Investigating pupillometry to detect emotional regulation difficulties in post-traumatic

stress disorder

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Abstract

Objective

Individuals with posttraumatic stress disorder (PTSD) have been found to exhibit emotional regulation difficulties. However, the specific neural mechanisms that underlie these difficulties remain understudied. This study aimed to use pupillometry as an index function of parasympathetic nervous system activation, to investigate the mechanisms underlying emotional regulation difficulties in individuals with PTSD.

Method

A total of 87 trauma-exposed mothers (34 with PTSD and 53 non-PTSD controls) completed an eye tracking assessment in which pupillary dilation in response to emotionally valenced stimuli was measured. The participants also completed two self-report measures of emotional regulation, namely the Difficulties in Emotional Regulation Scale and the Emotional Regulations Questionnaire. Linear mixed-effect modelling was used to assess potential group differences.

Results

The PTSD group exhibited increased pupillary dilation to positively valenced stimuli compared to the non-PTSD group. However, no significant associations between the self-report measures and pupillary response to emotionally valenced stimuli were found.

Conclusion

Increased pupillary dilation in PTSD may reflect impaired parasympathetic nervous system processes. The lack of association of these measures with self-reported emotion regulation may suggest reporting biases. Larger studies with more generalized populations are required to consolidate these preliminary findings.

Keywords

Emotional regulation, Eye tracking, Parasympathetic nervous system, Posttraumatic Stress

Disorder, Pupillometry

Introduction

Posttraumatic Stress Disorder (PTSD) has been associated with impaired emotional regulation (Weiss et al., 2018); a multi-faceted psychological construct that involves (1) an awareness, understanding, and acceptance of emotions; (2) an ability to control impulsive behaviours when experiencing emotional distress; and (3) the availability of adaptive strategies for modulating the duration and/or intensity of negative emotional experiences in accordance with individual goals and situational demands (Gratz and Roemer, 2004). Emotional dysregulation in PTSD involves cognitive, behavioral, and autonomic deficits, which may present as persistent negative emotions, irritable behaviours, anger outbursts, and avoidance of emotional stimuli that remind the individual of the traumatic event (APA, 2000).

Although several PTSD neuroimaging studies have focused on emotional dysregulation, the specific neural underpinnings of such dyregulation are not well understood (Tull and Kimbrel, 2020). Individuals with PTSD may have alterations in neurocircuitry involving the amygdala, insula, hippocampus, anterior cingulate cortex, and prefrontal cortex, and in autonomic processes (Fitzgerald et al., 2018). More specifically, they may have amygdala hyperresponsivity in the amygdala, which is accompanied by increased emotional reactivity and hyperarousal to emotional stimuli (Joshi et al., 2020).

Pupil dilation is a physiological index of emotional regulation that measures peripheral nervous system (PNS) processes (Cohen et al., 2015). Using pupillometry as an objective measure of emotional regulation difficulties in individuals with PTSD has a number of advantages; it is relatively inexpensive and it can be used across all age groups. There have been only a few studies measuring pupillary dilation in individuals with PTSD (Cascardi et al., 2015; Felmingham et al., 2011; Kimble et al., 2010), with inconsistent results and following

limitations. First, the existing studies have used only negative and neutral stimuli. Both Cascardi et al. (2015) and Kimble et al. (2010) used neutral images and that of high-threat content, whereas Felmingham et al. (2011) used only neutral and trauma-relevant lexical words (e.g., blood, attack, radio). Positive stimuli are an important addition, as it has been found that individuals with PTSD have aberrant processing of positively valenced stimuli (Clausen et al., 2016). Second, these studies contained small sample sizes of only 19-40 participants (Cascardi et al., 2015; Felmingham et al., 2011; Kimble et al., 2010). Third, pupillary light response may have affected the results as the onset of the emotional stimuli coincided with a change in display luminance (Yrttiaho et al., 2017).

Despite consistent evidence that emotion regulation difficulties are associated with PTSD and other varied negative mental health outcomes, the processes through which impairment leads to psychopathology remains unclear. To our knowledge, no study has utilized pupillometry to examine the role of emotional regulation in the association between trauma exposure and PTSD symptomatology. In this study, we employed eye tracking technology to determine whether trauma exposed individuals with PTSD differ in their response to positively and negatively emotionally valenced stimuli compared to trauma-exposed individuals without PTSD. We addressed the limitations in the existing literature that have measured pupillary response to emotionally valenced stimuli by including positive valenced stimuli, using a larger sample size, and controlling for pupillary light reflex. Given the previous findings of increased pupil size to emotional stimuli (Steinhauer et al., 2004), we made the following hypotheses. 1) We hypothesized that compared to trauma-exposed, non-PTSD controls, individuals with current or lifetime PTSD would exhibit larger pupillary diameter in response to positive and negatively valenced stimuli. 2) We also hypothesized that the dilation response would increase with selfreport difficulties in emotion regulation.

