demonstrated that the pupillary response correlates positively with the level of working memory load; increasing the span of digits to be remembered is associated with a parallel increase in the pupillary response (Laeng et al., 2012). In addition, studies have demonstrated a relationship between the degree of interference or competition between stimuli and/or responses and the task-evoked pupillary response. For instance, Laeng and colleagues investigated the pupillary response in observers performing a color Stroop task (Laeng et al., 2011). Their results showed that the pupil dilation in response to the stimulus was larger for incongruent words compared to congruent words. That is, the task-evoked dilation was larger when the task created a cognitive conflict, due to mismatch between color of ink and the written word, compared to when no such conflict occurred. Figure 1 illustrates the mean differences in pupil dilations during performance on the color Stroop task, in response to both congruent and incongruent words (Laeng et al., 2011).
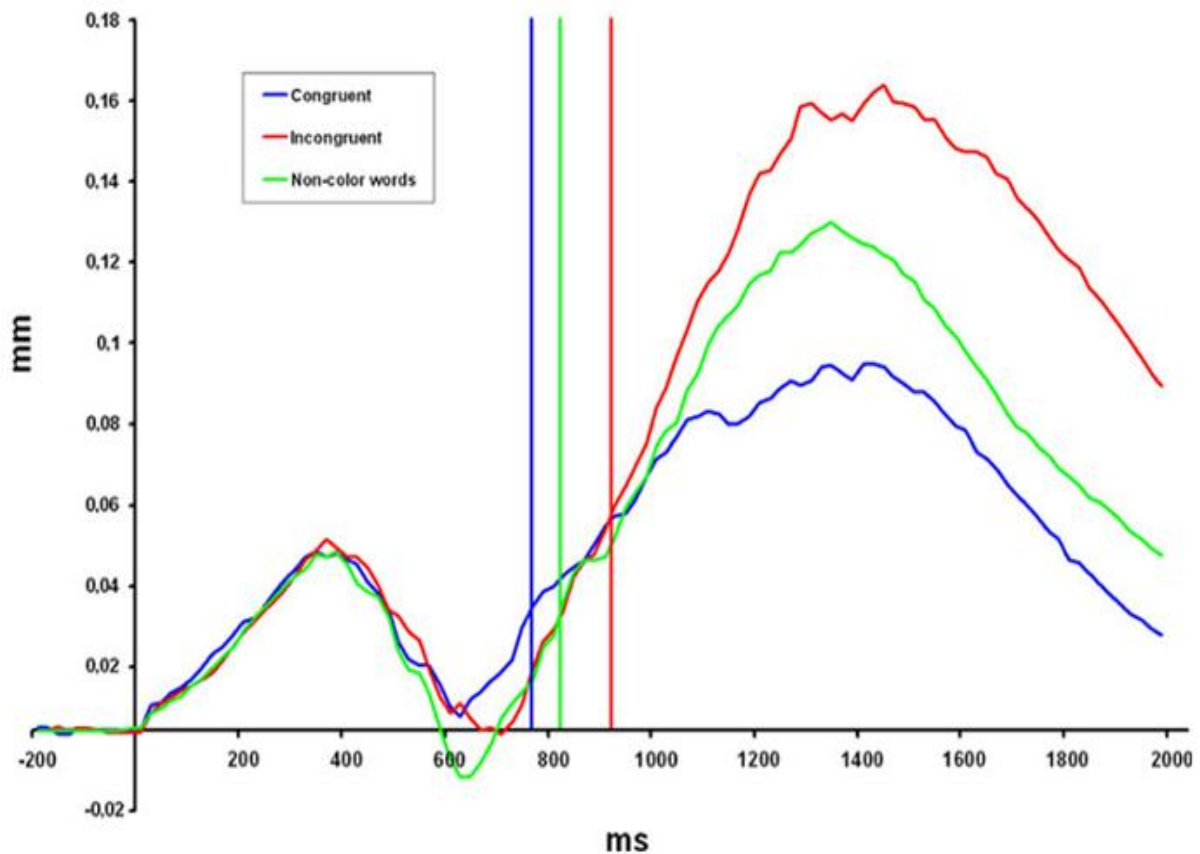
Figure 1. Mean pupil diameters (in mm) at each 20-ms sample for three conditions of a color-Stroop task. Time 0 indicates the onset of each stimulus. The colored vertical lines represent the point in time of each condition's mean RT (from Laeng et al., 2011).

The Locus Coeruleus – Norepinephrine System

Earlier research on monkeys suggests that task-evoked pupil dilations correlate negatively with the size of the pupil during rest, referred to as the baseline pupil diameter. More specifically, large baseline pupil diameters are found to be associated with decrements in task performance, accompanied by small task-evoked pupil dilations. Conversely, small or intermediate baseline pupils are typically associated with enhanced performance in a given task, as well as large dilations in response to targets (Clayton, Rajkowski, Cohen, Aston-Jones, 2004; Rajkowski, Majczynski, Clayton & Aston-Jones, 2004; Usher, Cohen, Servan-Schreiber & Aston-Jones, 1999). The inverse relationship between pupillary changes (baseline pupil diameter to task-evoked pupil dilation in a given trial) to behavior resembles the observed relationship between activity mode of locus coeruleus (LC) activity - and behavioral performance.

The LC is a small nucleus situated deep in the pons and sends projections to almost all brain regions (with the exception of the basal ganglia). Importantly, the LC is the source of norepinephrine (NE) release in the brain (Nieuwenhuis, Aston-Jones & Cohen, 2005), and is often referred to as the locus coeruleus-norepinephrine (LC-NE) system. NE is a neuromodulator that affects cortical processing by increasing the responsivity of neuronal units to their inputs (Gilzenrat, Nieuwenhuis, Jepma & Cohen, 2010). LC activity is shown to work under two modes of function – phasic and tonic (Usher, Cohen, Servan-Schreiber, Rajkowski & Aston-Jones, 1999). The phasic mode is associated with lower baseline NE release from the LC, in addition to high phasic NE bursts in response to task-relevant events. In the tonic LC mode, there is typically an absence of phasic NE bursts to task-relevant events, in addition to elevated baseline NE firing rate (Aston-Jones & Cohen, 2005). Animal studies have demonstrated rapid pupil dilations during task-related processing, in addition to large baseline pupils during periods of task-disengagement and distractive behavior (Clayton et al., 2004; Rajkowski et al., 2004; Usher et al., 1999). An important dimension of cognitive control is the adaptive regulation of the balance between pursuing known sources of reward and seeking new ones (Gilzenrat et al., 2010).This is a well-known fundamental trade-off in computational theories of reinforcement learning that distinguishes between states that favor exploration within the environment versus exploitation of a currently known source of reward or value. According to the adaptive gain theory (Aston-Jones & Cohen, 2005), the pattern of LC mode and the correlated pupillary behavior are both shown to correspond to exploration or exploitation (Laeng et al., 2012).

