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Atypical attention and saccade vigor in post-traumatic stress disorder

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A B S T R A C T

Effective attention control is essential for behavioral adaptation to different environmental contexts. In Post-traumatic Stress Disorder (PTSD) altered attention has been described in trauma-related and other emotional contexts. Nevertheless, atypical attention is also seen with neutral stimuli. The mechanisms of attention alterations in PTSD associated with neutral stimuli are poorly understood.

The present study investigates alerting and orienting responses in PTSD participants using emotionally neutral stimuli in a saccade eye movement task incorporating both spatially predictable and temporally unpredictable conditions. We studied 23 PTSD patients and 27 Non-PTSD controls, using repeated-measures mixed modeling to estimate group and task condition differences in behavioral and psychophysiological measures. We explored the relationships among saccade characteristics, pupil size, and PTSD symptoms, including CAPS hypervigilance scores. PTSD, compared to Non-PTSD, participants showed differences in their saccade 'main sequence', reflected by higher peak velocities adjusted for amplitude. PTSD participants had smaller primary position errors in the unpredictable saccade condition. They also exhibited greater hyperarousal, reflected by larger pupil size during fixation that was greater in the unpredictable condition.

Our results suggest that a heightened state of arousal and hypervigilance in PTSD leads to a state of atypical attention bias, even in emotionally neutral contexts. These differences may reflect higher saccade vigor. The observed differences suggest atypical attention in PTSD, which goes beyond possible distraction associated with emotional or threat-related stimuli.

1. Introduction

In Post-Traumatic Stress Disorder (PTSD), increased tonic alerting with heightened arousal and reactivity is one of the four symptom clusters. Typical clinical manifestations of heightened arousal are hypervigilance, exaggerated startle responses, and impairments in concentration (American Psychiatric Association, 2013). These phenomena may result in altered attention.

Efficient attention control is essential for behavioral adaptation to different stimuli and tasks. Concentration requires successful filtering of ambient noise, and it is adaptive to remain alert to novel, potentially relevant, environmental changes. Petersen and Posner proposed three networks within the attention system: 1) the alerting network, related to brain stem arousal and maintenance of sustained vigilance during tasks; 2) the orienting network, prioritizing sensory stimulus selection; and 3) the executive network, to switch the focus of attention (Petersen and Posner, 2012). In daily life, most situations contain information about when (alerting) and where (orienting) a stimulus event will occur. However, alerting and orienting are believed to be separate physiological processes that involve different anatomical areas and brain mechanisms. As previous studies have demonstrated, the alerting and orienting networks show functional independence of each other and their efficiency estimates are not correlated (Fan et al., 2002; Fernandez-Duque and Posner, 1997).

Meta-analytical evidence has demonstrated biased attention to threat-related stimuli in anxious individuals, including PTSD subjects (Bar-Haim et al., 2007). In PTSD, biased attention has also been postulated as a possible mechanism underlying atypical attention regulation to trauma-related and emotional stimuli (Aupperle et al., 2012). In those situations, attention appears to be biased towards heightened sensitivity to task-irrelevant trauma-related or emotional cues (Bangel et al., 2017; Bardeen, 2020).

Some evidence, however, suggests that attention alterations in PTSD may be more general and extend beyond increased distraction

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associated with emotional stimuli. For instance, altered attention in individuals with PTSD has been found in neuropsychological tests involving neutral cues (Golier and Yehuda, 2002). Further, behavioral data from an attention-shift paradigm demonstrated attention alterations in highly anxious subjects independent of the emotional value (including neutral) of the stimulus (Bar-Haim et al., 2005). In line with this finding, we previously observed atypical visual sensory processing in PTSD compared to non-PTSD subjects that could not be explained by the emotional salience (neutral, positive, negative) of the presented pictures (Mueller-Pfeiffer et al., 2013). A possible explanation of these findings are alterations of the alerting network in PTSD that led to a context-independent hyper-aroused state. This would imply that the attentional alterations caused by PTSD may be much more fundamental and may also involve altered processing of neutral stimuli and tasks. Understanding how PTSD patients cope in neutral contexts is central to developing a deeper comprehension of the nature of attentional alterations and the areas of life potentially affected by them. Considering that optimal attention is essential for successful behavioral adaptation in daily life, emotionally non-specific attentional alterations in PTSD may also be operative in stimulus-rich work environments and daily life.

Eye movement kinematics are widely used to study attention (Gooding and Basso, 2008) during saccades, which are rapid and conjugate eye movements (Mahanama et al., 2022). In experimental research, saccades performed between consecutive fixation points are characterized by their onset latency, peak velocity, amplitude and spatial error (Gooding and Basso, 2008). One approach to probe the attention alerting system is to present a warning signal before displaying a target cueing a subsequent saccade, leading to a state of variable hyperarousal in anticipation of the expected target. The neural mechanism may be that the warning signal results in suppression of ongoing activity and prepares the attention alert system for target detection, which facilitates rapid response to the upcoming cue to move (Petersen and Posner, 2012).