Materials and Methods

Study Design

This was a nested case control study of the ongoing Drakenstein Child Health Study (DCHS), a population-based birth cohort study in the Drakenstein area, a low socio-economic, semi-urban area in the Cape Winelands, Cape Town, South Africa. Pregnant women were enrolled in their second trimester and followed through childbirth; thereafter mother-child pairs were followed until the children are five years of age (Zar et al., 2015). Maternal and child health were investigated through longitudinal assessment of a range of clinical, environmental, genetic, nutritional, immunological, and psychosocial risk factors age (Zar et al., 2015).

Ethical considerations

All participants provided written informed consent, and ethical approval to conduct the larger study was obtained from the Human Research Ethics Committee of the Faculty of Health Sciences, University of Cape Town (UCT) (HREC REF: 401/2009) and by the Western Cape Provincial Health Research Committee. Approval to conduct the sub-study was obtained from the Human Research Ethics Committee of the Faculty of Health Sciences, UCT (HREC REF: 689/2016). All methods were carried out in accordance with the Declaration of Helsinki. Mothers provided informed consent at enrollment and were re-consented annually. Consent was done in mother's preferred language: English, Afrikaans or isiXhosa.

Recruitment and Enrolment

Mothers in the parent-study were originally recruited at 20-28 weeks' gestation from two primary care clinics - TC Newman and Mbekweni - in the Drakenstein sub-district between April 2012 and September 2015 (Zar et al., 2015). TC Newman serves a predominantly Mixed Ancestry community, while Mbekweni serves primarily a Black African community. The Drakenstein sub-district has been selected for its accessibility, population (of stable, but low socioeconomic status), high trauma burden, and cost-free public health system. For this substudy, a cohort of 100 participants were drawn using random computerised sampling. Within this cohort cases were identified based on maternal reports of trauma exposure and PTSD diagnostic assessments conducted antenatally (20-28 weeks) and during the post-partum period (timepoints: 10 weeks, 6 months, 12 months, 18 months, 24 months, and 36 months) using validated psychometric measures. Participants were assigned to either a clinical group (those who reported trauma exposure and were diagnosed with either a lifetime or current PTSD diagnoses) or a control group (mothers who reported trauma exposure, but did not receive a clinical PTSD diagnoses) (Stein et al., 2015). Cascardi et al (2015) reported a large effect size of 0.75 when comparing pupil dilation between PTSD and non-PTSD trauma-exposed groups in response to threat-relevant stimuli. A power analysis was conducted using this effect size, with the significance level set to 0.05 and power set to 0.80. The analysis indicted that a minimal sample of 29 was recommended to detect any potential group differences. Given that this study incorporated emotionally-valenced stimuli that are not necessarily threat-relevant, possibly leading to a smaller effect size, a larger sample was collected.

Inclusion criteria for the present sub-study included (a) mothers aged older than 18 years and (b) completion of psychometric measures of PTSD and trauma exposure during the study period (i.e., during the perinatal period until offspring three years of age). Exclusion criteria included (a) head injury or neurological disorder, (b) current psychotic disorder, and (c) history of substance abuse lasting longer than one year.

Research procedures and data collection methods

In a single session at the baseline visit, participants completed an eye tracking assessment, a series of questions via completion of self-report measures, and a structured clinical interview. Each session started with a briefing and consent period in which the participants were informed of the day's schedule and told that they were allowed to refuse participation without any consequences. The participants' data has been previously included in a larger study sampling the same database (Yrttiaho et al., 2020).

Pupil measurement

Procedure:

A participant was brought into a dimly lit, sound-proof room and sat 60 cm in front of a Tobii eye tracking system. To calibrate the eye tracker, the participant's seated height and distance from the eye tracker was adjusted and the participant was told to fixate on targets that appeared in various spots across the monitor. The participant was then presented with three experimental blocks, each consisting of eight different images of infant faces. The images appeared in randomized order and were either positively or negatively valenced. A scrambled, non-face pattern preceded each stimulus. Preceding the second and third blocks, the participants were given a break from viewing infant faces. During the break, positive music and images (i.e., an ocean scene) appeared for 10 seconds and eye tracking data was not recorded.

The assessment was broken down into four different parts: (1) a foreperiod with a black screen for 1000 ms; (2) a pre-stimulus period with randomized face pixels for 2000 ms; (3) stimulus onset, in which positively or negatively valenced images appeared for 4000 ms; (4) an ending indicator, in which a white rectangular border appeared over the stimulus for 1000 ms.

Additionally, before the emotionally valenced image appeared, there was a signalling sound for 2500 ms. The eye tracking test took approximately 10 minutes to complete.

Stimuli:

Facial stimuli used were of Caucasian male and female genders. 36 grayscale photographs were chosen from a pool of 208 images, which have been previously validated in a South African population (Yrttiaho et al., 2017). The images were selected based on similar face-background ratio, infants' head orientation, and infants' age (Yrttiaho et al., 2017). The images of infant's faces displayed front views of infants with positive (smiling) and negative (crying) facial expressions. This method of using images of facial expressions depicting various emotions is frequently used in eye tracking assessments of emotional responsiveness (Priebe et al., 2015; Proverbio et al., 2007).