The phasic mode is associated with lower baseline LC activity, as well as a high phasic firing in response to task-relevant events. Additionally, studies have demonstrated that the phasic mode is related to increased task-engagement and high performance on tasks, while the tonic mode is related to lower performance and task-disengagement (Aston-Jones & Cohen, 2005; Gilzenrat et al., 2010; Sara, 2009). According to the adaptive gain theory of LC's role in adaptive behavior, the tonic LC mode produces a persistent increase in gain, which consequently renders the system more sensitive to task irrelevant stimuli (Aston-Jones & Cohen, 2005). Although this mode is clearly disadvantageous with respect to the current task, a tonic increase in gain might enable a change in behavior in response to more valuable reward opportunities, or changes in behavioral requirements (Aston-Jones & Cohen, 2005). Accordingly, a high tonic LC level is hypothesized to correspond to an exploratory, broad sensitivity mode to either external or internal (mental) events (Laeng et al., 2012). According to the neurocomputational model of LC function (Usher et al., 1999), high tonic LC discharge

might provide a mechanism that supports sampling new stimuli and corresponding behavioral responses to unexpected or novel stimuli. Usher and colleagues (Usher et al., 1999) recorded directly from LC neurons in four Cynomolgus monkeys while performing a visual discrimination task. The task required the monkey to respond to infrequent targets, and to inhibit any response to frequent distractors. During each of the recording sessions, tonic LC fluctuations were associated with parallel alterations and improvements in task performance. Increased tonic LC discharge was associated with decreased responsivity of LC neurons' phasic discharge in response to target stimuli. This three-way association of tonic LC, phasic LC responses, and level of task performance was consistent across all recordings (Usher et al., 1999).

Based on these results, a neuro-computational model of LC function and its effect on performance was developed in order to elucidate the mechanisms that might underlie this relationship. The two-component hybrid model, consisting of an LC network and a behavioral network, suggests that electrotonic coupling is a crucial mechanism involved in the underlying patterns of LC activity, and that this pattern may play a role in regulating behavioral performance. This model proposes that during optimal task performance, the LC phasic mode provides adaptive adjustments in gain. These adjustments enhance the LC responses to target stimuli, which in turn serve to facilitate behavior that is relevant for the task-goal. These findings led the authors to suggest that the LC may play an important role in attentional modulation, as well as the regulation of goal-directed versus exploratory driven behaviors (Usher et al., 1999). Similarly, Yu and Dayan (2005) suggest that the tonic LC mode signals unexpected global changes in the external environment, and can be seen as a signal that serves as an alarm system for contextual switches (Yu & Dayan, 2005). It has been suggested that anxious individuals are more easily distracted due to a lowered threshold for "possible-threat" interpretations, or as constantly "looking out for danger" (Bishop, 2007; Notebaert et al., 2010). A tonic LC mode might support such exploratory behavior associated with people suffering from anxiety.

Recently, several studies have suggested that pupil diameter can be used as an indirect marker of activity within the LC-NE system in humans (Einhäuser, Stout, Koch & Carter, 2008; Gabay, Pertzov, Henik, 2011; Gilzenrat et al., 2010; Jepma & Nieuwenhuis, 2011; Privitera, Renninger, Carney, Klein & Aguilar, 2010). Pharmacological research has demonstrated that the baseline pupil diameter changes in parallel with the current level of NE in the human brain (Jepma et al., 2011). Together, these and similar findings indicate that both pupillary responses and baseline pupil diameter track the activation level within the LC-NE

system: The baseline pupil diameter corresponding to the baseline level of LC, while the task-evoked pupillary response corresponding to the phasic NE burst in the LC (Laeng et al., 2012).

Current Study

The aim of this study was to investigate the relationship of pupil diameter to attentional state during visual orienting in a neutral vs. threatening context. To do this we used a modified version of a visual search task. The additional singleton task (AST) was originally developed by Theeuwes (1991) and Theeuwes and colleagues (Theeuwes, Kramer, Hahn, Irwin & Zelinsky, 1999). In the standard trials, the task-goal is to search for a target among distractors and report the identity of a small object located inside the target. The target in this task is a salient color singleton which creates a pop-out effect. In the distractor trials, an additional salient distractor is presented simultaneously as the color-singleton, resulting in a competition between the two most salient objects in the search display (Theeuwes, 2010). Figure 2 gives an example of the display.
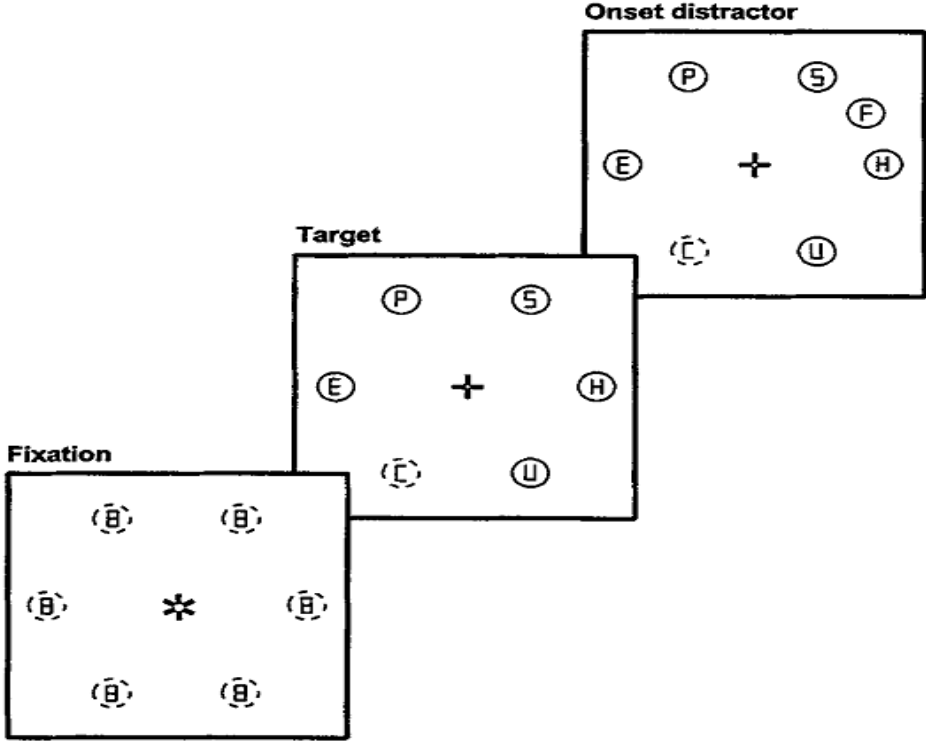

Figure 2. Example of stimulus display in the additional singleton task. The "Target" frame and the "Onset distractor" frame represent the two different trial types (from Theeuwes et al., 1999).