To date, only two studies have employed saccadic eye movement tasks to investigate attention control in PTSD. Both applied pro- and anti-saccade tasks, using a warning signal (circle or cross) as a cue before target presentation. Participants were instructed to either look toward the target (pro-saccade) or away from it (anti-saccade). These studies employed trauma-related or trauma-unrelated negative (Blekic et al., 2021; Reinhard et al., 2017), or positive stimuli (Blekic et al., 2021). Results were divergent, showing shorter pro- (Blekic et al., 2021) or anti-saccade (Reinhard et al., 2017) onset latencies in PTSD participants compared to controls and comparable (Reinhard et al., 2017) or higher (Blekic et al., 2021) error rates in PTSD participants compared to controls.

Given the neuropsychological evidence for attentional alterations in non-emotional attention tasks in PTSD, these equivocal findings raise the question of whether all the attention system differences seen in PTSD are independent of emotional cues (Golier and Yehuda, 2002). The aim of this study was therefore to investigate attentional alterations in PTSD with emotionally neutral stimuli, using a predictable and unpredictable saccade task (Konen et al., 2004). We hypothesized more pronounced performance alterations and greater saccade vigor in PTSD than in non-PTSD subjects. Findings of attention alterations even under neutral conditions would further question the longstanding cognitive theory that threat-related attentional biases are the predominant cause for atypical attention with increased alerting in PTSD (Lazarov et al., 2019).

2. Methods

2.1. Study design and sample characteristics

PTSD participants were recruited from the psychiatric outpatient department of the University Hospital of Zurich, from individual local psychotherapists, and by advertisement. Non-PTSD participants were recruited by advertisement. We included trauma-exposed (meeting DSM-5 criterion A) male and female individuals between 18 and 60 years of age, with (PTSD group) and without (Non-PTSD group) a current DSM-5 PTSD diagnosis, as assessed using the Clinician-Administered PTSD Scale (CAPS) (Schnyder and Moergeli, 2002). Trauma history was assessed using the CAPS (Wittmann et al., 2021) and the Childhood Trauma Questionnaire (CTQ) (Wingenfeld et al., 2010).

The following exclusion criteria were applied: 1) inadequate knowledge of the German language, 2) lifetime episode of unconsciousness >10 min, 3) psychosis (current or lifetime), 4) substance abuse (current or past 6 month), 5) substance addiction (current or lifetime), 6) current dissociative disorder, 7) psychiatric disorder caused by an underlying medical or neurological condition, 8) suicidality, 9) neurological or physical condition affecting the brain (current or lifetime), 10) cognitive impairment (intelligence quotient [IQ] < 70 according to the Wortschatztest (verbal IQ) (P, 1992) and Wiener Matrizen-Test (non-verbal IQ) (Piswanger, 1979)), 11) current use of beta blockers, anticholinergics or psychotropic drugs (except non-tricyclic antidepressants, allowed with a wash out period of 2 weeks). As the presented results were part of a larger fMRI study investigating functional neuroanatomy of bottom-up hyper-responsiveness in PTSD (Naegeli et al., 2018), the following fMRI-associated exclusion criteria were also applied to our sample: pregnancy, impaired hearing, and skin conductance non-response. Psychiatric exclusion criteria were assessed using the Mini International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998) and the Structured Clinical Interview for DSM-IV Dissociative Disorders - Revised (SCID-D-R) (Steinberg, 2000).

Prior to the experimental procedures, we assessed anxiety and depression using questionnaires including the trait portion of the State-Trait Anxiety Inventory (STAI) (Spielberger et al., 1983) and the Beck Depression Inventory (BDI). All questionnaires were German-adapted and validated versions. The study was approved by the Ethics Committee of Canton Zurich (2022–01451). All participants provided written informed consent prior to their inclusion according to the Helsinki declaration.

2.2. Experimental task procedures

We used a predictable and unpredictable saccade task that has been employed in a previous study of healthy individuals (Konen et al., 2004). The experimental task consisted of 7 blocks of predictable and 7 blocks of unpredictable saccades which alternated. Each block comprised 10 predictable or unpredictable saccades. A centrally located white fixation cross on a dark background indicated the beginning of a trial. The white cross changed to a colored circle after 400 msec, providing a cue for the subsequent saccade. The duration of the cue presentation was pseudorandomized between 400 and 800 msec to avoid anticipatory saccades. A red cue predicted a shift of the target to the right visual field (i.e. $+9^{\circ}$ on the horizontal meridian) and a green cue predicted a shift to the left visual field (i.e. -9-° on the horizontal meridian). A central blue cue signaled an upcoming target in either the right or left visual field. The target remained on for 1000 msec before returning to the center, becoming the central fixation target. The participants were instructed to fixate on the central cue, await the appearance of the peripheral target, look at it as quickly and accurately as possible, and return their gaze to the central cue upon target offset. Fig. 1 depicts the sequence of events during the task, in which eye movements were executed under both spatially predictable and unpredictable conditions (Condition).