Non-face patterns with matching grayscale intensity to the upcoming infant image were also adapted and were presented before each facial stimulus in order to minimize luminance-related variability in pupil size across trials (Yrttiaho et al., 2017). These stimuli were generated by randomly permuting the face pixels within square-shaped bounding areas spanning the entire figure (Yrttiaho et al., 2020).

Acquisition and analysis of pupil data:

Eye tracking technology (Tobii X2-60) was used to measure pupil response to infant face stimuli. The Tobii eye tracking system was based on Pupil Centre Corneal Reflection (PCCR), that is, near infrared illumination and its reflections from the cornea relative to the centre of the pupil. The light reflections were captured by two cameras. A general 3D model of the eye and the angles, distances, and other geometrical features of the reflections were used to calculate the position of the pupils and the direction of gaze. Pupil and gaze data were acquired, and the stimuli were presented, using MATLAB scripts, the Talk2Tobii toolbox, and Psychtoolbox. Pupil size from each eye was recorded from the pre-stimulus period throughout to the offset of the face stimulus.

GazeAnalysisLib was used to process the eye tracker's output, consisting of a timestamp, X-Y coordinates of the two eyes, and pupil diameter of the two eyes (in mm) at a sampling frequency of 60 samples/second (Leppänen et al., 2015). Pre-processing of the pupil signal followed a study using a similar procedure and eye tracking equipment (Yrttiaho et al., 2017). Pupil dilation was found to occur between 3000-4000-ms. Therefore, the time window for extracting pupil size was placed at this interval. For each block, the mean pupil size during this time window was calculated and reported as the pupillary response to the emotionally valenced stimuli. The mean pupil size was baseline-corrected by subtracting the mean pupil diameter during the pre-stimulus interval from the mean pupil size during the 3000-4000-ms response time window. Therefore, if the pupil had constricted from baseline, then pupil size received a negative value. Each individual data set underwent quality control. Criteria for quality control included that the participant maintained focus on the stimulus display and that there were no errors during the trial.

Emotional regulation self-assessments

The *Difficulties in emotion regulation scale (DERS)* is a 36-item self-report measure that assesses an individual's typical levels of emotion dysregulation across six domains: (1) non-acceptance of emotional responses, (2) difficulties pursuing goal-directed behaviours when experiencing negative emotions, (3) difficulties controlling impulsive behaviours when experiencing negative emotions, (4) lack of emotional awareness, (5) limited access to emotion

regulation strategies, and (6) lack of emotional clarity (Gratz and Roemer, 2004). Higher values indicate greater difficulties in emotion regulation.

The *Emotion Regulation Questionnaire (ERQ)* is a 10-item scale that can be scored on a 7-point Likert scale: endpoints 1 ('strongly disagree') to 7 ('strongly agree') (Gross and John, 2003). The ERQ measures two specific constructs related to emotion control: cognitive reappraisal and expressive suppression. Cognitive reappraisal assesses how a respondent positively regulates emotions to reduce psychological impact of the current situation. Emotion suppression examines how the respondent consciously hides/conceals uncomfortable feelings and/or thoughts in an adaptable way.

Trauma exposure, PTSD, and comorbid mental disorders assessment

For this study, trauma exposure was defined as a traumatic event(s) where the individual is confronted with actual or threatened death, serious injury or sexual violation, or exposure to the death, injury, or suffering of others per Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) criteria. Trauma exposure and PTSD symptoms were assessed using the following psychometric measures:

The *Beck Depression Inventory (BDI-II)* is a widely-used, 21-item measure of depressive symptoms (Beck et al.,1961, 1988, 1996). Each item assesses the severity of a symptom of major depression on a scale ranging from 0 (absence of symptoms) to 3 (severe, often with functional impairment). A higher total score is indicative of more severe depressive symptoms. The BDI-II has shown good validity, reliability and internal consistency in both psychiatric and non-psychiatric populations (Beck et al.,1961, 1988, 1996). It has been used in numerous studies conducted in South Africa (Kagee et al., 2014; Kagee & Martin, 2010; Nel & Kagee, 2013).

The *Intimate Partner Violence (IPV) questionnaire* was adapted for this study from the WHO multi-country study and the Women's Health Study from Zimbabwe (Krug et al., 2002; Shamu et al., 2011). The IPV questionnaire assessed lifetime and recent emotional, physical, and sexual abuse by one's intimate partner. For each type of abuse, a 4-point frequency scale was used ('never', 'once', 'few times', and 'many times'). A detailed description of the IPV questionnaire was previously published (Koen et al., 2014). Participants were considered to be trauma-exposed if they had any history of IPV (i.e., they did not report 'never' in all responses).