People suffering from clinical anxiety have described anxiety as the feeling of constantly looking out for danger (Notebaert et al., 2010). Thus, in order to investigate the effect of state anxiety in a non-clinical sample, we modified the AST paradigm by adding a "context"- variable with two levels: a neutral and a threatening context to the original version of the task. As such, we expected the threatening context to induce an attentional state similar to state anxiety as described above. A within-subject design was used so that all participants experienced both the neutral- and the threatening context. Considering the problem concerning selection bias, this design makes it possible to compare the effects of the two affective states (neutral and state anxiety), without taking into consideration the possible confound related to any differences between two groups (e.g., a clinical group vs. a non-clinical group).

Hypothesis and Predictions

The attentional control theory proposes that anxiety affects task performance by suppressing the impact from the endogenous attentional control mechanisms, and by enhancing exogenous processing. We tested this theory in a non-clinical sample. In line with this theory we hypothesized that a threatening context would impair task performance in a similar way as in anxious individuals. Thus, we expected the RTs for the distractor trials to increase during the threatening context. Furthermore, we predict that the attentional control states associated with each context will affect task performance. As such, we expect the RTs in the threatening context to be longer than the RTs in the neutral context. The adaptive gain theory suggests that the size of the pupil varies according to current attentional control state: a focused attentional state would be associated with a moderate or small baseline pupil diameter together with a large task-evoked pupillary response, while a reflexive attentional state would be associated with a larger baseline pupil diameter and smaller task-evoked pupil dilations. Taken together, we predict that the pupillary pattern described above will vary in accordance with the current attentional state. That is, the threatening context will be associated with a larger baseline pupil with smaller task-evoked pupil dilations compared to the neutral context. Given that our predictions stated above are confirmed, our findings will demonstrate the relationship between pupillary dynamics to task performance as stated by the adaptive gain theory of LC-NE function (Aston-Jones & Cohen, 2005).

Materials and Methods

Participants

The experiment group consisted of 20 volunteer students recruited from the University of Oslo (Department of Psychology). Two of the participants were excluded due to technical problems (i.e., poor pupil calibration), leaving 18 participants (N = 18; females = 9) in total. Ages ranged from 20-32 (M 24.71; SD 4.11). The participants were fluent Norwegian and/or English speakers. All observers had normal or corrected-to-normal vision, as well as normal color vision (according to self-reports). Observers gave their written informed consent before taking part in the experiment. All procedures conformed to national and institutional guidelines and the Declaration of Helsinki. Participants were compensated with 200 NOK at the end of the session.

Setup

Throughout all sessions, the participants' pupil diameter of the left eye was measured at a sampling rate of 240Hz (pupil size measurements were recorded every 4 ms) using an iView X Hi-Speed eye-tracking device (SensoMotoric Instruments SMI® GmbH). The pupil data were collected with the integrated iView X Software provided by SMI. Stimuli were presented on a 21-inch Eizo FlexScan T966 Color Display Monitor with a viewable image size of 19.6 inches (Dell Optiplex 760). In order to achieve a more accurate color and brightness representation of the stimulus display, the monitor used in this experiment was gamma-calibrated using a Spyder2 PRO. Participants were seated 80 cm from the computer screen. A chin rest was used in order to minimize head movements. Stimulus presentation was implemented in E-Prime 2.0 (Psychology Software Tools, Inc., Pittsburgh). A response box (Cedrus RB-420) was used to collect the responses. The sounds were presented through a pair of head phones (Sony MDR-XD100).

Sound stimuli. All sounds were chosen from the International Affective Digitized Sounds database/IADS (Bradley & Lang, 2007). The International Affective Sounds (IADS) was developed to provide a set of normative emotional stimuli for experimental investigations of emotion and attention. The database is being developed and distributed by the NIMH Center for Emotion and Attention (CSEA) at the University of Florida in order to provide standardized materials that are available to researchers (Bradley & Lang, 2007). In order to minimize habituation effects, four different sounds were used throughout the session. All four

sounds used in the experiment were rated high on arousal and low on pleasantness (see Table 1 for sound specifications)

Table 1
Table lists the sounds used in the threatening context. Mean ratings (on a 9-point rating scale for each dimension) and SDs for the sounds are based on the ratings performed by Bradley and Lang (2007), using the Self-Assessment Manikin (SAM).

	SoundNo.	Pleasure		Arousal	
		Mean	SD	Mean	SD
Scream	275	2.05	1.62	8.16	1.62
FemScream2	276	1.93	1.63	7.77	1.63
CarWreck	424	2.04	1.52	7.99	1.52
BikeWreck	600	2.13	1.55	7.28	1.55

Stimulus display. (see Fig.3). Participants performed a feature singleton search task, in which they searched for a circular color singleton and responded to the element located inside the singleton. For the standard trials, each trial began with a fixation display, consisting of a small, black (RGB values: 0, 0, 0) crosshair in the center of an otherwise white (RGB: 255, 255, 255) display (DVA = 12.271). After 200 ms fixation, six equispaced and equiluminant gray (RGB: 128, 128, 128) circles (radius = 1.2 cm), each containing a small black figure eight symbol, were presented on an imaginary circle. Distance from the center of the screen to the center of the circles was 8 cm. Pen width of the circles measured in pixels equaled 6. The six circles appeared at clock positions 1, 3, 5, 7, 9, and 11 on the larger imaginary circle. After 800 ms, all the gray circles, changed to red (RGB: 255, 0, 0), except from the target circle which remained gray. Simultaneously with the color change, the figure eights masks inside each circle were replaced by letters. The letters inside the red circles were distractor letters, randomly sampled without replacement from the set A, H, J, D, L, and G. The letter inside the gray circle was the target and consisted of either an E or a reversed E (3-digit using the font DS-Digital, font size = 22), with the orientation of the letter determining the response: participants pressed the leftmost-button for reversed E and the rightmost-button if the target was an E. Because the letters were relatively small, a fast response required the

participants to make a saccade towards the location of the gray circle in order to identify the target letter. The search display was presented for 1000 ms. Responses given outside this period were not registered. Based on earlier findings, and initial piloting data, demonstrating a ~ 2000 ms time period for the pupil to return to its baseline diameter (Einhäuser et al., 2008; Laeng et al., 2011; Privitera et al., 2010), each trial ended with a fixation display was presented for 1800 ms immediately after target offset.

