# Enhanced Emotional Response to Both Negative and Positive Images in Post-Traumatic Stress Disorder: Evidence from pupillometry

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**Abstract**

Post-traumatic stress disorder (PTSD) is characterised by alterations in the function of the autonomic nervous system. However, it is unclear if this dysfunction is threat-related or related to arousing stimuli in general. Pupillometry offers a simple non-invasive measure of ANS activity that can separate parasympathetic and sympathetic arousal. Participants viewed images with emotional or neutral content: 20 met diagnostic criteria for PTSD, 28 were trauma-exposed (but with no PTSD), and 17 were controls. Initial pupil constriction (a marker of parasympathetic function) was reduced for the PTSD group, while dilation due to the emotional content of the image (a marker of sympathetic activity) was greater in the PTSD group. Individuals with PTSD demonstrated enhanced physiological arousal to both threat-related and positive images. The results suggest reduced parasympathetic arousal and increased sympathetic arousal in the autonomic nervous system, which has been linked to a range of adverse health outcomes in PTSD.

*Keywords*: Post-traumatic stress disorder, PTSD, trauma, autonomic arousal, emotion, eye tracking, pupillometry

**Highlights**

- The processing of emotive, but trauma-unrelated, stimuli has not been studied in individuals with PTSD.
- Changes in the size of the pupil while viewing emotive images (happy, sad, and fear) were used to index autonomic nervous system responses.
- Individuals with PTSD showed a reduced constriction of the pupil to a change in light level, suggesting reduced parasympathetic arousal.
- Emotional images caused greater pupil dilation in all participants. Individuals with PTSD showed greater emotional sensitivity to both threat-related and happy images.
- Rather than a threat-specific response, these results suggest generalised hyperarousal and sensitivity to emotional stimuli in individuals with PTSD.

# Enhanced emotional responsivity to both negative and positive images in post-traumatic stress disorder: Evidence from pupillometry

People who have experienced traumatic events often show predictable psychological harm. In a significant number of individuals, the symptoms of this harm persist in the months after the event leading to a diagnosis of post-traumatic stress disorder (PTSD). PTSD involves reexperiencing, intrusive recollections, avoidance of trauma reminders, and alterations in cognition, mood, and arousal (*Diagnostic and Statistical Manual of Mental Disorders, 5th ed.; DSM-V;* American Psychiatric Association [APA], 2013). These symptoms are driven by a strong sense of current threat, which persists long after danger has passed (Ehlers & Clark, 2000). Hypervigilance to threat sets up a vicious cycle, which is thought to play a key role in both the maintenance and predisposition to PTSD (Dalgleish et al., 2001).

There is clear evidence for hyperarousal responses to standardised and ideographic trauma cues in PTSD (see Pole, 2007 for a meta-analysis) as well as persistently elevated levels of baseline arousal (Clancy et al., 2017). However, it is unclear whether hyperarousal is specific to trauma and threat-based cues, or if traumatised individuals' elevated baseline hyperarousal leads to an automatic hyperarousal and preparation for threat in any emotional context, including an enhanced response to positive emotional stimuli. To date, no studies have investigated primary physiological responses to emotional, but trauma-unrelated stimuli. In addition, alterations in basic emotional processing in PTSD remain understudied (Litz et al., 2000). This paper presents a novel physiological assessment paradigm to assess alterations in emotion processing in individuals with and without trauma-exposure and PTSD.

Arousal to different categories of emotive images (positive, negative-threat and negative-distress) were assessed using pupillometry as measure of emotional responsivity.

Psychophysiological symptoms have always been a key marker of PTSD (Mott, 1919). They are unique in that they can be objectively assessed in the laboratory and are not reliant upon subjective self-report (which can be subject to levels of insight and introspection). The persistent state of threat and fear associated with PTSD results in a shift in the physiological functioning of the autonomic nervous system (ANS) to promote fight and flight behaviours (Williamson, Porges, Lamb & Porges, 2015). Dysregulated arousal levels are a consequence of hypearousal in the sympathetic branch (Sherin & Nemeroff, 2011), as well as hypoactivity in the parasympathetic branch, of the ANS (Agorastos et al., 2013; Streeter et al., 2012). There is emerging evidence that this altered ANS function is associated with increased mortality rates through cardiovascular and metabolic disease biomarkers (Dedert, Calhoun, Watkins, Sherwood & Beckham, 2010). Chronic hyperarousal occurs at the expense of an intervening state of calm and, on this level, PTSD may be understood as a disorder of autonomic imbalance and dysregulation.

There is robust psychophysiological evidence for alterations in arousal in individuals with PTSD at rest and in response to trauma symptom provocation (tonic versus phasic arousal; for example, Forneris, Butterfield, & Bosworth, 2004; Liberzon, Abelson, Flagel, Raz, & Young, 1999; see Pole, 2007 for a metanalysis). A diverse range of physiological assessment measures have been used to demonstrate elevations in resting heart rate, skin conductance, blood pressure, and eye blink in facial electromyography (EMG) (Pole, 2007). More recent studies employ the use of heart-rate variability (HRV) to demonstrate reductions in parasympathetic function as an index of an individual's ability to cope with stress (Tan, Dao, Farmer, Sutherland & Gevirtz, 2011; Meyer et al, 2016). We argue here that pupillometry should be added to the toolbox of measures that are able to index the disorder of

autonomic imbalance and dysregulation in PTSD and that it has many strengths to support its use.

Pupillometry is the assessment of changes in the size of the pupil. These small fluctuations in size can be used to index changes in the physiological functioning of the ANS that happen during processing of psychological stimuli. The mechanism of control for the pupil is comprised of opposing contractions of two muscles within the iris: the sphincter and dilator pupillae. Pupil dilation is caused by either an increase of activity in the sympathetic nervous system, innervating the dilator muscle, or by inhibition of parasympathetic innervation to the sphincter muscle (Steinhauer et al., 2004). Hence, the pupil can be used as a physiological indicator to assess alterations in the function of the ANS. Alterations can be studied through measurement of changes in pupil responses to changes in luminance, or by looking at pupil responses which are modulated by a psychological or cognitive process (such as attention, effort, and emotion). In cognitive pupillometry paradigms, pupil dilation and constriction can be used as an index of emotional processing (Bradley, Miccoli, Escrig, & Lang, 2008; Bradley, Spigao & Lang, 2017; Partala & Surakka, 2003; Snowden et al., 2016) and to assess individual differences in traits and symptoms associated with mental disorder (e.g., Burkhouse, Siegle, Woody, Kudinova, & Gibb, 2015; Burley, Gray, & Snowden, 2017; 2019). Given the proposed centrality of persistent threat-induced alterations in ANS function in PTSD, pupillometry could provide a useful, quick, and non-invasive, method by which to explore the altered (or dysregulated) function of the ANS and any improvements in this following effective treatment.

Pupillometry allows for exploration of rapid responses. The modulation of the pupil occurs within one to two seconds of the onset of an emotional stimulus. The temporal resolution of this measure therefore allows for the assessment of rapid, pre-cognitive, effects of emotional processing, preventing consciously-mediated emotional regulation strategies

that may be adopted by the individual. This makes the index of affective modulation of the pupil response resistant to attempts at distortion or fabrication.

Pupillometry has been employed as a physiological measure in PTSD in a small number of studies, but the methodology has been variable, and has solely focussed on trauma cues and threat stimuli. Kimble, Fleming, Bandy, Kim, & Zambetti (2010) compared veterans assigned to high and low PTSD symptom groups. Participants viewed either a trauma image (war scenes) or a negative image (e.g. vehicle accident) on a split screen next to a neutral image. Participants in the high-PTSD group had larger pupils to both trauma and negative images, but also spent more time looking at these images in comparison to the neutral images. Felmingham, Rennie, Manor, and Bryant (2011) used a word viewing paradigm and assessed multiple indices of physiological reactivity. Participants were exposed to an array of four words one of which could be a trauma cue. Whilst individuals with PTSD had larger pupils when viewing words, there was no difference when related to the presence of the trauma cue words. The individuals with PTSD also spent more time looking at trauma-related words. Cascardi, Armstrong, Chung, and Paré (2015) presented single pictures containing either threatening or neutral stimuli for 30 seconds duration. In comparison to trauma-exposed controls, participants with PTSD had no overall differences in pupil size or reactivity to the threatening images. However, when pupil size was extracted during fixations to the "threat components" of the images (e.g., a knife), pupil area was greater for the PTSD group. Cascardi et al. conclude that pupil reactivity to threatening images shows promise as a physiological marker for PTSD.