The *Peri-traumatic distress inventory (PDI)* is a 13-item self-report measure that provides a quantifiable measure of level of distress experienced during and immediately after a traumatic event (Brunet et al., 2001). Each item assessed symptoms of distress related to the event, scored between 0 ('not at all') and 4 ('extremely'). A total score was obtained by calculating the mean response across all 13 items, with higher scores indicating greater distress related to the event. This measure was only completed by participants who reported experiencing a life-threatening trauma.

The Clinician Administered PTSD scale (CAPS) is a clinician evaluation of the participants' current and lifetime PTSD using criteria from the DSM-IV (APA, 2000). The CAPS is the most widely used structured interview for diagnosing PTSD and has excellent test-retest reliability (r=0.92-0.99) and internal consistency (alpha=0.80-0.90) (APA, 2017; Weathers et al., 2001). The CAPS is administered to participants who scored above threshold for PTSD on the Mini-International Neuropsychiatric Interview (MINI) in order to confirm the diagnosis.

The *MINI* was administered by a psychiatrist or clinical psychologist in order to diagnose PTSD (lifetime and current) and comorbid disorders based on DSM-IV-TR, and to exclude current substance use or psychotic disorders (Sheehan et al., 1998). The MINI was administered

antenatally (28-32 weeks), age six to 10 weeks, six months, and 18 months. The MINI was administered again on the same day as the eye tracking assessment. The participants were assigned to the PTSD group if they were diagnosed with lifetime or current PTSD using the MINI and CAPS at any time point.

Statistical Analysis

All statistical analyses were done using R Statistical Package 2017 and Stata Statistical Software: Release 14. Two-sample Wilcoxon rank-sum (Mann-Whitney) tests were used (1) to compare scores on emotion regulation measures with PTSD status, and (2) to compare maternal age between the clinical and control groups. Linear mixed-effect (LME) modelling was utilised to (1) compare participants' pupillary dilation according to PTSD status and (2) to assess the potential association between emotional regulation subscales and pupillary dilation. LME modelling is advantageous as it can account for within-participant variability in pupillary dilation by block (i.e., random-effect) when estimating group effects (i.e., fixed-effect). In order to ensure that PTSD groups don't differ on important demographic factors such as education, income and employment, chi-square tests were run.

Results

Demographics

Of the total 100 participants enrolled in this sub-study, 13 individuals were excluded from the final analysis because they did not meet the minimum criteria for trauma exposure. No participants were excluded on the basis of eye tracking quality control. Of the remaining 87 participants, 34 received a diagnosis of lifetime or current PTSD and were allocated to the PTSD group. The remaining 53 trauma-exposed participants were assigned to the control group. Demographic data was collected at previous time points within the parent-study. Table 1 below represents the demographic data for the two groups. Case and control participants did not differ significantly in terms of age, socioeconomic status (SES), or level of education.

Table 1 here

Self-report questionnaires

Of the 87 participants included in the study, 100% completed the DERS and ERQ self-report questionnaires. Table 2 indicates that the PTSD group had greater scores of emotional regulation difficulties, as indicated by lower scores on the ERQ and greater scores on the DERS. Only one of the six DERS subscales (Awareness) trended in the opposite direction to that predicted. However, univariate analyses showed that none of the score differences were statistically significant.

Table 2 here

Pupil response

The PTSD group showed a significantly greater pupillary response (0.03 mm) towards the positive stimuli compared to non-PTSD controls (p=0.04). There was no significant difference in pupillary response towards the negatively valanced stimuli between the PTSD group and the control group. Pupillary response according to PTSD status is summarised in Table 3 below. As shown in Table 4, no association was found between self-reported emotion regulation difficulties (in all participants) and pupillary response to positive infant stimuli. The impulse subscale of the DERS was the only subscale found to have a statistically significant correlation with negative infant stimuli. However, there was no statistically significant correlation between negative infant stimuli and the cumulative DERS score.

Table 3 here

Table 4 here

Figure 1 here

Discussion

To our knowledge, this study was the first to employ pupillometry to investigate emotional regulation difficulties by unique pupillary response to emotionally valenced stimuli in individuals with PTSD. Consistent with our main hypothesis, we found that trauma-exposed participants with PTSD exhibited larger pupillary dilation as compared to non-PTSD participants. These findings suggest that the pupillary response may be used to distinguish between individuals with trauma exposure who develop PTSD from those who do not. Only three studies have investigated pupillary dilation in response to emotionally valenced stimuli in individuals with PTSD (Cascardi et al., 2015; Felmingham et al., 2011; Kimble et al., 2010). Two of these studies found increased pupillary dilation in PTSD compared to healthy controls (Cascardi et al., 2015; Kimble et al., 2010). In the third study there was no increased pupillary dilation in PTSD (Felmingham et al., 2011), presumably due to the use of lexical stimuli, which may have low salience (Cascardi et al., 2015) compared to photographic images. Of note, none of the existing studies included positively valenced stimuli. Thus, the present study is the first to find that individuals with PTSD have increased pupil dilation to positive stimuli compared to matched control participants. Steinhauer et al. (2004) has suggested that increased pupil size to an emotional stimulus is a result of PNS inhibition due to demanding cognitive load. Increased cognitive load in individuals with PTSD is associated with emotional regulation difficulties (Moore & Zoellner, 2012). Our findings are consistent, then, with a link between emotional regulation difficulties and increased PNS response in individuals with PTSD. There was no association between PTSD status and pupil dilation in response to the negatively valenced stimuli. This was an unexpected result, as two previous studies found an association between pupil dilation and PTSD using negative stimuli (Cascardi et al., 2015; Kimble et al.,