For the distractor trials (see Fig. 1b), an additional red circle was presented at target display onset. The distractor could appear in four possible locations (at the 2, 4, 8, or 10 o'clock position). The position of the additional onset distractor was randomly sampled with replacement across trials, and was not possible to predict in advance.
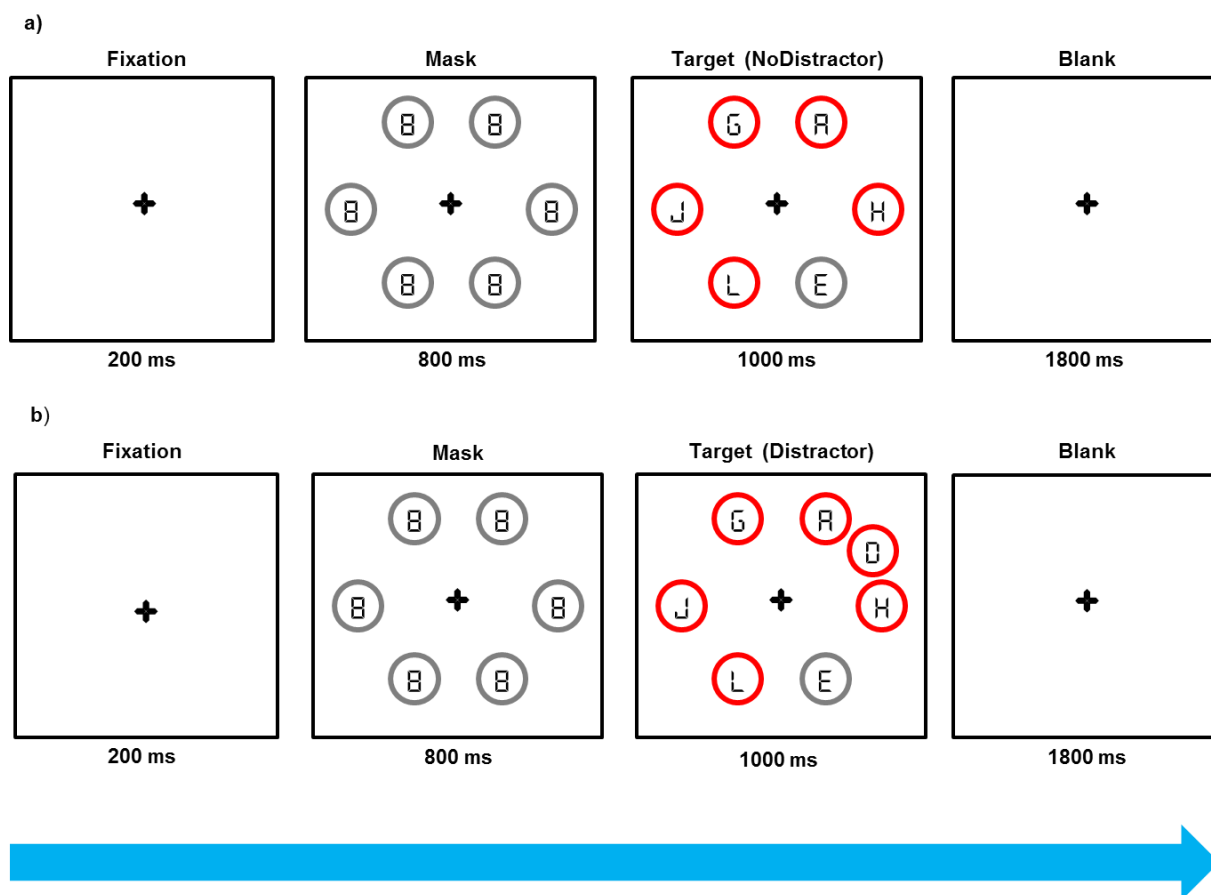
Figure 3. Illustration of the sequence of events in a trial. The blue arrow indicates the order of the sequence. After a 200 ms fixation, all gray circles changed to red, except for the target circle which remained gray. At the same time, all the premasks changed into letters. In the distractor condition (b) an additional red circle was added to the display with a 0 ms stimulus onset asynchrony (SOA). Participants had to make a speeded eye-movement to the gray circle and respond to the identity of the small letter located inside. The stimuli are not drawn to scale.

Design

This design was a 2 x 2 factorial design, with context (neutral and threat) and distractor (distractor and no-distractor) as independent variables. Participants performed the task in both levels of context: (a) a neutral context and (b) a threatening context. Within each context, a trial could be presented both with (distractor condition) and without (no-distractor condition) an additional onset distractor.

Procedure

Participants were tested in a quiet, and dimly illuminated room. The eye-tracker and the chair were adjusted to the height of each participant in the beginning of each session. The experimenter remained present throughout the session in order to adjust pupil and corneal reflection thresholds if necessary. Observers were asked to remain as static as possible during the experiment, and avoid eye blinks if possible. Due to a large amount of total number of trials, the participants were informed that they were allowed to take shorter brakes in between each run. The participants were instructed to search for the uniquely gray colored circle and to respond to the letter located inside of it, by pressing the appropriate response button with their index fingers resting on the right- or left button of the response box. Participants were instructed to keep their eyes on the fixation point until the target display appeared. During this display, the participants were told to make a speeded eye-movement towards the odd colored circle to identify the letter, and to respond as fast and accurate as possible. After responding, participants were instructed to re-fixate the centered crosshair. In order to familiarize the participants with the four sounds, each sound was played in a fixed ordered sequence before the experiment. During this sequence, the sound level was adjusted to each participant: we told the participants to adjust the sound level to be as loud as possible, without being painful. This sequence was followed by a practice session, consisting of 30 neutral trials (both no-distractor and distractor trials). Calibration of the eye-tracker followed immediately after. The calibration was validated by sequentially presenting fixation-spots at 9 random locations on the screen.

For both contexts, the two trial types described in the previous section were randomly drawn from a total of 896 trials (448 of each type), which was divided into 8 separate experimental runs (112 trials). Each run started and ended with a baseline recording of the pupil, lasting for 3000 msec. During these recordings, the participants were instructed to focus on a small white (RGB: 255, 255, 255) circle positioned in the center of an otherwise gray (RGB: 127, 127, 127) background. Within each of the 8 runs, shorter blocks of the neutral

14

trials and the context trials were presented interchangeably (see Fig. 4). A neutral block was presented in the beginning and at the end of each experiment round. These blocks consisted of 8, 9, or 10 neutral trials. The threat blocks consisted of 3, 4, or 5 trials. Except for the last neutral block within a round, a threat block always followed the neutral condition periods. The trials in this condition were identical to those in the neutral condition, with one exception: a sound was presented on the last trial of each block in the 3- and 4-trial blocks. In the 5-trial blocks, the sound would appear in 15 out of 32 blocks in total, leaving 17 blocks without sound. The no-sound threat blocks were included in order to prevent the participants from being able to predict the trial in which the sound would appear. To indicate the start of a threat block, a beep-sound lasting for 1000 ms was played before the onset of the first threat trial. After completion of the last trial in a threat period, the beep-sound was played again, this time to indicate the end of a threat period. In total, each participant performed 624 neutral trials and 272 threat trials, divided into 136 and 64 blocks, respectively. The time to complete the task was about 80 min. Figure 4 illustrates an example of a sequence of trials in a round.
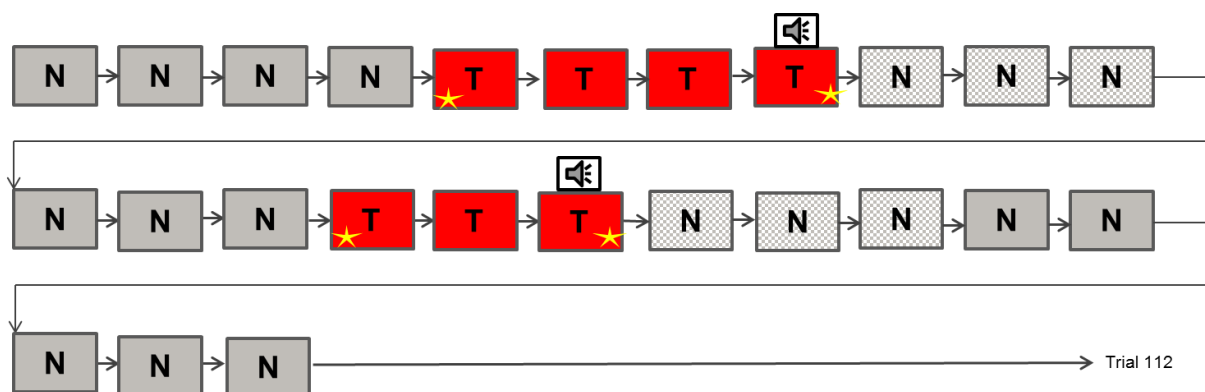