Groups of both PTSD and Non-PTSD participants were assessed. Measures of interest were saccade Onset Latency, saccade Peak Velocity, saccade Amplitude, saccade Primary Position Error and Pupil Size during fixation. Following the study of Konen et al. (2004) the saccade onset was determined using a defined velocity criterion (three samples above 10% of the saccade maximum). Pupil size (PS) served as an autonomic measure.

All tasks were implemented using E-Prime Professional 2.0 and E-

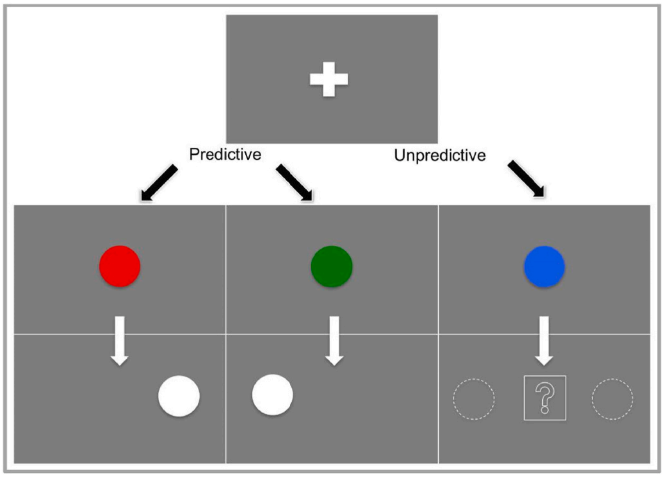

Fig. 1. Experimental design of the predictable and unpredictable saccadic eye movement task.

Prime Extensions for fMRI (Psychology Software Tools, Inc., Sharpsburg, PA). Stimuli were presented to the participants in a Philips Ingenia 3 T MR scanner. The fMRI results are not part of the present report.

2.3. Recording of eye movements and pupil size

Oculomotor data collection was performed in the MRI scanner, while scanning was performed in the background. Eye movements and pupil size were recorded monocularly from the right eye using an EyeLink 1000 Plus system (SR Research, Ltd., Ottawa, Canada). The camera was mounted behind the magnet bore and recorded the right eye position through an infrared mirror placed directly on the head coil. The video capture frequency was 1000 Hz. Saccade task instructions and stimulus cues were presented using Eye Link software.

2.4. Statistical analysis

For socio-demographic and clinical variables, we present descriptive between-group standardized mean differences.

Eye movement analysis was performed using R 4.4.1. To confine the analysis to saccades performed according to task instructions, outlier trials were excluded from the analysis. Outliers were defined as trials with 1) saccade latency less than 100 ms or greater than 600 msec, 2) saccade duration greater than 80 msec, 3) peak velocity <750, 4) peak velocity latency <70 msec, 5) saccade amplitude less than 4.5 deg or greater than 12.5 deg, 6) Q Ratio <3.0 (Q ratio = ratio of peak velocity to average velocity during the saccadic interval computed to determine abnormally fast or slow saccades) and 7) pupil size at fixation <4000, and 8) primary position error <3.5 deg. Outliers were excluded in all groups (PTSD versus Non-PTSD) and task conditions (predictable versus unpredictable).

To estimate the differences in kinematic and psychophysiological measures, repeated-measures mixed modeling was used. The effect of Group and Condition factors, as well as their interaction (Group x Condition), was tested on each measure. Subject was included as a random effect. To explore the relationships among kinematic, autonomic and PTSD symptoms, linear mixed models (estimated using maximum-likelihood with the nloptwrap optimizer) were calculated for saccade measures, including saccade Onset Latency, saccade Primary Position Error, saccade Peak Velocity and saccade Amplitude. In addition, pupil size during fixation and CAPS hypervigilance scores were calculated. Hypervigilance scores were used because of the strong connection between these PTSD symptoms and attention dysfunction.

3. Results

3.1. Clinical characteristics

We studied 50 (68% female) trauma-exposed individuals with (n = 23) and without (n = 27) PTSD. There were more females with than without PTSD. The index trauma differed between PTSD and Non-PTSD participants, PTSD participants reported more sexual and repeated physical violence. PTSD participants showed a higher severity of state anxiety and depression (group characteristics are presented in Table 1).

3.2. Saccade characteristics

Trials were filtered to confine the analysis to movements performed according to task instructions. The cleaning procedure reduced the number of saccades used for statistical modeling. The saccade numbers after exclusion were lower, with 63%/78% (predictable/non-predictable) remaining for Non-PTSD participants and 52%/60% remaining for PTSD participants. Statistical modeling of the cleaning effects on counts with a Poisson mixed model incorporating Group, Condition and Cleaning as fixed effects and Subject as a random effect revealed an overall reduction in saccades related to Cleaning (Incidence Rate Ratio = 0.57, 95% CI [0.52–0.61], t = −14.17). The interaction of Condition × Clean (Incidence Rate Ratio = 1.31, 95% CI [1.18–1.46], t = 5.00) revealed larger saccade exclusions in the Predictable condition. No effects of Group or its interactions with other variables were observed.

Table 1
Demographic and clinical characteristics of PTSD and Non-PTSD participants.