2010). Mothers have been found to exhibit increased pupil dilation when shown images of infants in distress or discomfort, compared to when they are shown images of infants with positive facial expressions, perhaps reflecting heightened ANS arousal (Yrttiaho et al., 2017). In the present study, lack of difference between the two groups min response to negatively valenced stimuli may indicate that all mothers, regardless of PTSD status, responded with heightened autonomic arousal to the distressing infant images. Heightened ANS arousal to negatively valenced stimuli may also explain the significant correlation between negatively valenced stimuli and the impulse subscale of the DERS (Herman et al., 2018).

PTSD status and pupillary dilation did not significantly correlate with self-report assessments of emotional regulation Several factors may have influenced the validity of the self-report measures used in this study, including the participants' self-awareness, their ability to ignore social biases, their willingness to accurately respond, and their comprehension of the instructions and questions (Choi and Pak, 2005; Mauss and Robinson, 2009). These limitations highlight the need for more objective measures of emotional regulations, such as pupillometry.

Several limitations of this study deserve emphasis. First, the cross-sectional design, makes causal inference problematic. Second, in several cases, mothers performed the assessment while their child remained in the room; this may have interfered with the validity of the study. Third, our study is limited by a relatively small sample, although a power analysis indicated that it was sufficient to assess our primary hypotheses. Our small effect size highlights the need for further studies with larger samples to replicate these findings. Fourth, trauma exposure is a complex phenomenon – our findings may have been influenced by the time-elapsed since trauma, the cumulative violence exposure, and the type of trauma that participants experienced,. Finally, the

specificity of our sample (only female participants of low SES with civilian PTSD) may well limit generalizability of results to other populations.

In conclusion, our finding of greater pupil dilation in response to positive stimuli in women with civilian PTSD compared to trauma-exposed controls is consistent with the presence of emotional regulation difficulties associated with greater cognitive load and PNS impairment. However, given that we were unable to demonstrate a correlation between pupillary response and self-reported measures of emotion regulation, this conclusion is a tentative one. Future research to better understand the mechanisms underlying increased pupillary response in PTSD is needed, and may ultimately inform the use of interventions to target the relevant underlying mechanisms..

Acknowledgments

We thank the mothers and their children for participating in the study and the study staff, the clinical and administrative staff of the Western Cape Government Health Department at Paarl Hospital and at the clinics for support of the study. We acknowledge Gerdia Harvey for her help with data collection.

Declaration of Interest

The study was funded by the Bill and Melinda Gates Foundation (OPP 1017641). Additional support for HJZ and DJS was provided by the Medical Research Council of South Africa. DJS has received research grants and/or honoraria from Lundbeck and Servier. This research was also supported by a joint project grant from the Academy of Finland and National Research Foundation, South Africa (# 2501271617). The fifth author received a grant from the Emil Aaltonen Fountain, Finland. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The remainder of the authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- APA. (2000). *Diagnostic and statistical manual of mental disorders*. (4th ed.). American Psychiatric Publishing.
- APA. (2017). Clinical Practice Guideline for the Treatment of Posttraumatic Stress Disorder (PTSD) in Adults.
- Beck, A., Steer, R., & Brown, G. (1996). *Manual for the Beck Depression Inventory-II*.Psychological Corporation.
- Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An Inventory for Measuring Depression. Archives of General Psychiatry, 4(6), 561–571. https://doi.org/10.1001/archpsyc.1961.01710120031004
- Beck, Aaron T., Steer, R. A., & Carbin, M. G. (1988). Psychometric properties of the Beck
 Depression Inventory: Twenty-five years of evaluation. *Clinical Psychology Review*, 8(1),
 77–100. https://doi.org/10.1016/0272-7358(88)90050-5
- Brunet, A., Weiss, D. S., Metzler, T. J., Best, S. R., Neylan, T. C., Rogers, C., Fagan, J., & Marmar, C. R. (2001). The Peritraumatic Distress Inventory: A proposed measure of PTSD criterion A2. *American Journal of Psychiatry*, *158*(9), 1480–1485. https://doi.org/10.1176/appi.ajp.158.9.1480
- Cascardi, M., Armstrong, D., Chung, L., & Paré, D. (2015). Pupil Response to Threat in Trauma-Exposed Individuals With or Without PTSD. *Journal of Traumatic Stress*, 28(4), 370–374. https://doi.org/10.1002/jts.22022
- Choi, B. C. K., & Pak, A. W. P. (2005). A catalog of biases in questionnaires. *Preventing Chronic Disease*, 2(1). /pmc/articles/PMC1323316/