Figure 4. Example of a sequence of trials in a round. N = Neutral trial, T = Threat trial, N (chequered) = Recovery trial. Yellow star indicates a trial with a "cue"-sound. Speaker icon indicates a threat-sound.

Pupil data preprocessing

The raw pupillometry data were preprocessed following similar procedures for all pupil data analyses. Pupil data were preprocessed using a custom written MATLAB (MathWorks, Natick, USA) script developed in the laboratory (Center for the Study of Human Cognition, University of Oslo). The data points recorded 200 ms preceding mask onset and up until 2000 ms after mask onset were converted from pixels into millimeters. This time window was chosen to account for the large variation in pupil peak latencies across the

participants. In order to exclude physiologically improbable pupil sizes, we removed those data points in which the pupil was smaller than 2 mm and larger than 7 mm, together with their neighboring data points (50 ms before and after the removed data point). For each of the remaining trials, we calculated the mean horizontal and vertical pupil size, as well as their standard deviations (SDs). Measurement noise (e.g., blinks) was defined as pupil sizes more than 2.5 SD away from the mean. These trials were removed from the data set. Also, if the task period during a trial was considered too noisy (with more than 50% of the horizontal or vertical data points removed), these trials were removed during the preprocessing steps. To assess the baseline pupil diameter for each trial, the horizontal and vertical size measurements representing the period 200 ms before mask onset were averaged. For a minor number of trials, this period was removed during the preprocessing steps. In order to assess the baseline for the removed trials, the data points representing the period 200 ms after mask onset were used to calculate baseline diameter. Thereafter, a single measure of pupil diameter was obtained for each trial by averaging the horizontal and vertical coordinates of the pupil diameter. The removed epochs were reconstructed through linear interpolation for the remaining task period. In order to further reduce high-frequency noise in the period of interest, the data representing a trial were smoothed using MATLAB's inbuilt '*rloess*' algorithm. This algorithm is a robust version of the *'loess'* algorithm found in MATLAB, which is a local regression method using weighted linear least squares and a 2nd degree polynomial model; the *'rloess'* algorithm assigns lower weight to outliers in the regression, and in addition assigns zero weight to data outside six mean absolute deviations.

Results

Behavioral data. Table 2 illustrates mean RTs and SDs for each condition. For the RTs, we conducted a 2 (Context: Neutral and Threat) x 2 (Distractor: Distractor and NoDistractor) analysis of variance (ANOVA) in SPSS. Error trials were not included in the analysis (Threat Distractor (TD) = 3%, Threat No-Distractor (TND) = 2%, Neutral Distractor (ND) = 2%, Neutral No-Distractor (NND) = 2%). Response latencies that exceeded each participant's mean by more than 2.5 standard deviations were treated as outliers and eliminated from the RT analyses as well as the RTs considered responder errors, defined as RTs shorter than 250 msec (3.65% of the total trials) were removed from the data set. Also excluded from the data set were those trials in which the negative sounds were presented (15 trials in total). In order to reduce any carryover effects due to the negative sound, the first

three neutral trials (recovery trials) immediately following a sound block were removed from the analysis (192 trials in total per subject). Considering the low error rate in all four conditions, accuracy was not analyzed. Our results showed a significant main effect of distractor, $F(1, 17) = 46.09$, $p < .0001$, and no main effect of context, $F(1, 17) = .410$, $p = .5$. The results revealed a significant interaction of context * distractor, $F(1, 17) = 4.691$, $p = .045$.

A paired samples t-test was conducted to compare the attentional capture effect between Threat Distractor – Threat NoDistractor (M = 33.99, SD = 22.89) vs. Neutral Distractor-Neutral NoDistractor (M = 26.85, SD = 17.22). Results revealed that the difference between Threat Distractor – Threat NoDistractor was significantly larger than the difference between Neutral Distractor – Neutral NoDistractor, $t(17) = 2.166$, $p = .045$. These results demonstrate a larger attentional capture in the threatening context, compared to the neutral context. Figure 5 illustrates mean RTs for all conditions.

Table 2
Group means for the RTs (in ms) and within-subject SDs for each condition.

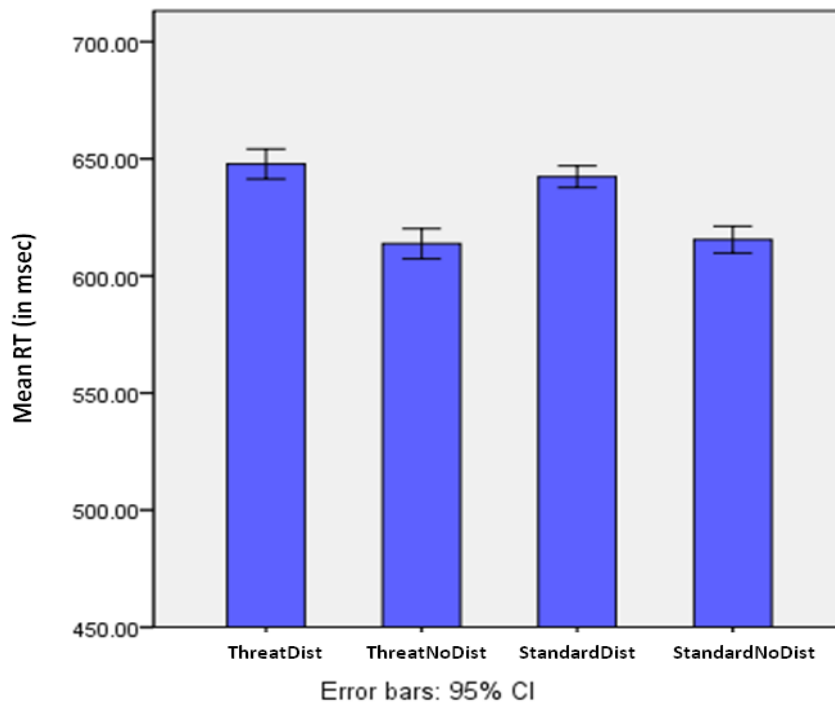| Condition	*M*	*SD*
Threat-Distractor	653.8	12.87
Threat-NoDistractor	619.8	12.94
Neutral-Distractor	648.4	9.3
Neutral-NoDistractor	621.6	11.5

Figure 5. Mean RTs for each of the four contexts. Bars indicate 95% confidence intervals for within-subject designs (Loftus & Masson, 1994).