Measure	Group				SMD
	PTSD (n = 23)		*Non-PTSD (n = 27)*		
	n	*%*	*n*	*%*	
Female	19	90.5	15	60.0	0.755
Medication					
Antidepressant	11	47.8	0	0.0	1.354
For physical medical conditions	4	17.4	0	0.0	0.649
Type of index trauma					
Accident	3	13.0	5	22.2	
Natural disaster	0	0.0	2	7.4	
Single physical violence	1	4.3	6	18.5	
Repeated physical violence	4	17.3	2	7.4	
Single sexual violence	8	34.8	1	3.7	
Repeated sexual violence	4	17.3	0	0.0	
Combat trauma	0	0.0	4	14.8	
Witnessed accident	0	0.0	1	3.7	
Witnessed suicide/violence	2	8.6	5	18.5	
	Mean	*SD*	*Mean*	*SD*	
Age (years)	39.0	14.28	41.32	11.50	0.179
Education (years)	14.57	2.58	15.16	3.76	0.183
CAPS Total	30.19	10.81	2.04	3.23	3.530
CAPS Re-experiencing	7.90	3.30	0.48	0.71	3.110
CAPS Avoidance	3.95	1.56	0.24	0.6	3.135
CAPS Negative cognition/mood	9.81	4.58	0.72	1.90	2.592
CAPS Hyperarousal	8.52	3.74	0.60	1.15	2.865
CTQ Emotional abuse	15.43	6.87	8.56	3.51	1.259
CTQ Physical abuse	10.81	5.14	6.64	2.25	1.05
CTQ Sexual abuse	10.10	6.41	5.80	1.94	0.907
CTQ Emotional neglect	15.67	6.46	10.44	4.88	0.913
CTQ Physical neglect	11.19	4.37	6.92	2.0	1.258
STAI Trait anxiety	52.19	12.46	34.72	9.54	1.574
BDI Total	21.43	9.60	5.44	4.44	2.137

CAPS: Clinician-Administered PTSD Scale, CTQ: Childhood Trauma Questionnaire, STAI: State-Trait Anxiety Inventory, BDI: Beck Depression Inventory, *SD*: Standard deviation, *SMD*: Standardized mean difference.

3.3. Behavioral and psychophysiological results

To examine Group and task Condition effects on saccade Onset Latency, we fitted a linear mixed model to predict Onset Latency (RT) by Condition and Group. The model's total explanatory power was moderate (conditional $R^2 = 0.30$). Within this model: 1) the effect of Condition [Unpredictable] was statistically significant and positive (beta = 20.73, 95% CI [15.80–25.67], t (3806) = 8.24, p < 00.001; Std. Beta = 0.30, 95% CI [0.23, 0.38]), 2) the effect of Group [PTSD] was statistically non-significant and negative (beta = −16.27, 95% CI [−36.72 – 4.17], t (3806) = −1.56; Std. Beta = −0.23, 95% CI [−0.53 – 0.060]), and 3) the interaction of Condition [Unpredictable] × Group [PTSD] was statistically significant and positive (beta = 7.70, 95% CI [0.0069–15.41], t (3806) = 1.96, p = 0.05; Std. Be]). Examination of the interaction shows that PTSD participants exhibited shorter latencies than Non-PTSD participants in thepredictable saccade condition (Fig. 2).

To examine effects on saccade Primary Position Error, we fitted a linear mixed model to predict PrimaryPositionError by Condition and Group. The model's total explanatory power was moderate (conditional $R^2 = 0.33$). Within this model: 1) the effect of Condition [Unpredictable] was statistically non-significant and negative (beta = −0.05, 95% CI [−0.10 - 5.49e-03], t (3663) = −1.76, p = 0.079; Std. Beta = −0.07, 95% CI [−0.14 - 7.53e-03]), 2) the effect of Group [PTSD] was statistically non-significant and positive (beta = 0.10, 95% CI [−0.14 - 0.34], t (3663) = 0.80, p = 0.425; Std. Beta = 0.13, 95% CI [−0.20 - 0.46]), and 3) the interaction effect of Condition [Unpredictable] × Group [PTSD] was statistically significant and negative (beta = −0.13, 95% CI [−0.22 to −0.05], t (3663) = −3.07, p = 0.002; Std. Beta = −0.18, 95% CI [−0.30 to −0.06]). Examination of the interaction showed that PTSD participants exhibited smaller errors than Non-PTSD participants in the unpredictable condition (Fig. 3).

The relationship between saccade Peak Velocity and saccade Amplitude ('main sequence') was examined using a linear mixed model to predict PeakVelocity with Amplitude, Condition and Group. The model's total explanatory power was high (conditional $R^2 = 0.74$). Within this model: 1) the effect of Amplitude was statistically significant and positive (beta = 34.90, 95% CI [33.34, 36.47], t (3663) = 43.65, p < 00.001; Std. Beta = 0.51, 95% CI [0.49–0.53]), 2) the effect of Group [PTSD] was statistically significant and positive (beta = 74.18, 95% CI [37.05, 111.32], t (3663) = 3.92, p < 00.01; Std. Beta = 0.37, 95% CI [0.02–0.72]), 3) the interaction of Amplitude × Group [PTSD] was statistically not significant and 4) the effect of Condition was not significant.). PTSD participants exhibited higher peak velocities at all amplitudes in both predictable and unpredictable conditions compared to Non-PTSD participants (Fig. 4).