- Clausen, A. N., Youngren, W., Sisante, J.-F. V., Billinger, S. A., Taylor, C., & Aupperle, R. L. (2016). Combat PTSD and Implicit Behavioral Tendencies for Positive Affective Stimuli: A Brief Report. *Frontiers in Psychology*, 7(MAY), 758. https://doi.org/10.3389/fpsyg.2016.00758
- Cohen, N., Moyal, N., & Henik, A. (2015). Executive control suppresses pupillary responses to aversive stimuli. *Biological Psychology*, 112, 1–11. https://doi.org/10.1016/j.biopsycho.2015.09.006
- 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
- Fitzgerald, J. M., Digangi, J. A., & Phan, K. L. (2018). Functional Neuroanatomy of Emotion and Its Regulation in PTSD. In *Harvard Review of Psychiatry* (Vol. 26, Issue 3, pp. 116– 128). Lippincott Williams and Wilkins. https://doi.org/10.1097/HRP.00000000000185
- Gratz, K. L., & Roemer, L. (2004). Multidimensional Assessment of Emotion Regulation and Dysregulation: Development, Factor Structure, and Initial Validation of the Difficulties in Emotion Regulation Scale. *Journal of Psychopathology and Behavioral Assessment*, 26(1), 41–54. https://doi.org/10.1023/B:JOBA.0000007455.08539.94
- Gross, J. J., & John, O. P. (2003). Individual Differences in Two Emotion Regulation Processes: Implications for Affect, Relationships, and Well-Being. *Journal of Personality and Social Psychology*, 85(2), 348–362. https://doi.org/10.1037/0022-3514.85.2.348
- Herman, A. M., Critchley, H. D., & Duka, T. (2018). The role of emotions and physiological arousal in modulating impulsive behaviour. In *Biological Psychology* (Vol. 133, pp. 30–43).

Elsevier B.V. https://doi.org/10.1016/j.biopsycho.2018.01.014

- Joshi, S. A., Duval, E. R., Sheynin, J., King, A. P., Phan, K. L., Martis, B., Porter, K. E., Liberzon, I., & Rauch, S. A. M. (2020). Neural correlates of emotional reactivity and regulation associated with treatment response in a randomized clinical trial for posttraumatic stress disorder. *Psychiatry Research - Neuroimaging*, 299, 111062. https://doi.org/10.1016/j.pscychresns.2020.111062
- Kagee, A., & Martin, L. (2010). Symptoms of depression and anxiety among a sample of South African patients living with HIV. *AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV*, 22(2), 159–165. https://doi.org/10.1080/09540120903111445
- Kagee, A., Nel, A., & Saal, W. (2014). Factor structure of the Beck Depression Inventory-II among South Africans receiving antiretroviral therapy. *AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV*, 26(2), 257–262. https://doi.org/10.1080/09540121.2013.802278
- 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
- Koen, N., Wyatt, G. E., Williams, J. K., Zhang, M., Myer, L., Zar, H. J., & Stein, D. J. (2014).
 Intimate partner violence: Associations with low infant birthweight in a South African birth cohort. *Metabolic Brain Disease*, *29*(2), 281–299. https://doi.org/10.1007/s11011-014-9525-4
- Krug, E. G., Mercy, J. A., Dahlberg, L. L., & Zwi, A. B. (2002). The world report on violence and health. *Lancet*, 360(9339), 1083–1088. https://doi.org/10.1016/S0140-6736(02)11133-0

- Leppänen, J. M., Forssman, L., Kaatiala, J., Yrttiaho, S., & Wass, S. (2015). Widely applicable MATLAB routines for automated analysis of saccadic reaction times. *Behavior Research Methods*, 47(2), 538–548. https://doi.org/10.3758/s13428-014-0473-z
- Mauss, I. B., & Robinson, M. D. (2009). Measures of emotion: A review. In Cognition and Emotion (Vol. 23, Issue 2, pp. 209–237). Taylor & Francis Group . https://doi.org/10.1080/02699930802204677
- Moore, S. A., & Zoellner, L. A. (2012). The Effects of Expressive and Experiential Suppression on Memory Accuracy and Memory Distortion in Women with and without PTSD. *Journal of Experimental Psychopathology*, *3*(3), 368–392. https://doi.org/10.5127/jep.024411
- Nel, A., & Kagee, A. (2013). The relationship between depression, anxiety and medication adherence among patients receiving antiretroviral treatment in South Africa. *AIDS Care -Psychological and Socio-Medical Aspects of AIDS/HIV*, 25(8), 948–955. https://doi.org/10.1080/09540121.2012.748867
- Priebe, J. A., Messingschlager, M., & Lautenbacher, S. (2015). Gaze behaviour when monitoring pain faces: An eye-tracking study. *European Journal of Pain*, 19(6), 817–825. https://doi.org/10.1002/ejp.608
- Proverbio, A. M., Matarazzo, S., Brignone, V., Zotto, M. Del, & Zani, A. (2007). Processing valence and intensity of infant expressions: The roles of expertise and gender. *Scandinavian Journal of Psychology*, 48(6), 477–485. https://doi.org/10.1111/j.1467-9450.2007.00616.x
- Shamu, S., Abrahams, N., Temmerman, M., Musekiwa, A., & Zarowsky, C. (2011). A
 Systematic Review of African Studies on Intimate Partner Violence against Pregnant
 Women: Prevalence and Risk Factors. *PLoS ONE*, 6(3), e17591.