Baseline pupil diameter analysis. External baseline pupil size was assessed for each participant by averaging the baseline measures recorded at the beginning and the end of each experimental run (in total: 48 seconds). The baseline diameter within each condition was corrected to this measure by subtracting the external baseline diameter from each of the four trial baseline means. We performed a paired samples t-test to investigate the difference in baseline pupil diameter between the threatening context (M = -.83, SD = .04) and the neutral context (M = -.91, SD = .04). The results showed a significant difference in baseline pupil diameter between the two contexts, $t(17) = 4.786$, $p = .000$. Thus, in line with our predictions, the analysis demonstrated a significant larger baseline pupil diameter in the threatening context, compared to the neutral context. Note that the values for each baseline measure are negative. This indicates that the task-related baselines are in fact a pupillary constriction compared to the external baseline measures. Figure 6 illustrates the differences in baseline pupil diameter across contexts.
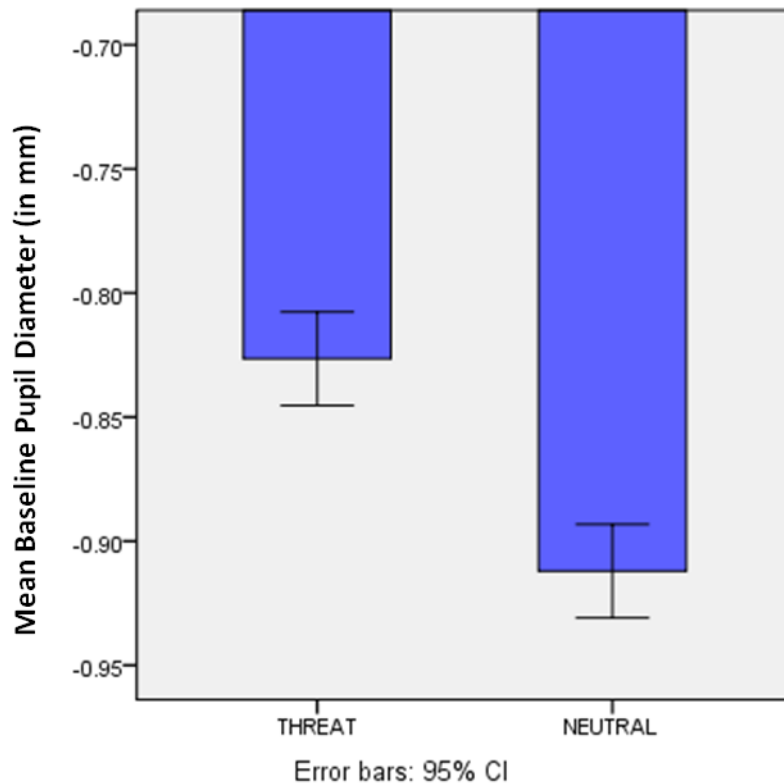
Figure. 6 Differences in mean baseline pupil diameter (in mm) across contexts, averaged over a 200-ms epoch from mask onset. Bars indicate 95% confidence intervals for within-subject designs (Loftus & Masson, 1994).

Pupil change analysis. To investigate whether or not there was an inverse relationship between baseline pupil diameter and task-evoked pupil dilations, we assessed the maximum task-evoked pupil increase from the external baseline corrected trial-baseline diameter on a trial-by trial basis. Maximum peak was defined as the maximum positive deviation from the baseline within each condition, occurring within the 1800 ms time-window following mask-display onset. To obtain this value, the baseline pupil diameter for each trial was subtracted from the maximum peak and averaged within each condition. We performed a paired samples t-test to investigate the difference in maximum peak size relative to the corresponding baseline between the neutral context (M = .41, SD = .04) and the threatening context (M = .35, SD = .04). The results showed a significant difference in pupil dilation diameter between the two contexts, $t(17) = 3.148$, $p = .006$. These results confirmed our predictions that pupillary change from baseline would be larger in the neutral context compared to the threatening context (see Fig. 7).
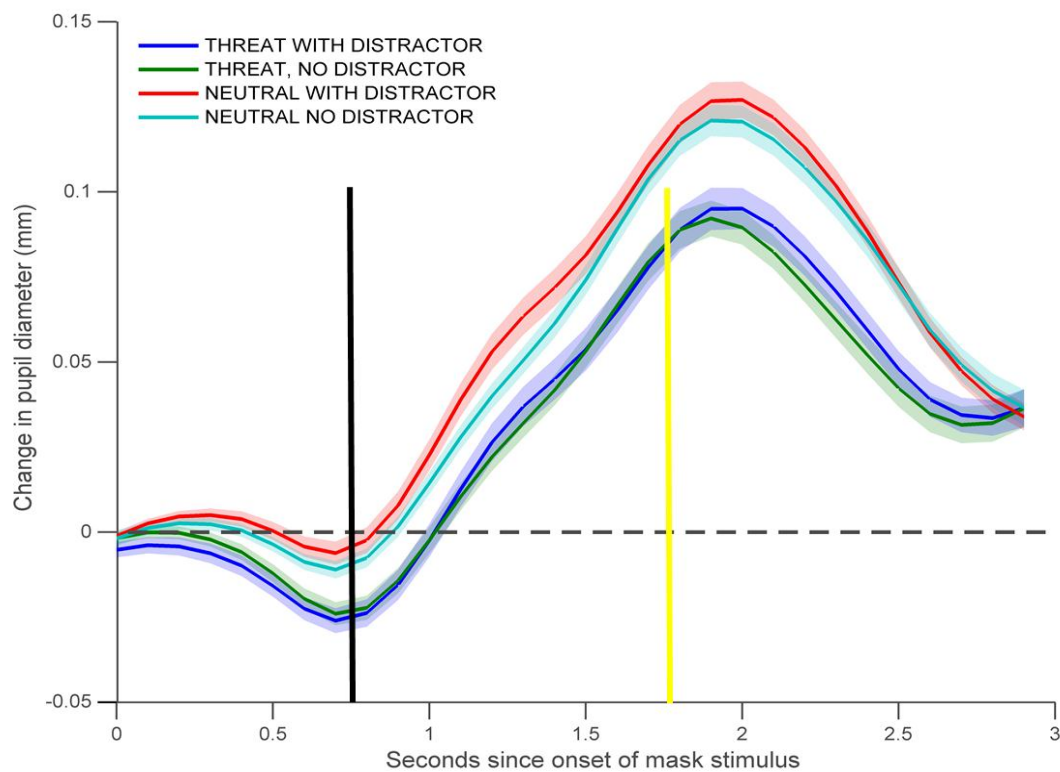
Figure 7. Time courses of averaged task-evoked pupil dilation from baseline for all four conditions. Solid black line represents the point in time of target onset. Solid yellow line represents the point in time of target offset.