To examine effects on Pupil Diameter at fixation, we fitted a linear mixed model to predict PupilSize atFixation with Condition and Group. The model's total explanatory power was high (conditional $R^2 = 0.86$). Within this model: 1) the effect of Condition [Unpredictable] was statistically significant and negative (beta = −51.28, 95% CI [−76.28 to −26.28], t (3663) = −4.02, p < 00.001; Std. Beta = −0.07, 95% CI [−0.11 to −0.04]), 2) the effect of Group [PTSD] was statistically non-significant and positive (beta = 247.69, 95% CI [−137.38–632.75], t (3663) = 1.26, p = 0.207; Std. Beta = 0.36, 95% CI [−0.20 - 0.91]), and 3) the interaction of Condition [Unpredictable] × Group [PTSD] was statistically significant and positive (beta = 69.90, 95% CI [30.47–109.34], t (3663) = 3.48, p < 00.001; Std. Beta = 0.10, 95% CI [0.04, 0.16]). PTSD participants exhibited a non-significant increase in pupil size during fixation in both the predictable and unpredictable conditions compared to Non-PTSD participants (Fig. 5).

To examine effects of CAPS Hypervigilance on saccade Onset Latency, we fitted a linear mixed model to predict Onset Latency with Amplitude, Group and CAPS Hypervigilance. The model's total explanatory power was low (conditional $R^2 = 0.27$). Within this model: 1) the effect of CAPS Hypervigilance was statistically significant and

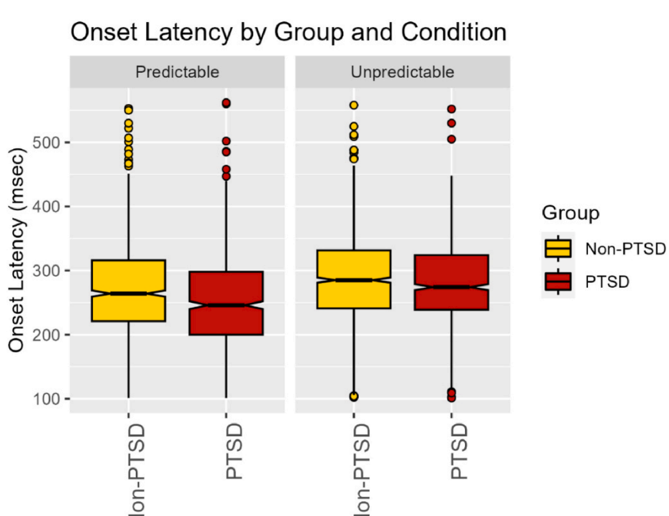

Fig. 2. Saccade Onset Latency is lower in the PTSD group in the predictable task condition.

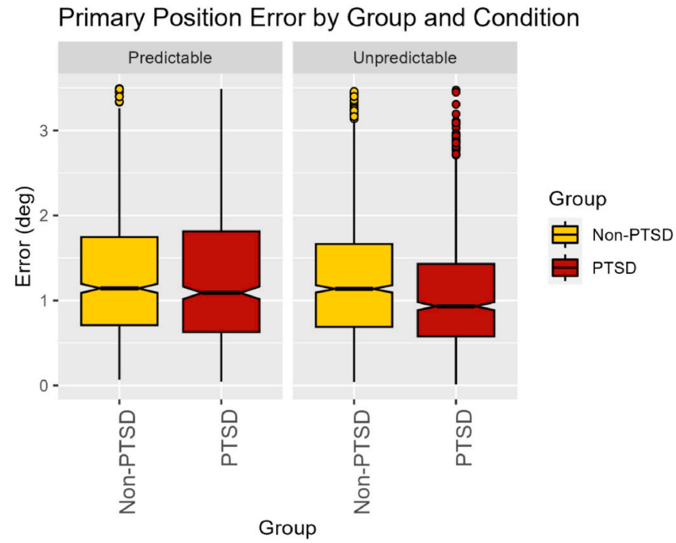

Fig. 3. Primary Position Error is lower in the PTSD group in the unpredictable task condition.

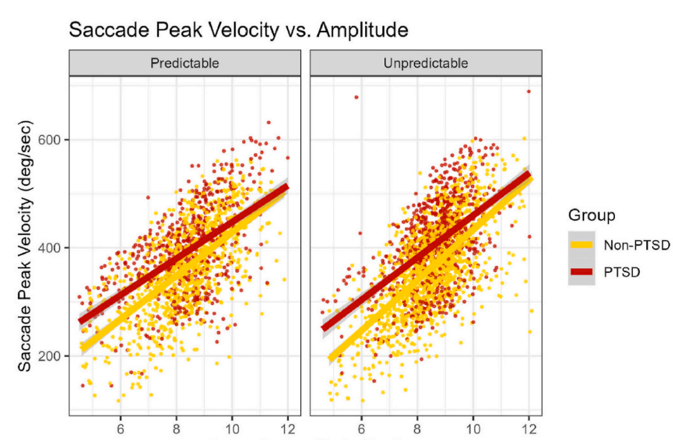

Fig. 4. The main sequence plot of Saccade Peak Velocity versus Amplitude shows linear increases in peak velocity with increasing amplitude and higher peak velocities for both predictable and unpredictable task conditions.