https://doi.org/10.1371/journal.pone.0017591

- Sheehan, D. V., Yves Lecrubier, K., Harnett, S., Amorim, P., Juris, J., Weiller, E., Hergueta, T., Baker, R., & Dunbar, G. C. (1998). The Mini-International Neuropsychiatric Interview (MINI): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *Journal of Clinical Psychiatry*, *59*(20), 22–33.
- Stein, D. J., Koen, N., Donald, K. A., Adnams, C. M., Koopowitz, S., Lund, C., Marais, A.,
 Myers, B., Roos, A., Sorsdahl, K., Stern, M., Tomlinson, M., van der Westhuizen, C.,
 Vythilingum, B., Myer, L., Barnett, W., Brittain, K., & Zar, H. J. (2015). Investigating the
 psychosocial determinants of child health in Africa: The Drakenstein Child Health Study. *Journal of Neuroscience Methods*, 252, 27–35.

https://doi.org/10.1016/j.jneumeth.2015.03.016

- Steinhauer, S. R., Siegle, G. J., Condray, R., & Pless, M. (2004). Sympathetic and parasympathetic innervation of pupillary dilation during sustained processing. *International Journal of Psychophysiology*, 52(1), 77–86. https://doi.org/10.1016/j.ijpsycho.2003.12.005
- Tull, M., & Kimbrel, N. (2020). *Emotion in posttraumatic stress disorder* (1st ed., Vol. 1). Elsevier.
- Weathers, F. W., Keane, T. M., & Davidson, J. R. T. (2001). Clinician-administered PTSD scale: A review of the first ten years of research. *Depression and Anxiety*, 13(3), 132–156. https://doi.org/10.1002/da.1029
- Weiss, N. H., Dixon-Gordon, K. L., Peasant, C., & Sullivan, T. P. (2018). An Examination of the Role of Difficulties Regulating Positive Emotions in Posttraumatic Stress Disorder. *Journal* of Traumatic Stress, 31(5), 775–780. https://doi.org/10.1002/jts.22330

- Yrttiaho, S., Bruwer, B., Zar, H. J., Donald, K. A., Malcolm-Smith, S., Ginton, L., Hoffman, N.,
 Vuong, E., Niehaus, D., Leppänen, J. M., & Stein, D. J. (2020). Pupillary and Attentional
 Responses to Infant Facial Expressions in Mothers Across Socioeconomic Variations. *Child Development*, cdev.13503. https://doi.org/10.1111/cdev.13503
- Yrttiaho, S., Niehaus, D., Thomas, E., & Leppänen, J. M. (2017). Mothers' pupillary responses to infant facial expressions. *Behavioral and Brain Functions*, 13(1), 1–12. https://doi.org/10.1186/s12993-017-0120-9
- Zar, H. J., Barnett, W., Myer, L., Stein, D. J., & Nicol, M. P. (2015). Investigating the early-life determinants of illness in Africa: The Drakenstein Child Health Study. *Thorax*, 70(6), 592– 594. https://doi.org/10.1136/thoraxjnl-2014-206242

Tables and Figures

Table 1 Demographic characteristics of sample

	PTSD - N (%)	Control - N (%)	Estimate ¹	p-value
Number of participants	34 (39%)	53 (61%)		-
Age - Median (IQR)	25.0 (22.2, 28.2)	26.3 (23.2, 30.8)	1013	0.33
Primary	5 (14.7)	2 (3.8)		
Some Secondary	19 (55.9)	31 (58.5)		
Completed Secondary	10 (29.4)	18 (34.0)		
Any Tertiary	0 (0)	2 (3.8)	4.52	0.21
Lowest SES	8 (23.5)	14 (26.4)		
Low-Moderate SES	14 (41.2)	10 (18.9)		
Moderate-High SES	7 (20.6)	16 (30.2)		
High SES	5 (14.7)	13 (24.5)	5.49	0.14
<r1000 m<="" td=""><td>15 (44.1)</td><td>24 (45.3)</td><td></td><td></td></r1000>	15 (44.1)	24 (45.3)		
R1000-5000/m	16 (47.1)	21 (39.6)		