The current evidence for emotional hyperarousal using pupillometry is therefore mixed and not without methodological limitations. Furthermore, these studies so far have only compared fear or trauma cue stimuli to neutral ones. Hence, it is not clear whether the proposed hyperarousal in PTSD is: (1) specific to trauma-related stimuli: (2) relates to

physiological hyperarousal to any threatening/fear stimuli (irrespective to whether it is trauma-related); or (3) if higher baseline physiological arousal leads to a more generalised hyperarousal to all affective information (both positive and negative).

The present study assessed differences in pupillary response according to PTSD diagnostic status, and the relationship between PTSD symptom severity, and indices of pupillary function using a passive image viewing paradigm. Furthermore, it examined differences in pupillary response in individuals with PTSD at rest, during the pupil constriction caused by the onset of a luminance change, and with emotional modulation by affective content, including both positive and negative affect.

Despite anecdotal accounts to suggest PTSD is associated with visibly larger pupils, there is no supporting research evidence measuring resting diameter of the pupil. However, there is some evidence that state anxiety can alter initial pupil diameter. For example, Hourdaki et al. (2005) found that participants under threat (of noise or electric shock) showed large pupil dilations even before any stimulus was presented. In line with the evidence for reduced parasympathetic tone and hyperarousal of the sympathetic nervous system, it was hypothesised that individuals with PTSD would show larger initial pupil diameter compared to control groups (hypothesis one).

Emotional arousal has been shown to reduce the constriction of the pupil that occurs in response to luminance changes (i.e. a flash of light). There is a reduced constriction in individuals anticipating an electric shock (Bitsios et al., 1996) and in individuals with anxiety disorder relative to controls (Bakes et al., 1990). Reductions in the light reflex have also been used as indicators of autonomic dysregulation in patients with schizophrenia (Bär et al., 2008). Due to the evidence for hypoarousal of the parasympathetic system, it was hypothesised that individuals with PTSD would show a reduced initial constriction reflex compared to control groups (hypothesis two).

It is unclear from previous literature as to whether the altered state of arousal and hypervigilance produced by the persistent sense of current threat in PTSD is specific to: a) trauma-related stimuli; b) threat/fear stimuli; c) any negative stimuli; or d) all affective stimuli (including positive). Due to the hyperarousal of the sympathetic system to threatening stimuli in people with PTSD, it was hypothesised that individuals with PTSD would show the greatest level of arousal to threat images during the pupil re-dilation phase (hypothesis three).

## Method

### Participants

The study was approved by the Research Ethics Committee at Cardiff University. All participants gave written informed consent to take part in the study.

Participants were recruited from the community through staff members within third sector military, addiction, homelessness, and women's shelter services across England and Wales. Eighty people volunteered to take part in the study, of whom fifteen violated exclusion criteria, providing a total sample of 65: 20 met diagnostic criteria for PTSD, 28 were trauma-exposed (but did not achieve diagnostic criteria for PTSD), and 17 control subjects did not report prior trauma exposure. Exclusion criteria for the study included self-reported current illicit substance use, history of dependent substance use, history of head injury, uncorrected visual problems, eye disease, and current use of any form of opiate drug (including codeine and heroin replacement prescriptions). Current substance abuse was evaluated by both self-report and report of staff members who knew the individual well. Individuals were not excluded for use of psychotropic medication, but this information was requested and recorded: 21 individuals reported a current prescription of psychotropic medication (primarily anti-depressants and anxiolytic medication) and there were no differences in the frequency of medication use across the three groups ($p$ = .33). A full

account of these statistical analyses of medication and co-morbid diagnoses, and their (lack of) effects on the results, are available in McKinnon (2017).

## Measures

### The Clinician Administered PTSD Scale for DSM-5 (CAPS-5).

The CAPS-5 (Weathers, Blake, Schnurr, Kaloupek, Marx, & Keane, 2013) is a 30-item structured interview, considered to be the gold-standard in PTSD assessment. The CAPS was used to assess participants for a current diagnosis of PTSD (symptoms within the last month). Within the current sample, the internal consistency of CAPS-5 ratings was high (Cronbach's alpha = .95). Interviews were transcribed for assessment of inter-rater reliability (IRR) between the main rater (AM) and a co-author who is a consultant clinical psychologist (NSG). Ten individuals were randomly selected for inter-rater reliability assessment with severity scores ranging between 2 – 59 ($M$ = 30, $SD$ = 20). All ten individuals met criterion A, with complete agreement between assessors (Cohen's $\kappa = 1.0$). Seven individuals met the criteria for a current diagnosis of PTSD, with complete diagnostic status agreement between assessors (Cohen's $\kappa = 1.0$). Reliability of symptom subscales was assessed through intra-class correlation statistics (ICC; Shrout & Fleiss, 1979). Throughout the 10 individual interviews, ICC values were high (Scale B = .95, Scale C = .97, Scale D = .96, Scale E = .97). There was complete agreement between ratings of functional impairment (level of distress, social impairment, and occupational impairment; Cohen's $\kappa = 1.0$).

### The Life Events Checklist with Extended Criterion A Assessment for DSM-5 (LEC-5).

The LEC-5 is a self-report measure designed to screen for potentially traumatic events in a respondent's lifetime (Weathers et al., 2013). The LEC-5 assesses exposure to 16 events known to potentially result in PTSD and includes one additional item assessing any 'other' extraordinarily stressful event not captured in the first 16 items. Previous versions of the LEC

have been shown to have adequate psychometric properties in both clinical and non-clinical samples (Gray, Litz, Hsu, & Lombardo, 2004), but there are no existing psychometric properties for the LEC-5. The LEC-5 was used to establish the presence and form of a Criterion A stressor.

**The Impact of Event Scale-Revised (IES-R).** The IES-R (Weiss & Marmar, 1997) is a 22 item self-report questionnaire measuring frequency of symptoms of posttraumatic intrusion (7 items), avoidance (8 items) and hyperarousal (7 items) occurring over the past seven days. Responses are measured on a 5-point Likert scale from 0 ('Not at all') to 4 ('Extremely'), with scores ranging from 0 - 88. Higher scores indicate higher symptom severity. Within the current sample, the internal consistency based upon 64 valid assessments was high (Cronbach's a = .96). As expected, there was a strong relationship between the CAPS-5 and the IES-R ($r$ = .88, $p$ <.001).

**Wechsler Abbreviated Scale of Intelligence.**

The Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) two-subscale assessment was used to evaluate intelligence quotient (IQ) of the participants. The two-subscale version takes around 20 minutes to administer and consists of verbal (oral word definitions to assess verbal concept formation) and performance subscales (matrix reasoning to assess perceptual organisation and broad visual intelligence). The measure produces an estimate of Full-Scale IQ (FSIQ).

**Pupillometry Task.**

The experimental paradigm employed was developed by O'Farrell (2016) and full details of task piloting and development are reported within the thesis. The task consisted of 40 images selected from the IAPS[1], divided into four emotive categories and presented in a

[1] IAPS reference numbers of stimuli used: Fear: 1220, 1300, 1301, 1321, 1930, 1932, 6250, 6300, 6370, 9405; Sad: 2800, 3230, 3350, 2730, 2710, 3180, 9040, 9410, 9250, 3266;

pseudo-random order. Negative-threat ('fear') images were selected from the affected category identified by Barke, Stahl, and Kroener-Herwig (2012). Negative-distress ('sad') images, positive-adrenaline ('happy') and neutral images formed the remaining categories. Fear, sad and happy images were matched on dimensions of arousal as well as on figural components and complexity of image. Images were converted to greyscale and matched on dimensions of image contrast and luminance using Adobe Photoshop Elements 12.0. Each test image was preceded by a grey screen presented for 2000ms. This blank screen included a fixation mark for the first 1000ms. The same blank screen was presented for 5000ms following the stimulus to allow the pupil to return to baseline. A short stimulus presentation (2000ms) was chosen to avoid problems due to boredom or lack of motivation and to assess the earlier, more automatic, pupil reactions to the stimuli (within 2000ms from stimulus onset), rather than those that might be evoked by purposeful emotion regulation strategies. Passive viewing of the stimuli was chosen to be in line with most previous studies that have examined these specific components of the pupillary response (Bradley et al, 2008; Bradley et al., 2017; Snowden et al., 2016). There were three main indices extracted from the data and used for the analysis: initial pupil diameter, initial constriction response, and the emotional modulation of the pupil by affective images in comparison to neutral images.