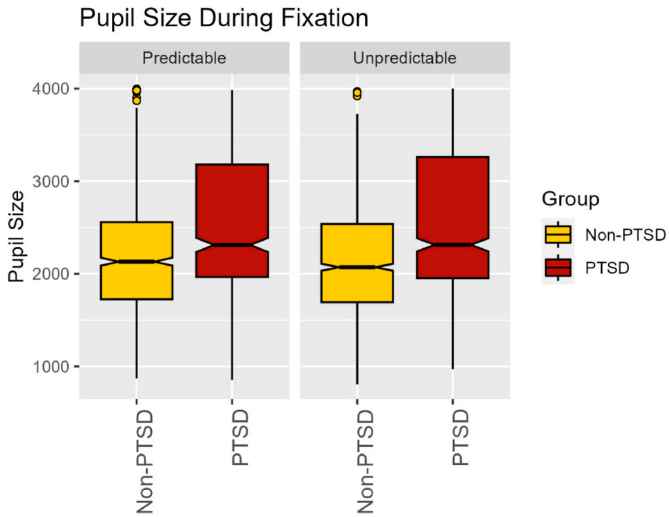

Fig. 5. Pupil Size during fixation is larger in both predictable and unpredictable task conditions.

negative (beta = −52.76, 95% CI [−100.59 to −4.92], t (3451) = −2.16, p = 0.031; Std. Beta = 0.19, 95% CI [−0.29 - 0.67]) and 2) the effect of Amplitude by CAPS Hypervigilance interaction was statistically significant and positive (beta = 7.64, 95% CI [2.97–12.30], t (3451) = 3.21, p = 0.001; Std. Beta = 0.16, 95% CI [0.06, 0.25]). PTSD, but not Non-PTSD, participants exhibited shorter saccade onset latencies associated with greater CAPS hypervigilance (Fig. 6).

For all models, standardized parameters were obtained by fitting the model on a standardized version of the dataset. Ninety-five % Confidence Intervals (CIs) and p-values were computed using a Wald t-distribution approximation. As groups differed in their characteristics regarding sex and total BDI score, we adjusted for both variables in our models. Neither sex, nor total BDI score accounted for the variation observed in the outcome variables.

4. Discussion

Summary of results. Using predictable and unpredictable saccades, we investigated alerting and orienting responses in participants with and without PTSD using visual stimuli devoid of emotional content.

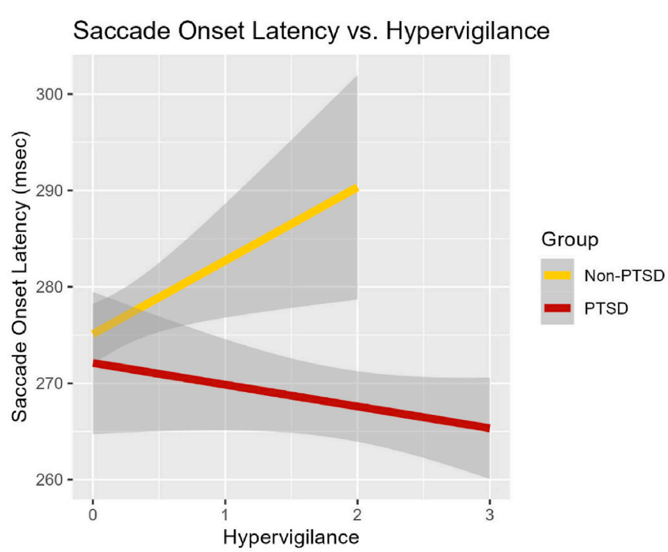

Fig. 6. Saccade Onset Latency decreases with increasing clinical hypervigilance (CAPS) in the PTSD group.

Visual targets were presented at both predictable and unpredictable times. While saccade latencies were lower in the predictable condition in both groups. PTSD participants demonstrated relatively shorter saccadic latencies in the predictable condition. PTSD, compared to Non-PTSD, participants also showed greater peak velocities adjusted for amplitude in both conditions, indicative of higher saccadic vigor. PTSD participants had smaller primary position errors in the unpredictable saccade conditions. They also exhibited greater hyperarousal, reflected by larger pupil size during fixation that was greater in the unpredictable condition. These results suggest that a heightened state of arousal and hypervigilance drive atypical attention in PTSD, even in emotionally neutral contexts. Thus, the observed effects go beyond possible distraction associated with emotional or threat-related stimuli.