Important to notice, however, figure 7 depicts the mean pupillary change relative from the baseline pupil diameter measured before target onset. Figure 8 illustrates the same curve for the uncorrected pupillary measures; that is the absolute pupil peak size (in mm). As this figure demonstrates, there was no difference in the absolute peak size across the two contexts.
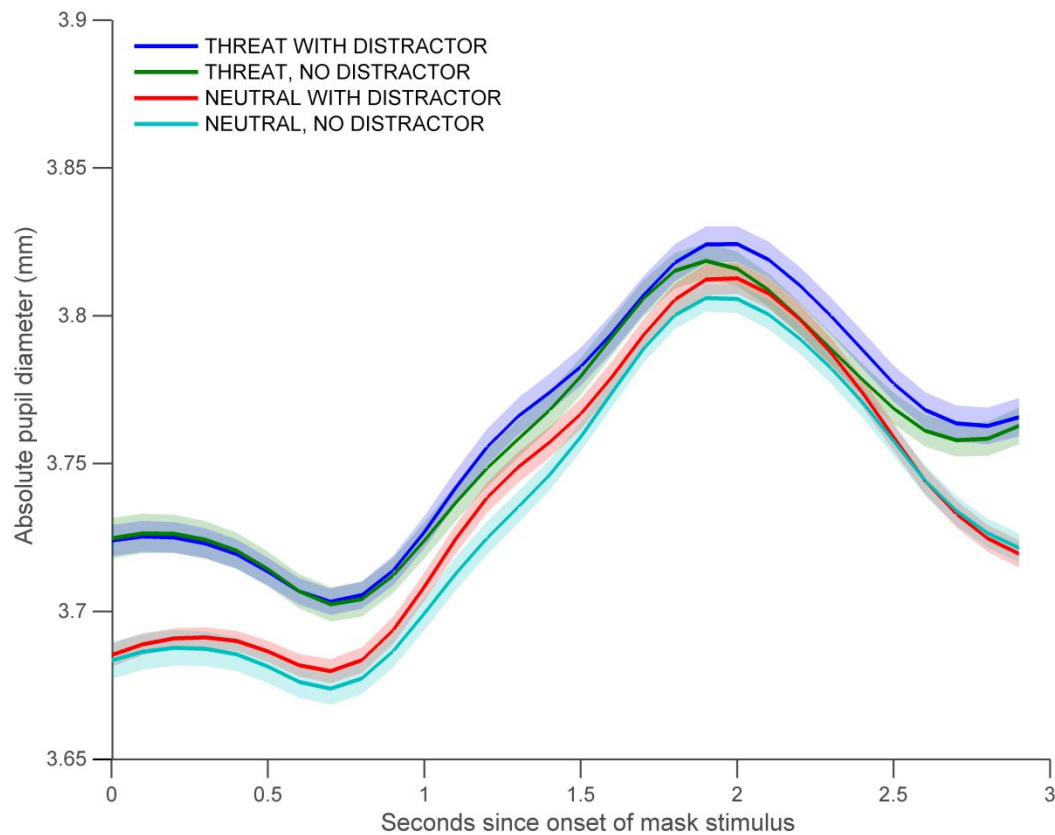
Figure 8. Time course of the pupil size (in mm) based on uncorrected pupillary measures. As the figure illustrates, there is a marginally higher pupillary response in the threatening context, indicating that the baseline pupil diameter is changing in response to contexts, and thus creating the differences in relative peaks from baseline across contexts.

A repeated measures ANOVA was performed on the absolute pupil peak diameters. The results revealed no main effect of either context, $F(17,1) = 2.281$, $p = .149$, or distractor, $F(17,1) = 1.039$, $p = .322$. There was no significant interaction of context * distractor, $F(17,1) = .439$, $p = .517$.

Discussion

In this experiment, we administered a task that was specifically designed to investigate pupillary dynamics in participants performing a modified version of the additional singleton task. The aim of the present study was to investigate the relationship between pupillary responses to behavioral performance during orienting of attention in a threatening and a

neutral context. With respect to the distractor trials, RT analysis revealed a main effect of distractor. Also, we found a significant interaction between context and distractor. A paired samples t-test revealed that the attentional capture of the additional distractor was larger in the threatening context, compared to the neutral context. This flexible attentional set in a threatening context seems behaviorally adaptive, since increased responsiveness to distracting stimuli would enable rapid detection of threatening stimuli in real life situations.

The pupil data analysis revealed a pupillary response pattern in line with our predictions. First, the baseline diameter pupil analysis demonstrated a significantly larger baseline pupil diameter in the threatening context trials as compared to the neutral trials. In addition, analysis of absolute pupil peak size revealed no significant differences in pupil dilation diameter across the four conditions. Thus, in line with our predictions, a larger baseline pupil diameter was associated with a smaller pupil peak relative to baseline and vice versa. The paired samples t-test on the differences in pupil change from baseline revealed a significantly larger pupillary change in the neutral context compared to the threatening context. Moreover, the absolute peak size analysis revealed no main effects of either context or distractor. We interpret these findings as evidence that the differences in pupillary change relative from baseline across contexts are the result of a change in baseline pupil diameter rather than pupillary peak sizes.

The larger attentional capture in a threatening context is consistent with the view that threat and anxiety affects the processes involved in goal-driven attentional control in visual selective attention. According to Eysenck and colleagues (Eysenck et al., 2007), the endogenously driven attentional component is impaired during threat processing. The result of this may be a system more responsive towards objects and events within a broader area than what is required for attention to be focused on a specific task-goal. Studies investigating the neural basis of fear and threat related processes in people suffering from clinical anxiety has consistently shown decreased activity in the prefrontal areas assumed to play a major role in endogenous orienting. This decrease is even more obvious during visual processing of negative emotional stimuli (e.g., pictures of spiders and snakes) (Bishop, 2007).