**Initial Pupil Diameter.**

In a typical pupillometry paradigm (see Snowden et al., 2016) a picture is presented to the participants for a short period of time. Standard responses are shown in Figure 1. The pupil starts at its resting level, termed the initial pupil diameter. The size of the pupil at rest reflects a balance in parasympathetic and sympathetic activity and has been used to examine

Happy: 8501, 8161, 2216, 8034, 8200, 8350, 2208, 4599, 8470, 8490; Neutral: 7002, 7004, 7006, 7009, 7010, 7020, 7025, 7030, 7031, 7150.

ANS function in many psychological and neurological conditions (e.g., Bär et al., 2008; Anderson & Colombo, 2009).

**Initial Constriction Response.**

Around 300ms after stimulus presentation the pupil begins a rapid constriction that typically nadirs at around 800ms (see Figure 1). This constriction response (also often termed the pupillary light reflex) is thought to be due to the physical properties of the stimulus such as brightness, contrast, and luminance (Barbur, 2004) and is mainly under the control of the parasympathetic system (Lowenstein & Loewenfeld, 1950; Giakoumaki et al., 2005). Hence, this component of the pupil's reactivity can be used as an index of parasympathetic function.

**Emotional Modulation of Pupil Response.**

Following the nadir of the constriction response, the pupil begins to dilate (see Figure 1). Typically, this dilation is greater when viewing an affective image (Bradley et al., 2008, Snowden et al., 2016) and is thought to reflect the activity of the sympathetic nervous system (Lowenstein & Loewenfeld, 1950; Bradley et al., 2008; Bradley et al., 2017). To index this reaction to the affective component of the stimulus, and therefore assess sympathetic activation, the size of the pupil to neutral stimuli can be subtracted from the size of the pupil to the affective stimuli.

The data cleaning methods are identical to those of Snowden et al. (2016). The diameters of the left and right pupils were recorded once every 16.7ms across trials for each condition. An average of the two eyes is reported in millimetres, where data is missing for one eye the monocular estimate is taken. Any pupil diameter change of ± 0.38mm within a 20ms interval was attributed to random fluctuation and removed (Partala & Surakka, 2003). Data within 33.3ms around these points were also removed to avoid anomalous readings. Missing data figures are reported after cleaning. A pre-stimulus onset 'baseline' period of 200 ms was calculated for each trial and subtracted from each subsequent data recording to

establish a change score metric. This 20ms baseline was averaged across trials to produce an initial pupil diameter. Graphs are displayed using a running median smoother for ease of visual representation, but data used for the analysis did not use this smoothing. The analysis was conducted using a script in Python using NumPy and Pandas extensions, and is available from https://doi.org/10.17605/OSF.IO/W2D67

**Procedure**

The researcher held an information session for staff and volunteers within each organisation to outline the purpose of the study and to describe the methods, procedure, and exclusion criteria. Potential participants were approached by a member of staff or volunteer team within the organisation, who offered an information leaflet and the opportunity to meet with the researcher to ask questions. Participants deemed eligible to take part were reimbursed for their time, which was either with cash or a voucher at the discretion of the participating organisation.

The study procedures took place in a private, artificially lit room. Participants gave written informed consent to all procedures. The full procedure took between one and a half to two and a half hours to complete, depending on whether the CAPS-5 interview was indicated (i.e. if the individual fulfilled Criterion A of the LEC-5).

For the pupillometry task, the participant was seated approximately 60cm away from a laptop screen, underneath which a Tobii X2-60 eye tracking device was secured. A calibration procedure was conducted for each participant using a 5-point calibration screen. During calibration, the participant was instructed to view a moving target (red dot) as it moved sequentially between 5 points on the screen over the course of 10s. The eye tracker then located the participant's pupils within an area of three-dimensional space, allowing for small head movements to occur without interrupting measurement, and negating the need for a head rest. Participants were told that a series of images would be displayed in greyscale in

the centre of the screen. Participants were informed that they were free to look at any aspect of the images, but should not take their eyes away from the screen at any point. Participants were informed that the task would take approximately five minutes, asked to pay attention throughout, and advised that they could blink during the task whenever needed.

The LEC-5 and Criterion A assessment were used to guide the assessment of PTSD using the CAPS-5 and IES-R. The respondent was asked to identify, at the end of the LEC-5, the single most stressful thing which had ever happened to them. The criterion A inquiry then followed. Individuals who did not satisfy the conditions of the criterion A assessment were not asked to complete the CAPS-5 interview, but still completed the IES-R. An example of a non-Criterion A trauma is a death by natural causes, or an injury in which there was no threat to life (perceived or actual).

## Results

### Demographic and Clinical Characteristics

From the sample of sixty-five individuals, forty-eight had been exposed to a Criterion A traumatic event. Twenty met diagnostic criteria for PTSD (termed PTSD group) and 28 did not (termed trauma group). The seventeen remaining participants who did not meet Criterion A formed the control group.

The groups were well matched on IQ and gender ratios (Table 1). There was no significant difference concerning IQ between the groups. There was no significant difference ($p$ = .14) in time since event in months between the PTSD (median = 108) and trauma control group (median = 234). However, there was a significant difference between group and age, with the PTSD group being statistically significantly younger than the control group ($p$ = .008). Age is controlled for in subsequent group analyses. As would be expected, the PTSD group had significantly higher scores on all clinical psychometrics.

### Pupillometry

Data averaged for all participants are presented in Figure 2 (these data were baseline corrected by subtracting the average pupil size in the time window 200ms prior to the test image). The data conformed to the expected pattern (see Figure 1), with a sharp decrease in pupil size commencing around 300ms and a nadir around 900ms. The pupil then increased in size during the remainder of the stimulus presentation. After the stimulus was removed (at 200ms) there was a second constriction (beginning 300ms after the stimulus was removed), before the pupil returned to baseline level over an approximate further 1500ms.

To extract the indices of performance, time windows that were established in previous research were used (Snowden et al., 2016). The initial pupil diameter was calculated as the average pupil size in the 200ms prior to stimulus presentation. The constriction response was calculated by averaging the pupil size in the window 500 – 1000ms post stimulus presentation (where the nadir occurs) for the baseline corrected data. Given the possible influence of the emotional content of the images on the initial constriction response (Henderson, Bradley & Lang, 2014), this was only performed for the neutral stimuli. The emotional modulation of the pupil response was taken by calculating the average pupil size in the 1000 – 2000ms post-target for the emotional stimuli and subtracting the pupil size for the neutral stimuli in the same time window. A positive modulation score means that the pupil was larger while viewing emotional images relative to neutral images.

**Initial Pupil Diameter.**

Total missing data within this window, after data cleaning, was 14.2%. Reliability was assessed through a split half measure. Correlational reliability analysis (corrected by the Spearman-Brown equation) showed excellent reliability ($r$ = .99).

The analysis of zero-order correlations (Table 2) indicated that initial pupil diameter was not significantly associated with any of the clinical variables, but was negatively associated with age (see also Winn, Whitaker, Elliott, & Phillips, 1994). Age has been used

as a covariate in later analyses. The finding that the initial pupil diameter was not related to PTSD symptom severity as assessed by either the CAPS-5 or the IES-R was important, as it suggested that individuals with greater symptom severity did not demonstrate abnormality in initial pupil diameter.