>R5000/m	3 (8.8)	8 (15.1)	0.92	0.63
Not Working	27 (79.4)	38 (71.7)		
Working	7 (20.6)	15 (28.3)	0.31	0.58
Maternal depression (BDI)				
Probable moderate/severe				
clinical	5 (19.2)	3 (6.8)		
Probable subthreshold	21 (80.7)	41 (93.2)	1.41	0.23

Note: ${}^{1}\chi^{2}$ for *Note:* ${}^{1}\chi^{2}$ for categorical variables. *W* for continuous variables. p-value < 0.05*; p-value < 0.01**; p-value < 0.001***

	PTSD – median	Control –	W	p-value
	(IQR)	median (IQR)		
Difficulties in emotional				
regulation				
Total	85.5 (72, 98)	82 (68, 101)	831	0.55
Awareness	14 (13, 18)	15 (13, 19)	1002	0.38
Clarity	11.5 (9, 14)	10 (7, 13)	803	0.39
Goals	12 (10, 15)	12 (10, 14)	830	0.54
Impulse	14 (11, 16)	13 (10, 16)	859	0.71
Non-Acceptance	15 (12, 17)	14 (9, 18)	753	0.20
Strategies	18 (14, 21)	18 (14, 20)	851	0.67
Emotional regulation				
questionnaire				
Cognitive Reappraisal	29.5 (21, 39)	32 (25, 37)	990	0.44
Expressive Suppression	16.5 (11, 22)	17 (13, 22)	965	0.58

Table 2 Self-Report Scores and PTSD Status

Note: p-value < 0.05*; p-value < 0.01**; p-value < 0.001***

	PTSD - median	Control -	Beta coefficient	p-value
	(IQR)	median (IQR)	[CI] ¹	
Positive			0.05 [0.01:0.09]	0.009*
Overall	.02 (01, .08)	01 (06, .03)		
Block 1	.02 (04, .05)	06 (12, .01)		
Block 2	.03 (05, .09)	.02 (04, .08)		
Block 3	.03 (02, .07)	.00 (10, .06)		
Negative			-0.01 [-0.05:0.02]	0.376
Overall	.02 (03, .04)	.03 (02, .10)		
Block 1	.00 (05, .04)	.03 (03, .09)		
Block 2	.03 (02, .13)	.02 (02, .10)		
Block 3	.00 (07, .09)	.04 (06, .11)		

Note: ¹ PTSD vs Non-PTSD group (Non-PTSD = reference group). Only fixed-effects displayed. p-value < 0.05*; p-value < 0.01**; p-value < 0.001***

	Positively Valenced Stimuli		Negatively Valenced Stimuli	
	Beta coefficient [CI]	p-value	Beta coefficient [CI]	p-value
DERS				
Cumulative	0.00 [-0.02:0.01]	0.610	-0.01 [-0.03:0.00]	0.156
Awareness	0.00 [-0.02:0.01]	0.720	0.00 [-0.02:0.01]	0.899
Clarity	0.01 [-0.01:0.03]	0.288	0.00 [-0.01:0.02]	0.772
Goals	0.00 [-0.02:0.02]	0.788	0.00 [-0.02:0.01]	0.502
Impulse	0.00 [-0.02:0.02]	0.855	-0.02 [-0.03: -0.001]	0.043*
Non-Acceptance	0.00 [-0.03:0.01]	0.370	0.00 [-0.02:0.01]	0.305
Strategies	-0.01 [-0.03:0.01]	0.316	-0.02 [-0.03:0.00]	0.059
ERQ				
Cognitive	0.00 [-0.02:0.01]	0.698	0.01 [-0.01:0.03]	0.279
Reappraisal				
Expressive	0.00 [-0.02:0.02]	0.943	0.00 [-0.01:0.02]	0.737
Suppression				

Table 4 Association	Between Emotionally	[,] Valenced Stimuli d	and Self-Report Measures

Note: Only fixed-effects displayed. p-value < 0.05*; p-value < 0.01**; p-value < 0.001***

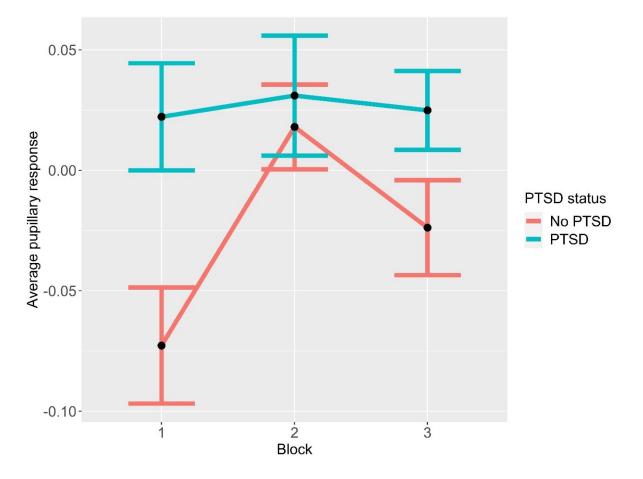


Figure 1 PTSD Status Differences in Average Pupillary Dilation to Positively Valenced Stimuli by Block