Saccade vigor. PTSD participants exhibited differences in their 'main sequence' – defined as the relationship between saccade peak velocity and saccade amplitude. These differences, with higher saccade peak velocity adjusted for amplitude are consistent with an underlying difference in saccade vigor, a relatively recent construct relating saccade kinematics to decision-making contexts (Korbisch et al., 2022; Reppert et al., 2015; Sedaghat-Nejad et al., 2019). In our experiment, the duration of cue presentation before target presentation was pseudorandomized between 400 and 800 msec to avoid anticipatory saccades and induce uncertainty. This resulted in both temporal and spatial uncertainty about the target onset in the unpredictable condition and temporal uncertainty in the spatially predictable condition. Thus, the task provoked a phasic change in alertness, preparing the participants for lateral target detection. PTSD participants showed greater hyperarousal, manifested in larger pupil size during the fixation period preceding target appearance. This hyperalert state was associated with a more vigorous response with shorter saccade latency in the predictable condition and more so in the PTSD group. Higher saccade peak velocities, adjusted for saccade amplitude, was seen in the PTSD group.

The relationship between saccade peak velocity and amplitude, the 'main sequence', has long been regarded as fixed (Bahill et al., 1975; Gibaldi and Sabatini, 2021); peak saccade velocity increases with saccade amplitude. Recent evidence has emerged suggesting a more flexible and voluntary modulation of peak velocity for given saccadic amplitudes, depending on the degree of intrinsic motivation (Chen et al., 2014; Muhammed et al., 2020). In our PTSD participants, we saw greater saccade vigor, reflected by higher saccade velocity and shorter saccade onset latency. As a possible explanation, we hypothesize greater motivation to respond to an upcoming stimulus in PTSD patients, as they are in a hyperalert state. The lower error rates in task performance may also be indicative to this increased vigor. Only recently, a coupled-vigor hypothesis (Kita et al., 2022) has been postulated, describing a link between the vigor of action execution (velocity) and action selection (accuracy) (Thura, 2020). Our findings support this hypothesis – PTSD participants showed higher peak velocities and smaller errors. The heightened alertness was also manifested in increased clinical hyperarousal in PTSD participants, which was associated with shorter saccade onset latency and larger pupil diameter.

There is robust evidence supporting higher sympathetic reactivity in PTSD in the presence of negatively-valenced stimuli (trauma-related or non-trauma related) (Felmingham et al., 2011; Kimble et al., 2010; Pole, 2007). A heightened sensitivity to trauma-related or emotional cues (Bangel et al., 2017; Bardeen, 2020), leading to a bias of attention, has been postulated as a potential mechanism underlying atypical attention regulation in PTSD (Aupperle et al., 2012). Even so, we observed this phenomenon in our more emotionally neutral context. In a previous fMRI study employing a picture-viewing task with varying emotional content, we found visual processing in PTSD, compared to Non-PTSD, participants to be substantially altered with reduced task-related activity in the visual cortex (Mueller-Pfeiffer et al., 2013). These effects of lower visual responsiveness were unrelated to the emotional salience of the pictures (Mueller-Pfeiffer et al., 2013). In the present study, using an eye movement task in an emotionally neutral context, we were able to show that increased saccade vigor occurs with neutral stimuli, which is presumably due to higher arousal and vigilance in the PTSD group.

To our knowledge, only two studies with pro- and anti-saccade task design have investigated saccadic eye movement as a function of altered attention in PTSD (Blekic et al., 2021; Reinhard et al., 2017). A recent study did not include neutral stimuli, but used positive and negative emotional pictures (Blekic et al., 2021). They reported more directional gaze errors with negative pictures in PTSD subjects compared to controls and shorter latencies of the first saccades. Only a single study has previously employed a saccadic eye movement (Reinhard et al., 2017). This study used neutral stimuli (circle/squares) in their standard condition. They found no group differences in latency or error rates between PTSD and non-PTSD participants; velocity was not studied (Reinhard et al., 2017). PTSD symptom severity in the arousal cluster was not correlated with error rates in standard condition. While Reinhard et al. captured directional gaze errors in their pro- and anti-saccade task paradigm, our use of positional errors may have provided a more refined approach to detecting subtle differences in error rate differences related to increased saccade vigor.

In prior research on fearful individuals, enhanced hypervigilance to visual stimuli (neutral or threat) has been demonstrated with heightened spatial attention during environmental scanning for a target cue (Weymar et al., 2013). Further, we previously observed atypical visual processing in PTSD in emotionally neutral pictures (Mueller-Pfeiffer et al., 2013), demonstrating sensory processing alterations in PTSD patients engaging in a picture viewing task. In another study, PTSD participants compared to controls showed similar evoked response potentials while viewing angry and neutral faces. Controls showed an expected differentiated pattern with faster responses to angry than neutral faces (Felmingham et al., 2003).