An ANCOVA was used to determine the effect of PTSD status on initial pupil diameter, controlling for age. After adjustment for a significant effect of age ($p < .001$), there was no significant difference in initial pupil diameter across groups, $F(2, 61) = 1.76$, $p = .18$. (PTSD: $M = 3.88$, 95% CI [3.59, 4.18]; trauma $M = 4.08$, 95% CI [3.66, 4.46]; control: $M = 4.07$, 95% CI [3.50, 4.21]).

**Constriction Response.**

Total missing data within this window (500-1000ms), after data cleaning, was 8.8%. Correlational reliability analysis (corrected by Spearman-Brown) showed excellent reliability ($r = .92$). Pupil sizes (with the initial pupil diameter subtracted) are illustrated in Figure 3, with the pupil size as a function of time depicted for the three groups (Figure 3. Left side), and the average pupil size in the constriction window (500 – 1000ms) in Figure 3 (right side).

A one-way ANCOVA to determine the effect of PTSD status on the constriction response was conducted, controlling for age. After adjustment for the effect of age ($p = .01$), there was a significant effect of PTSD status, $F(2, 61) = 5.00$, $p = .01$, $\eta_2 = .14$. Follow-up *t*-tests showed the PTSD group had a larger pupil size (and therefore a smaller constriction response) than the trauma group ($p = .006$, $d = 0.76$), and the control group ($p = .008$, $d = 0.91$), demonstrating that only the individuals who had experienced a traumatic event and met criteria for PTSD showed a reduction in the constriction response.

Analysis of zero-order correlations (Table 2) indicated that all the clinical variables were positively related to pupil size (i. e., greater levels of symptoms were associated with

larger pupils and therefore a smaller constriction response). The correlations suggest that all sub-scales of the CAPS-5 gave similar results.

**Emotional Modulation of the Pupil Response.**

Total missing data within this 1000 – 2000ms window, after data cleaning, was 10.2%. Correlational reliability analysis (corrected by Spearman-Brown) suggested good reliability for neutral ($r$ = .88); happy ($r$ = .89); sad ($r$ = .83); and fear ($r$ = .91) images within this window.

A mixed 4 x 3 ANOVA was conducted on pupil size (corrected for initial pupil size) to determine the effect of the within groups factor (emotion: neutral, fear, happy, and sad) and the between groups factor (PTSD status: PTSD, trauma-exposed, and control) on the pupil response in this time window. There was a significant main effect of emotion, $F(3, 186) = 38.34$, $p < .001$, $\eta_p^2 = .38$, and a significant main effect of PTSD status, $F(2, 62) = 5.29$, $p = .008$, $\eta_p^2 = .15$, and a significant interaction between emotion and PTSD status, $F(6, 186) = 2.50$, $p = .03$, $\eta_p^2 = .08$. Inclusion of age as a covariate did not alter this pattern of results.

In order to understand this interaction, we performed a series of planned comparisons. For each emotional category we computed an emotional index by calculating the difference between each affective stimulus type and the neutral stimuli. These are displayed stratified by PTSD group in Figure 4.

***Fear images.*** A univariate ANOVA found a significant effect of PTSD status on the emotional modulation of the pupil response by fear images, $F(2, 61) = 4.62$, $p = .01$, $\eta 2 = .13$. Planned comparisons showed that the PTSD group had a greater emotional modulation than both the trauma-exposed participants ($p = .003$, $d = 0.87$), and the control group ($p = .007$, $d = 0.85$).

***Happy Images.*** A univariate ANOVA showed a significant effect of group for happy images $F(2, 61) = 3.32$, $p = .04$, $\eta 2 = .10$. Planned comparisons showed the PTSD group had a

greater emotional modulation than both the trauma-exposed group ($p$ = .008, $d$ = 0.73) and the control group ($p$ = .003, $d$ = 0.97).

***Sad Images.*** A univariate ANOVA showed no significant effect of group for sad images $F(2, 61) = .24$, $p$ =.78.

The zero-order correlations (see Table 2) of the emotional modulation of the pupil response and the clinical variables show positive correlations for most of the clinical scales for the fear and happy stimuli (indicating greater responses to these stimuli for people with greater severity of PTSD symptoms). No significant results were found for the sad images.

## Discussion

This study assessed alterations in emotional responsivity in individuals with PTSD thus contributing to the developing body of evidence for the use of pupillometry in this population. Given the persistent sense of current threat posed within the PTSD model (Ehlers & Clark, 2000), this study explored whether enhanced emotional responsivity was specific to negative and threatening images, or whether this leads to an automatic preparation for threat when faced with any affective stimuli. The experimental stimuli produced the expected pattern of results, with a robust early constriction response of the pupil on presentation of an image, followed by a recovery that was strongly influenced by the emotional content of the image (Bradley et al, 2008; Snowden et al., 2016). Contrary to hypothesis one, individuals with PTSD did not show a larger initial pupil diameter. However, there was support for hypothesis two: individuals with PTSD showed a reduced initial constriction response to light, compared to trauma-exposed individuals (without PTSD) and controls (not trauma-exposed). There was partial support for hypothesis 3: individuals with PTSD had greater emotional modulation of the pupil response for both the emotional categories of threat and

happy images (but not sad images), indicating that sensitivity to emotional stimuli in PTSD was not limited to fear or threat stimuli.

The initial pupil diameter was not significantly related to any measure of PTSD or trauma. Bakes et al. (1990) found no significant difference in resting pupil size after dark adaptation in individuals with anxiety versus controls, and Felmingham et al. (2011) found no differences between individuals with and without PTSD assessed in a lit room. Hence, there are no existing published studies reporting alterations in initial pupil sizes at rest or at baseline in PTSD, despite anecdotal reporting of larger pupils. A study by Bitsios et al. (1996) found increased resting pupil diameter during fear-conditioning, suggesting larger initial pupil diameter can be linked to phasic task-related fear, and that initial pupil diameter is associated with state measures of affective response, rather than more stable trait or chronic symptoms.

In the PTSD group the amplitude of the pupil constriction response was significantly reduced, with a large effect size. The reduction in the constriction response was also related to greater symptom severity in dimensional analyses, but there is no specific symptom subscale that was associated with this. While we believe this is the first study to demonstrate reduced pupil constriction response in people with PTSD, previous studies have found changes in constriction response during anxious states (Bitsios et al., 1996) and in individuals with high trait anxiety (Bakes et al., 1990). However, these latter studies assessed pupil activity using the pupillary light reflex paradigm, which is typically done under conditions of dark adaptation to maximise the initial size of the pupil (see Bistios et al., 1996). This kind of dark adaptation paradigm is more powerful in assessing a reduction in constriction amplitude, as the resting pupil is larger in darkness, and the assessment presents only a brief flash of light. However, such an assessment requires the participant to dark adapt which can take tens of minutes of the participant sitting in a completely dark room. This is also prone to causing

the participant anxiety and therefore leading to a potentially important confound between anxiety response and sensitivity to sitting in darkness and an increased stress response in certain individuals.

Assessment in conditions of moderate light can be done without this period of adaptation and is a more appropriate paradigm for the assessment of pupil dilation due to the influence of affective stimuli (Steinhauer et al., 2004). That is, if the pupil is already maximally dilated, as in conditions of darkness, this leads to a ceiling effect for the emotional modulation parameter. We also argue that assessment of the pupil constriction response in moderate light conditions is less anxiety-provoking and more tolerable for individuals with PTSD and those who are anxious or hypervigilant. Anxious individuals would be likely not to feel comfortable sitting silently within a dark room for many minutes waiting to dark adapt.

The reduction of the constriction response in PTSD is suggestive of a reduction in parasympathetic activity. Parasympathetic dysfunction appears in several psychiatric disorders and physical diseases. For instance, Wang et al. (2016) found 30 out of 36 studies reviewed reported parasympathetic dysfunction based on pupillary light reflex measurements in a diverse range of patient groups (including Parkinson's Disease, schizophrenia, diabetes, heart failure etc.) versus healthy controls.