However, our data conflict with recent studies demonstrating how experimentally induced anxiety inhibit processing of non-target information, and thus enhance performance on selective attention tasks (Finucane, 2011). These divergent findings may be explained by the different properties of the tasks used across different studies. For instance, the Posner cueing task has frequently been used in order to investigate the effect of perceived threat, or state anxiety, on cognitive performance. In this task, observers are presented a valid or invalid

cue, indicating the possible location of an upcoming target. Results from studies using this task to investigate the effect of stress or anxiety on task performance typically show that anxious states in the observer are associated with faster RTs compared to neutral mental states. This difference in performance between groups is assumed to reflect a smaller interference effect of the invalid cue, which in turn improves processing of the upcoming target (Finucane, 2011). According to a classic paper by Easterbrook (1959), emotional arousal reduces the range of cues that an observer processes, which results in a sharpening of attention in a central location and impairs the processing of peripherally located stimuli. This theory may explain the smaller effect of the invalid cue associated with state anxiety. Theeuwes and colleagues (1999) demonstrated that the stimulus onset asynchrony (SOA) determined whether the additional onset distractor captured attention or not. That is, if SOA was more than 150 msec, there was no capture by the abrupt onset of an irrelevant distractor. Furthermore, the size of the attentional capture was largest when SOA was 0, and became smaller as the SOA approached 90 msec. From this, the authors concluded that for competition between two objects to take place, the two objects must be presented simultaneously, or within the timeframe of ≤ 90 msec. Considering the results from studies using the Posner task in light of Theeuwes and colleagues' (Theeuwes et al., 1999) findings, due to SOA exceeding 90 msec, competition between an invalid cue and the target may not take place. Hence, the abrupt onset of the following target may not require any attentional control processes other than stimulus-driven orienting mechanisms, which in our study did not seem to be attenuated by a threatening context. Furthermore, as is proposed in the Easterbrook hypothesis, state anxiety impairs the processing of a peripherally located stimulus. In this experiment, initial capture of attention by a distractor makes the target a peripherally located stimulus. In line with predictions derived from the Easterbrook hypothesis, experimentally induced threat impaired target processing indicated by increased RTs when a distractor was presented in the target display.

An alternative explanation for the disparity between ours and earlier results could be that the threatening context in our study was not threatening enough. However, with respect to our pupillary findings, results revealed significantly larger baseline pupil dilation, in the threatening context. Furthermore, our results showed that the pattern of pupil dynamics across the two contexts is a result of changes in baseline pupil diameter, and not the peak itself. This pattern of pupil dynamics demonstrated in this study resembles the pattern of the tonic LC mode described by Aston-Jones and Cohen (2005). Clinical studies have revealed that the LC is activated by stress, and responds to it by increasing NE secretion, and by altering the

activity in the prefrontal cortex (Laeng et al., 2012).The LC neurons that project primarily to the forebrain regions are involved in the organization of stress and anxiety responses (Goddard, Ball, Martinez, Robinson, Yang, Russel & Shekhar, 2009). Supporting evidence for the role of the LC in emotional activation comes from results that link the LC-NE system as a mediator of the typical emotional responses measured by EEG, and autonomic measures such as blood pressure, heart rate, and galvanic skin response (Aston-Jones et al., 1996). Moreover, maximal discharge in the LC neurons during waking is associated with highly aroused conditions, including stress (Jones, 2003). In addition, a considerable amount of clinical evidence has suggested the relationship between the central noradrenergic system and anxiety states or depression (Itoi & Sugimoto, 2010). Consistent evidence from studies considering the role of noradrenergic system in anxiety demonstrates a higher baseline (tonic) NE activity during situations involving stressors (Kalk, Nutt & Lingford-Hughes, 2011). During acute stress responses, the release of NE occurs in phasic bursts when attending to the threat cue, as well as an increase in tonic NE release, which in turn increases arousal (Benarroch, 2009). Findings associated with NE release during adaptive and maladaptive responses to stress has shown that chronic stress may contribute to enduring dysregulation of the LC-NE system, and pharmalogical interventions that modify NE functioning are being used on patients with anxiety and depression (Goddard et al., 2009). According to Goddard and colleagues (2009), the LC-NE system can be described as a modulator with anxiogenic (anxiety enhancing) or anxiolytic (anxiety suppressing) effects that vary according to acute or chronic levels of stress. Acute stressors associated with a high level of threat demand rapid attention, and the LC-NE neuronal pathway is said to respond to such stressors, and thus functions as an attentional gatekeeper (Goddard et al., 2009).

It has been suggested that a combination of high trait and high state anxiety might be required for the threat-related processing pattern to be observed in non-clinical populations (Bishop, 2007). Recent neuroimaging studies of conditioned fear and negative affective states indicate a common amygdala-prefrontal circuitry underlying threat processing and fear responses. Findings from such studies suggest that the balance of activity within this circuitry is altered in anxious individuals resulting in decreased activity in the prefrontal control areas (Bishop, 2007). While decreased prefrontal activity has not been demonstrated during transient state anxiety in the healthy population, decreased prefrontal activity during threat-related processing has been well documented in the clinical population. It is assumed that the prefrontal cortical areas are involved in the regulation of activity triggered by the occurrence of threat induced processes (Bishop, 2007). Thus, there is a possibility that the differences in

the neural basis for threat-processing results in different attentional impairments between the healthy and clinical population. According to the attentional control theory (Eysenck et al., 2007), anxiety is expected to enhance the stimulus-driven detection of salient events. However, there were no significant differences in RT scores for the no-distractor trials across contexts. A reason for this might be the effect of regulation from the frontal areas in response to the contextual change.

Limitations

Despite the compelling findings in this study, there are certain limitations in the design that must be taken into consideration. First, our experiment did only include a threatening context in addition to the neutral context. Including a second emotional context, for instance a positive or happy context, would enable us to investigate the effect of other types of contexts on behavioral performance and pupillary responses. Thus, including a second emotional context would be necessary for follow-up studies. Furthermore, due to the within-subject design, and the large number of total trials, the experiment session was quite long. Thus, factors such as motivation and degree of task (dis-)engagement must be taken into consideration. Considered the overweight of neutral trials compared to threatening trials, it is a possibility that the difference across contexts observed on both RTs and pupillary responses may have been in part related to such factors. Nevertheless, the skewed relationship between the neutral and threatening trials was necessary in order to induce a sense of unpredictability in the participants. Furthermore, there was very little difference in variance across the two contexts Moreover, pupillary responses are at best only indirect measures of cognitive processes, and factors like luminance- and color effects must be taken into consideration. Although the colors used to present the stimuli in this experiment were controlled for differences in luminance, we did not measure the subjective perceived brightness of the stimuli in each participant. Differences in luminance could also have effect on the subjective perceived degree of salience of the target compared to the distractors. However, as this would affect both contexts similarly, an effect due to luminance effects is rather unlikely. Another limitation of the design could be related to the use of auditory cues. Although the three consecutive trials following a sound were removed from the analysis, we do not know whether or not there were any carry-over effects. Another possible confound is the possibility that there was a ceiling effect, or that the differences in pupil change across context was due to the pupil reaching its maximum limit of dilatation in the threatening context. Recently,

several studies have investigated the pupillary response using dark testing rooms (except for the light from the monitor). Future studies may consider using monitor lightning as the only light source in order to test the pupil range during such conditions. Furthermore, a combination of pupillometry and fMRI may be advantageous for future studies. Recording pupillary responses during fMRI and ERP has shown to be successful in linking pupillary responses with various brain activations and processes (Sara, 2009).

Conclusions

In this study, we found a change in baseline pupil diameter in response to an experimentally induced contextual change. Lastly, our findings provide additional support for a relationship between the pattern of pupillary responses and attentional state. Insofar as these pupillary patterns conforms to the pattern of LC activity predicted by the adaptive gain theory (Aston-Jones & Cohen, 2005), these findings provide further indirect evidence that pupil diameter may be a useful index of LC activity

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