Attention in PTSD. Preliminary evidence from non-eye movement research indicates that attention alterations in PTSD may be more generalized and extend beyond attention bias attributable to trauma-related or emotional stimuli (Golier and Yehuda, 2002). Standardized neuropsychological tests involving neutral stimuli have hinted at altered attention in PTSD affecting cognitive (Qureshi et al., 2011) and executive functioning (Block and Liberzon, 2016). Based on the Posner and Petersen attention model, a recent article reviewing findings from non-affective tests in PTSD suggested that alterations in orienting were one component of attention bias in PTSD (Block and Liberzon, 2016). Evidence related to the alerting network in PTSD, however, is scarce (Block and Liberzon, 2016). Based on our findings from a task involving spatial and temporal uncertainty, we have evidence for differences in both the alerting and orienting networks in PTSD, possibly resulting from a context-independent hyperarousal state and attention bias. The components of attention bias have been conceptualized by Cister and Koster to include: 1) facilitated attention (faster detection of threat stimuli), 2) difficulty in disengagement from threat stimuli vs. neutral stimuli)and 3) attentional avoidance to threat stimuli (Cisler and Koster, 2010). This framework provides insight into attention bias in PTSD in the context of threat. Nevertheless, it fails to explain the altered attention observed in our paradigm employing neutral stimuli. We therefore believe that the constructs of saccade vigor and an attention model including alerting and orienting may help to fill the gaps in the understanding of altered attention in PTSD.

5. Strengths and limitations

The analysis of saccadic eye movements in PTSD offers a promising approach to the investigation of atypical attention in PTSD. A strength of our paradigm is the deliberate use of neutral stimuli. This provided us with evidence of altered attention beyond trauma-related contexts. In addition, in our analyses, we explored effects of clinical hypervigilance, an approach advocated in a recent review on sensory processing, (Harricharan et al., 2021) and which allowed a more differentiated analysis of attention bias in PTSD in the framework of our experiment. In our paradigm, we did not test for group differences in attentional bias related to trauma-related or emotional stimuli. Thus, we cannot exclude the possibility that PTSD participants may demonstrate even greater attentional interference with emotionally salient cues. In view of the existing literature, this would be expected. Rather, our study primarily aimed to identify possible mechanisms that could explain attentional alterations in PTSD, under neutral conditions.

Some limitations must be considered in interpreting our findings. First, our oculomotor data were collected in a non-naturalistic environment as part of a larger fMRI study. Both groups were exposed to the same environmental conditions and we did see group differences in saccade properties. However, it would be valuable to transfer our approach to natural conditions to see if these effects can also be observed outside the fMRI scanner. In our study, we did not perform standardized screening for altered visual function prior to the experiment, but assessed visual function implicitly by determining that participants could read instructions on the stimulus screen. Therefore, we cannot exclude with certainty that our results were influenced by differences in visual function. Future studies could use standardized measures of visual function to address this uncertainty. In our study, female participants predominated in both groups. In our models, we adjusted for sex, which had no significant effect on any outcome variables. Given the imbalanced sex distribution of our sample, however, the power to detect sex-related differences may have been too low, which could bias our results and affect their generalizability. In addition, our sample reflected more man-made trauma (particularly sexual abuse and childhood abuse) than other types of trauma (e.g., accidents), and the distribution of index trauma type between groups differed.

Not unexpectedly, the PTSD group also showed significantly higher anxiety and depression scores and corresponding medication use than the Non-PTSD group. We therefore cannot exclude the possibility that the results may have been influenced by comorbid effects. Nevertheless, depression has been associated with lower saccade velocity (Wen et al., 2022). This suggests a downward effect (lower saccade velocity) would be expected in PTSD with increasing depressive symptoms, which would have been expected to reduce the observed group effects. Adjusting for depression in the PTSD group did not result in effects on the measured variables. Regarding error rates, depression has not been associated with an altered accuracy of saccades (Carvalho et al., 2014). Anxiety, in turn, has been linked to higher eye-movement errors (Hepsomali et al., 2017), so that a concomitant anxiety disorder would be expected to lead to more errors.

6. Conclusions

In a predictable and unpredictable saccade paradigm, PTSD participants demonstrated shorter latencies and higher peak velocities. Using neutral, emotionally non-salient stimuli, our results challenge the assumption that threat-related attentional biases are the main cause of atypical attention in PTSD. Rather, we suggest that greater saccade vigor in PTSD is due to greater arousal driving altered attention control. Our findings broaden knowledge of the mechanisms of atypical attention in PTSD and may be particularly valuable for understanding the extent of attentional alterations in PTSD and the scope of daily life potentially affected. Saccade vigor could be a useful biomarker to index treatment response in PTSD.

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Data availability statement

The data underlying this article cannot be shared publicly due to privacy or ethical restrictions. The results supporting our conclusion will be shared on reasonable request to the corresponding author.

CRediT authorship contribution statement

Lena Jellestad: Writing – original draft, Methodology. **Thomas Zeffiro:** Writing – review & editing, Formal analysis, Data curation. **Hanspeter Mörgeli:** Writing – review & editing, Formal analysis. **Marco Piccirelli:** Writing – review & editing, Software, Methodology, Investigation, Data curation. **Assia Jaillard:** Writing – review & editing, Methodology. **Patrick Pasi:** Writing – review & editing. **Naomi Ruth Shepherd:** Writing – review & editing, Data curation. **Christoph Mueller-Pfeiffer:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Data curation, Conceptualization.

Declaration of competing interest

The authors have no conflicts of interest to declare that are relevant to the content of this article.

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