Previous studies that provide evidence for reduced parasympathetic activity in PTSD have relied mainly on studies of heart rate and heart rate variability (Hopper, Spinazzola, Simpson, & van der Kolk, 2006; Sahar, Shalev & Porges, 2001; Tan, Dao, Farmer, Sutherland, Gervitz, 2011). However, dissociating low parasympathetic activity from high sympathetic activity is not easy in these paradigms, and the use of pupillometry may prove to be a useful addition with which to examine nervous system functioning in PTSD due to titration of the parasympathetic response.

Autonomic hyperarousal during symptom provocation (i.e. emotional responsivity secondary to trauma reminders) has been well documented in PTSD (Pole, 2007). The result of increased pupil reactivity to threatening stimuli in PTSD appears in line with the findings of Cascardi et al. (2015), but the two paradigms differ in several important ways. First, the stimuli in Cascardi et al. (2015) were presented for a long time (30s) and the pupil dilation response was not isolated by a standardised analysis window, but was measured during fixations on specific threat elements of these images. Such a paradigm is prone to possible differences in fixation patterns between the groups. Thus, if the PTSD group is vigilant to threat and focus more on threat stimuli contained within an image then this may lead to differences in pupil response. Second, the study of Cascardi et al. (2015) differed from the current study in that the majority of participants were women who had been subject to violent trauma. Fifty-five percent of the current sample were men, and experiences of trauma-type varied widely due to the sampling technique. These differences between the studies, yet the common finding of a categorical difference in pupil response between PTSD and controls, add to the robustness of the finding and strengthens the argument for the potential of the use of pupillometry in the assessment of PTSD.

The finding of increased emotional modulation of the pupil response in PTSD across positive and negative affective categories, rather than that of a specific threat response, was unexpected. This suggests that the emotional hyperarousal found in PTSD is not confined to just threat-related stimuli, nor indeed to just negatively-valenced stimuli. However, other studies of trauma-unrelated emotional processing using indices of autonomic activity are rare. A study by Litz, Orsillo, Kaloupek, and Weather (2000) assessed heart rate and skin conductance to positive, neutral, and negatively arousing images from the International Affective Picture Set (IAPS) in veterans with PTSD and well-adjusted veteran controls. They found that the PTSD group showed higher heart rate reactivity to all images. Litz et al.

suggested that this was indicative of automatic preparation for threat during uncertain emotional contexts, a conclusion supported by the present findings. Further, White, Costanzo, Blair, and Roy (2015) found that greater PTSD symptom levels (although all were sub-threshold to a diagnosis of PTSD) in veterans were associated with increased amygdala activation to both positive and negative emotional stimuli.

While these results suggest that PTSD may be related to a hypersensitivity to all categories of emotional stimuli, we did not find evidence for this thesis when using sad images. It is notable (see Figures 2 and 4) that these sad images produce the greatest pupil response in all of the groups and that the control group produced much greater pupil responses to these sad images than to the fear or happy images. There is also a trend in the data for the PTSD group to show the greatest pupil response to sad images. Therefore, it may be that the strong pupillometry responses produced by these sad images might lead to a "ceiling effect" whereby the pupil's ability to grow larger in individuals with PTSD begins to saturate as the baseline responses grow larger and hence the clinical groups appear more similar than for lower levels of emotional modulation. Future studies are needed to examine these hypotheses more closely, but we predict that the PTSD group will show greater responses than the control groups for sad images that are "less sad" than the images used in the present experiment.

There are a number of limitations to the present study. First, the sample sizes used were modest, but in line with most previous comparable research. However, the sample size was not well powered to detect small effect sizes such as possible differences in the correlations between the different symptom types of PTSD.

Second, the study design was cross sectional, sampling individuals at one point in time post-traumatic event. Hence, it is not clear whether the presence of PTSD caused affective sensitivity, or whether this sensitivity represented a pre-existing trait vulnerability to

the disorder in certain individuals. Further study would be required to see if these atypical pupil responses are due to significant trauma leading to PTSD or whether they are present before exposure to traumatic events, leading to vulnerability to acquire PTSD in the face of trauma.

Third, the samples were not matched on age due to quasi-experimental, opportunistic sampling. This confound was considered and statistically controlled for within all statistical analyses. Comorbidity in mental disorder is high, but use of a diagnostic measure to obtain a clinical sample (as opposed to looking at symptoms alone), as well as two control-comparison groups (trauma-exposed but no PTSD, and no trauma) were employed to partly address this limitation. Thus, the pattern of significant results in PTSD can be compared to both trauma-exposed groups and control groups, with slightly different demographics and symptom levels in each. To reduce sampling bias, we recruited our entire sample from charitable and third sector organisations, rather than recruiting a 'typical' healthy control sample with no symptoms. Future studies could employ the use of an anxiety disorder control group, such as a group of individuals with generalised anxiety disorder, to assess whether these emotional processing differences are unique to PTSD.

Finally, the sample was formed of individuals who had experienced a heterogenous array of potentially traumatic events. This is not necessarily a limitation, as it demonstrates that the construct of PTSD was associated with alterations in pupil response and arousal in a diverse clinical sample. However, it is an atypical group as most studies employ samples of individuals who have been exposed to similar types of trauma, such as with military samples.

In future studies, the use of a pre-test and post-test design measuring pupil activity before and after a treatment intervention for PTSD would provide a further powerful test of changes in autonomic function in PTSD alongside symptom reduction and improvements in clinical presentation. Overall, this study demonstrates that the use of pupillometry is sensitive to

alterations in arousal that are hypothesised to occur due to mental disorder and demonstrates the utility of examining the full waveform of pupil activity, from resting baseline, to constriction, to re-dilation.

Overall, the pattern of results reported (i.e., no alteration in initial pupil diameter, reduced reactivity to visual stimulation, and greater responsivity to emotional stimuli) suggest that people with PTSD have altered autonomic function. The approach herein fits with strategies that encourage the exploration of underlying pathophysiological mechanisms in mental health and mental disorder, such as the Research Doman Criteria (RDoC; Insel et al., 2010) in development by the US National Institute of Mental Health. RDoC aims to form a biologically valid framework for the understanding of mental disorders (e.g., via genetic analysis and neuroscience) as distinct from a focus upon symptomatology and clinical presentation. The implications of *hypo*arousal in the parasympathetic system are similar to those of *hyper*arousal in the sympathetic system, resulting in a chronic hyperarousal and sensitivity to emotional stimuli. Heightened emotional processing is coupled with a corresponding failure to regulate arousal. Such a system may be valuable in the short-term (e.g. for maintaining vigilance, detecting danger, and responding quickly). However, in the long-term, these characteristics can be biologically costly and are associated with a large range of poor health outcomes, including increased mortality (Williamson et al., 2005), in a manner similar to those under constant stress (McEwen, 2007). The emotional vigilance demonstrated here via pupillometry suggests PTSD could be maintained by rapid, pre-cognitive, autonomic hyperarousal to both positive and negative categories of affective stimuli. It is possible that individuals misattribute this heightened arousal (Schachter, 1962; Cotton, 1981), such that even benign positive stimuli contribute to the vicious cycle of hypervigilance and threat sensitivity. Individuals with PTSD are so prepared to encounter threat in their day-to-day lives that any emotional stimulation (either positive or negative) can

feel over-whelming, requiring additional emotional regulation resources on an already over-burdened system (Seligowski, Lee, Bardeen & Orcutt, 2015).

## References

Agorastos, A., Boel, J. A., Heppner, P. S., Hager, T., Moeller-Bertram, T., Haji, U., … Stiedl, O. (2013). Diminished vagal activity and blunted diurnal variation of heart rate dynamics in posttraumatic stress disorder. *Stress*, *16*(3), 300–310. https://doi.org/10.3109/10253890.2012.751369

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders: DSM-5*. (5th ed.). Washington, DC.

Anderson, C. J., & Colombo, J. (2009). Larger tonic pupil size in young children with autism spectrum disorder. *Developmental Psychobiology, 51*(2), 207-211. https://doi.org/10.1002/dev.20352

Bakes, A., Bradshaw, C. M., & Szabadi, E. (1990). Attenuation of the pupillary light reflex in anxious patients. *British Journal of Clinical Pharmacology*, *30*(3), 377–381. https://doi.org/10.1111/j.1365-2125.1990.tb03787.x

Bär, K.-J., Boettger, M. K., Schulz, S., Harzendorf, C., Agelink, M. W., Yeragani, V. K., … Voss, A. (2008). The interaction between pupil function and cardiovascular regulation in patients with acute schizophrenia. *Clinical Neurophysiology:19*(10), 2209–2213. https://doi.org/10.1016/j.clinph.2008.06.012

Barbur, J. L. (2004). Learning from the pupil - studies of basic mechanisms and clinical applications. In L. M. Chalupa & J. S. Wener (Eds.), *The Visual Neurosciences* (pp. 641- 656). Cambridge, MA, USA: MIT Press.

Barke, A., Stahl, J., & Kröner-Herwig, B. (2012). Identifying a subset of fear-evoking pictures from the IAPS on the basis of dimensional and categorical ratings for a German sample. *Journal of Behavior Therapy and Experimental Psychiatry*, *43*(1), 565–572. https://doi.org/10.1016/j.jbtep.2011.07.00

Bitsios, P., Szabadi, E., & Bradshaw, C. M. (1996). The inhibition of the pupillary light reflex by the threat of an electric shock: a potential laboratory model of human anxiety. *Journal of Psychopharmacology*, *10*(4), 279–287. https://doi.org/10.1177/026988119601000404

Bradley, M. M., Miccoli, L., Escrig, M. A., & Lang, P. J. (2008). The pupil as a measure of emotional arousal and autonomic activation. *Psychophysiology*, *45*(4), 602–607. https://doi.org/10.1111/j.1469-8986.2008.00654.x

Bradley, M. M., Sapigao, R. G., & Lang, P. J. (2017). Sympathetic ANS modulation of pupil diameter in emotional scene perception: Effects of hedonic content, brightness, and contrast. *Psychophysiology*. https://doi.org/10.1111/psyp.12890

Burkhouse, K. L., Siegle, G. J., Woody, M. L., Kudinova, A., & Gibb, B. E. (2015). Pupillary reactivity to sad stimuli as a biomarker of depression risk: Evidence from a prospective study of children. *Journal of Abnormal Psychology*, *124*(3), 498–506. https://doi.org/10.1037/abn0000072

Burley, D. T., Gray, N. S., & Snowden, R. J. (2017). As far as the eye can see: Relationship between psychopathic traits and pupil response to affective stimuli. *PLOS ONE*, *12*(1), e0167436. https://doi.org/10.1371/journal.pone.0167436

Burley, D. T., Gray, N. S., & Snowden, R. J. (2019). Emotional modulation of the pupil response in psychopathy. *Personality Disorders: Theory, Research, and Treatment*, *10*(4), 365-375. http://dx.doi.org/10.1037/per0000313

Cascardi, M., Armstrong, D., Chung, L., & Paré, D. (2015). Arousal-related pupil response to threat: A comparison of trauma-exposed individuals with and without PTSD. *Journal of Traumatic Stress*, *28*(4), 370–374. https://doi.org/10.1002/jts.22022

Clancy, K., Ding, M., Bernat, E., Schmidt, N. B., & Li, W. (2017). Restless 'rest': Intrinsic sensory hyperactivity and disinhibition in post-traumatic stress disorder. *Brain: A Journal of Neurology*, *140*(7), 2041–2050. https://doi.org/10.1093/brain/awx116

Cotton, J. L. (1981). A review of research on Schachter's theory of emotion and the misattribution of arousal. *European Journal of Social Psychology*, *11*(4), 365-397. https://doi.org/10.1002/ejsp.2420110403

Daluwatte, C., Miles, J. H., Christ, S. E., Beversdorf, D. Q., Takahashi, T. N., & Yao, G. (2013). Atypical pupillary light reflex and heart rate variability in children with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *43*(8), 1910–1925. https://doi.org/10.1007/s10803-012-1741-3

Dedert, E. A., Calhoun, P. S., Watkins, L. L., Sherwood, A., & Beckham, J. C. (2010). Posttraumatic stress disorder, cardiovascular, and metabolic disease: a review of the evidence. *Annals of Behavioral Medicine, 39*(1), 61-78. https://doi.org/10.1007/s12160-010-9165-9

Felmingham, K. L., Rennie, C., Manor, B., & Bryant, R. A. (2011). Eye tracking and physiological reactivity to threatening stimuli in posttraumatic stress disorder. *Journal of Anxiety Disorders*, *25*(5), 668–673. https://doi.org/10.1016/j.janxdis.2011.02.010

Forneris, C. A., Butterfield, M. I., & Bosworth, H. B. (2004). Physiological arousal among women veterans with and without posttraumatic stress disorder. *Military Medicine*, *169*(4), 307–312. https://doi.org/10.7205/milmed.169.4.307

Gabella, G. (1976). *Structure of the Autonomic Nervous System*. London: Chapman and Hall.

Giakoumaki, S. G., Hourdaki, E., Grinakis, V., Theou, K., & Bitsios, P. (2005). Effects of peripheral sympathetic blockade with dapiprazole on the fear-inhibited tight reflex. *Journal of Psychopharmacology, 19*(2), 139-148. https://doi.org/10.1177/0269881105048994

Granholm, E., Morris, S., Galasko, D., Shults, C., Rogers, E., & Vukov, B. (2003). Tropicamide effects on pupil size and pupillary light reflexes in Alzheimer's and Parkinson's disease. *International Journal of Psychophysiology*, *47*(2), 95–115. https://doi.org/10.1016/S0167-8760(02)00122-8

Gray, M. J., Litz, B. T., Hsu, J. L., & Lombardo, T. W. (2004). Psychometric properties of the Life Events Checklist. *Assessment, 11*(4), 330-341. https://doi.org/10.1177/1073191104269954

Henderson, R. R., Bradley, M. M., & Lang, P. J. (2014). Modulation of the initial light reflex during affective picture viewing. *Psychophysiology*, *51*(9), 815–818. https://doi.org/10.1111/psyp.12236

Hopper, J. W., Spinazzola, J., Simpson, W. B., & van der Kolk, B. A. (2006). Preliminary evidence of parasympathetic influence on basal heart rate in posttraumatic stress disorder. *Journal of Psychosomatic Research, 60*(1), 83-90. https://doi.org/10.1016/j.jpsychores.2005.06.002

Hourdaki, E., Giakoumak, S. G., Grinakis, V., Theou, K., Karataraki, M., & Bitsios, P. (2005). Parametric exploration of the fear-inhibited light reflex. *Psychophysiology*, *42*(4), 447-455. https://doi.org/10.1111/j.1469-8986.2005.00301.x

Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D. S., Quinn, K., ... & Wang, P. (2010). Research domain criteria (RDoC): toward a new classification framework for research on mental disorders. https://doi.org/10.1176/appi.ajp.2010.09091379

Kimble, M. O., Fleming, K., Bandy, C., Kim, J., & Zambetti, A. (2010). Eye tracking and visual attention to threating stimuli in veterans of the Iraq war. *Journal of Anxiety Disorders*, *24*(3), 293–299. https://doi.org/10.1016/j.janxdis.2009.12.006

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1997). International affective picture system (IAPS): Technical manual and affective ratings. *NIMH Center for the Study of Emotion and Attention*, 39–58.

Liberzon, I., Abelson, J. L., Flagel, S. B., Raz, J., & Young, E. A. (1999). Neuroendocrine and psychophysiologic responses in PTSD: A symptom provocation study. *Neuropsychopharmacology*, *21*(1), 40. https://doi.org/10.1016/S0893-133X(98)00128-6

Litz, B. T., Orsillo, S. M., Kaloupek, D., & Weathers, F. (2000). Emotional processing in posttraumatic stress disorder. *Journal of Abnormal Psychology*, *109*(1), 26–39. https://doi.org/10.1037//0021-843x.109.1.26

Lowenstein, O., & Loewenfeld, I. E. (1950). Mutual role of sympathetic and parasympathetic in shaping of the pupillary reflex to light: Pupillographic studies. *Archives of Neurology & Psychiatry*, *64*(3), 341-377. https://doi.org/10.1001/archneurpsyc.1950.02310270030002

McEwen, B. S. (2007). Physiology and neurobiology of stress and adaptation: Central role of the brain. *Physiological Reviews*, *87*(3), 873-904. https://doi.org/10.1152/physrev.00041.2006

McKinnon, A. (2017). *Assessing physiological sensitivity in Post-Traumatic Stress Disorder*. PhD Thesis, Cardiff University. http://orca.cf.ac.uk/id/eprint/110198

Meyer, T., Albrecht, J., Bornschein, G., Sachsse, U., & Herrmann-Lingen, C. (2016). Posttraumatic Stress Disorder (PTSD) patients exhibit a blunted parasympathetic response to an emotional stressor. *Applied psychophysiology and biofeedback*, *41*(4), 395-404.

Micieli, G., Tassorelli, C., Martignoni, E., Pacchetti, C., Bruggi, P., Magri, M., & Nappi, G. (1991). Disordered pupil reactivity in Parkinson's disease. *Clinical Autonomic Research, 1*(1), 55–58. https://doi.org/10.1007/BF01826058

Mott, F. W. (1919). *War neurosis and shell shock.* London: Oxford University Press.

O'Farrell, K. R. (2016). *Assessment of emotional processes and psychopathy among offenders using both behavioural and physiological measures* (PhD Thesis). Cardiff University, Cardiff, UK. http://ethos.bl.uk/OrderDetails.do?uin=uk.bl.ethos.699372

Partala, T., & Surakka, V. (2003). Pupil size variation as an indication of affective processing. *International Journal of Human-Computer Studies*, *59*(1–2), 185–198. https://doi.org/10.1016/S1071-5819(03)00017-X

Pole, N. (2007). The psychophysiology of posttraumatic stress disorder: A meta-analysis. *Psychological Bulletin, 133*(5), 725–746. https://doi.org/10.1037/0033-2909.133.5.725

Sahar, T., Shalev, A. Y., & Porges, S. W. (2001). Vagal modulation of responses to mental challenge in posttraumatic stress disorder. *Biological Psychiatry, 49*(7), 637-643. https://doi.org/10.1016/s0006-3223(00)01045-3

Schachter, S., & Singer, J. (1962). Cognitive, social, and physiological determinants of emotional state. Psychological review, 69(5), 379. https://doi:10.1037/h0046234

Seligowski, A. V., Lee, D. J., Bardeen, J. R., & Orcutt, H. K. (2015). Emotion regulation and posttraumatic stress symptoms: A meta-analysis. *Cognitive Behaviour Therapy*, *44*(2), 87-102. https://doi.org/10.1080/16506073.2014.980753

Sherin, J. E., & Nemeroff, C. B. (2011). Post-traumatic stress disorder: the neurobiological impact of psychological trauma. *Dialogues in Clinical Neuroscience*, *13*(3), 263–278.

Shrout, P. E., & Fleiss, J. L. (1979). Intraclass correlations: Uses in assessing rater reliability. *Psychological Bulletin, 86*(2), 420–428.

Shvil, E., Rusch, H. L., Sullivan, G. M., & Neria, Y. (2013). Neural, psychophysiological, and behavioral markers of fear processing in PTSD: A review of the literature. *Current Psychiatry Reports, 15*(5), 358. https://doi.org/10.1007/s11920-013-0358-3

Snowden, R. J., O'Farrell, K. R., Burley, D., Erichsen, J. T., Newton, N. V., & Gray, N. S. (2016). The pupil's response to affective pictures: Role of image duration, habituation, and viewing mode. *Psychophysiology, 53*(8), 1217–1223. https://doi.org/10.1111/psyp.12668

Steinhauer, S. R., Siegle, G. J., Condray, R., & Pless, M. (2004). Sympathetic and parasympathetic innervation of pupillary dilation during sustained processing. *International Journal of Psychophysiolog, 52*(1), 77–86. https://doi.org/10.1016/j.ijpsycho.2003.12.005

Streeter, C. C., Gerbarg, P. L., Saper, R. B., Ciraulo, D. A., & Brown, R. P. (2012). Effects of yoga on the autonomic nervous system, gamma-aminobutyric-acid, and allostasis in epilepsy, depression, and post-traumatic stress disorder. *Medical Hypotheses, 78*(5), 571–579. https://doi.org/10.1016/j.mehy.2012.01.021

Tan, G., Dao, T. K., Farmer, L., Sutherland, R. J., & Gevirtz, R. (2011). Heart rate variability (HRV) and posttraumatic stress disorder (PTSD): a pilot study. Applied psychophysiology and biofeedback, 36(1), 27-35. https://doi.org/10.1007/s10484-010-9141-y

Wang, Y., Zekveld, A. A., Naylor, G., Ohlenforst, B., Jansma, E. P., Lorens, A., … Kramer, S. E. (2016). Parasympathetic nervous system dysfunction, as identified by Pupil Light Reflex, and its possible connection to hearing impairment. *PLOS ONE, 11*(4), e0153566. https://doi.org/10.1371/journal.pone.0153566

Weathers, F. W., Blake, D. D., Schnurr, P. P., Kaloupek, D. G., Marx, B. P., & Keane, T. M. (2013). The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5). Interview available from the National Center for PTSD at www.ptsd.va.gov.

Wechsler, D. (1999). *Wechsler Abbreviated Scale of Intelligence*. San Antonio, TX: The Psychological Corporation.

Weiss, D. S., & Marmar, C. R. (1997). The Impact of Event Scale—Revised. J. P. Wilson, & T. M. Keane (Eds.). In *Assessing psychological trauma and PTSD: A handbook for practitioners.* (pp. 399–411). New York: Guilford Press.

White, S. F., Costanzo, M. E., Blair, J. R., & Roy, M. J. (2015). PTSD symptom severity is associated with increased recruitment of top-down attentional control in a trauma-exposed sample. *NeuroImage: Clinical*, *7*, 19–27. https://doi.org/10.1016/j.nicl.2014.11.012

Williamson, J. B., Porges, E. C., Lamb, D. G., & Porges, S. W. (2015). Maladaptive autonomic regulation in PTSD accelerates physiological aging. *Frontiers in Psychology*, *5*. https://doi.org/10.3389/fpsyg.2014.01571

Winn, B., Whitaker, D., Elliott, D. B., & Phillips, N. J. (1994). Factors affecting light-adapted pupil size in normal human subjects. *Investigative Ophthalmology & Visual Science*, *35*(3), 1132–1137.

**Figure Legends**

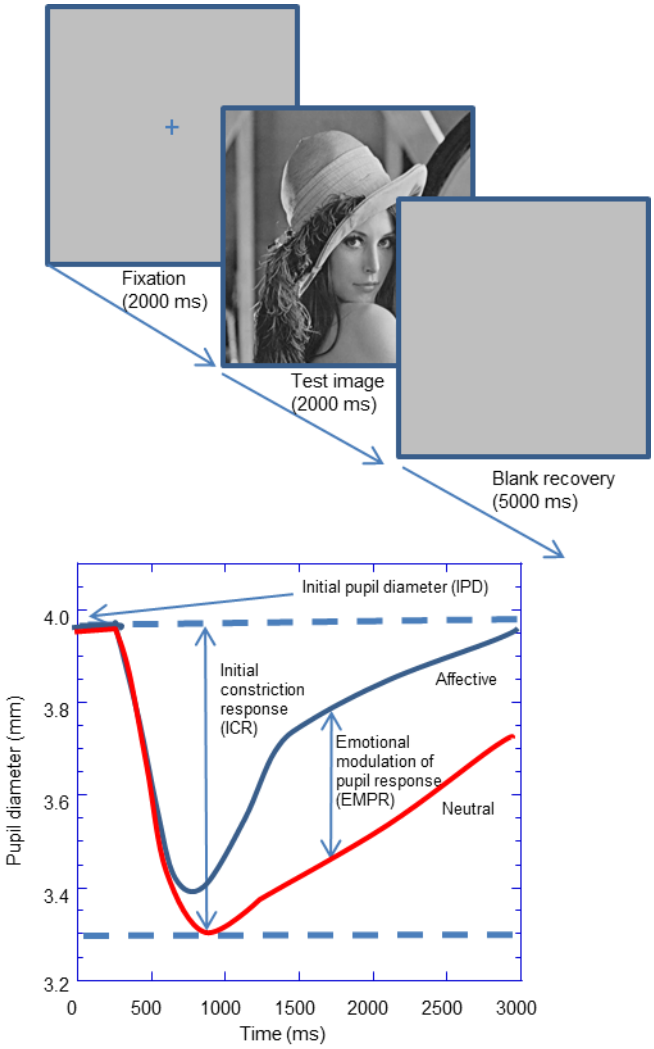


Figure 1. A visual representation of an experimental trial and the prototypical response of the pupil.

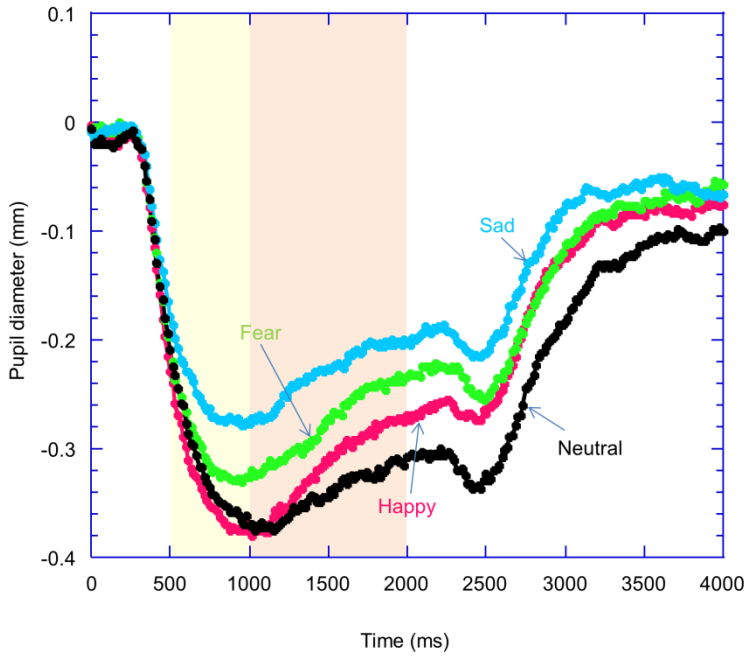


Figure 2. Mean change in pupil diameter from stimulus onset to 4000ms for *N* = 65 participants. The shaded areas represent the two analysis windows of interest. a = 500–1000ms: the constriction response, and b = 1000– 2000ms: the re-dilation response.

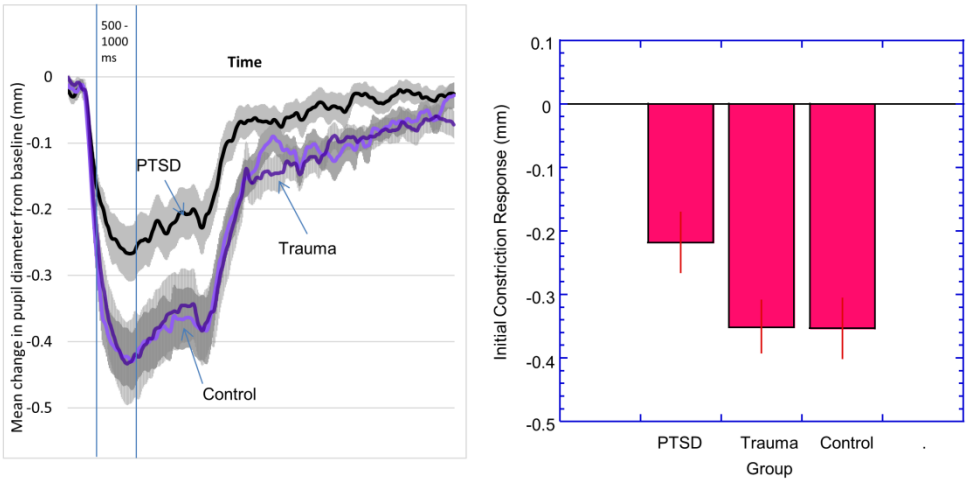


Figure 3. Left side. Response over time to the neutral stimuli stratified by group. Light gray bars indicate 95% confidence intervals. Right side. Mean pupil size to the neutral images by group within the 500 – 1000ms window. Error bars represent +/- 1 standard error.

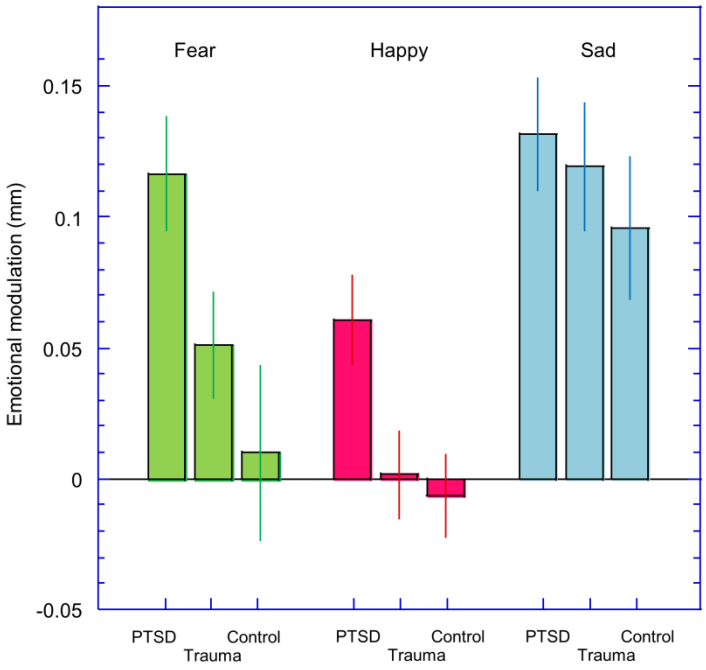


Figure 4. Group differences in the emotionally modulated pupil response to fear, happy and sad images. Error bars represent +/- 1 standard error.

Table 1.
*Group demographics and clinical characteristics.*

| | PTSD (*n* = 20) | Trauma (*n* = 28) | Control (*n* = 17) | Internal consistency |
|---|---|---|---|---|
| Age | 38.3 (*10.3)* | 45.2 *(15.4)* | 50.3 *(12.8)* | |
| Gender | 50% female | 43% female | 47% female | |
| IQ | 103.6 *(20.3)* | 104.8 *(16.6)* | 109.5 *(22.8)* | |
| CAPS-5 | 41.9 *(14.1)* | 8.5 *(9.3)* | - | .95 |
| IES-R | 55.6 *(15.8)* | 18.1 *(18.5)* | 9.9 *(19.6)* | .97 |

*Note.* Mean *(Standard deviation).* Internal consistency is represented by Cronbach's Alpha.

Table 2

*Zero-order Correlations between PTSD severity and pupil responses within the sample (N = 65 for measures not using the CAPS-5, n = 48 for CAPS-5 measures)*

| | CAPS-5 | CAPS-B Intrusion | CAPS-C Avoidance | CAPS-D Negative Cognition | CAPS-E Hyperarousal | IES-R | Age |
|---|---|---|---|---|---|---|---|
| Initial pupil diameter | .03 | .06 | .06 | .01 | .00 | -.15 | -.47* |
| Constriction response | .35** | .29* | .26* | .36** | .31* | .26* | .19 |
| EMPR-fear | .29* | .28* | .18 | .29* | .21 | .15 | -.11 |
| EMPR-sad | .00 | -.12 | .01 | .01 | .00 | .02 | -.12 |
| EMPR - Happy | .29* | .29* | .21 | .28* | .18 | .08 | -.22 |

*Note*. EMPR = Emotional Modulation of the Pupil Response. * $p < .05$, ** $p < .01$