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EEG theta/beta ratio: a marker of executive control and its relation with anxiety-linked attentional bias for threat

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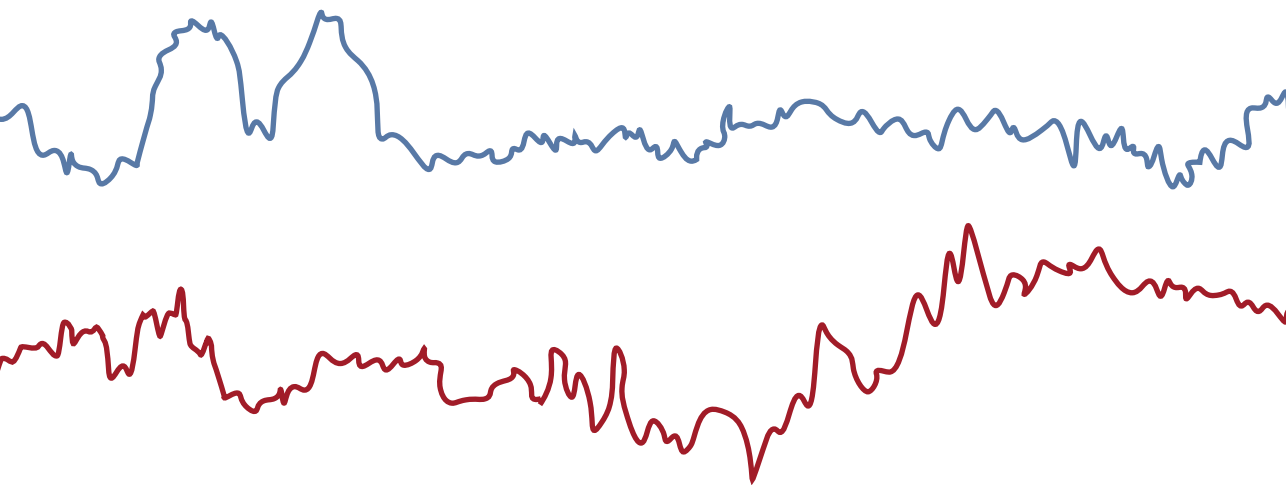
CHAPTER 1.

Early and late dot probe attentional bias to mild and high threat pictures:
relations with EEG theta/beta ratio, self-reported trait attentional control and trait
anxiety

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ABSTRACT

Frontal EEG theta/beta ratio (TBR; negatively associated with attentional control, or AC) was previously reported to moderate threat-level dependent attentional bias in a pictorial dot-probe task (DPT), interacting with trait anxiety. Unexpectedly, this was independent from processing stage (using cue-target delays of 200 and 500 ms) and also not observed for self-reported trait AC. We therefore aimed to replicate these effects of TBR and trait anxiety and to test if effects of early versus late processing stages are evident for shorter cue-target delays. This study also revisited the hypothesis that TBR and self-reported trait AC show similar effects. Fifty-three participants provided measurements of frontal TBR, self-reported trait AC, trait anxiety and DPT-bias for mild and high threat pictures using the same DPT, but this time with 80 and 200 ms cue-target delays. Results indicated that higher TBR predicted more attention to mild than high threat, but this was independent from trait anxiety or delay. Lower self-reported trait AC predicted more attention to mild than high threat, only after 200 ms (also independent of trait anxiety). We conclude that the moderating effect of TBR on threat-level dependent DPT-bias was replicated, but not the role of trait anxiety, and this study partially confirms that effects of trait AC are more dominant in later processing.

Vigilance to highly threatening stimuli is a natural and adaptive response (Ohman, 1993, 1994; Whalen, 1998). An efficient response when task-irrelevant stimuli are subjectively evaluated as being only mildly aversive, would be to direct attention away from them (e.g. Bradley, Mogg, Falla, & Hamilton, 1998; Koster, Verschuere, Crombez, & Van Damme, 2005; MacLeod, Mathews, & Tata, 1986). Highly anxious individuals have a tendency to appraise mildly threatening stimuli and situations as highly threatening (see Mogg & Bradley, 1998; 2016; Cisler & Koster, 2010). Many studies have indeed demonstrated a vigilant bias to high threat in most people, which extends toward mild threat when people are more anxious (for reviews and meta-analysis, see Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, van IJzendoorn, 2007; Cisler & Koster, 2010; van Bockstaele, Verschuere, Tibboel, De Houwer, Crombez, & Koster, 2014). This attentional over-processing of mild threat, or 'attentional bias to threat', may occur automatically and is probably a maintenance factor of anxiety disorders (van Bockstaele et al.). In highly anxious individuals, however, attentional avoidance might also occur (e.g. Koster et al., 2005; Mogg, Bradley, Miles, & Dixon, 2004; Schoorl, Putman, van der Werff, & van der Does, 2014; Wald, Shechner, Bitton, Holoshitz, Charney, Muller, et al., 2011). This attentional avoidance may occur especially for highly threatening stimuli (Mogg & Bradley, 2016), e.g., phobia- or trauma-related stimuli or scenes cueing immediate threats to physical integrity (e.g., Koster et al., 2007; Schoorl et al., 2014; Mogg, Philippot & Bradley, 2004; Pine et al., 2005). Trait attentional control may have a crucial influence in this (Mogg & Bradley, 1998; 2016). Attentional avoidance may result from a secondary process, mediated by strategic, top-down attentional control (Mogg & Bradley, 2016). The question of whether such avoidance is indeed controlled or if it also occurs automatically is still open to empirical study. For instance, more avoidance of trauma-related pictures was observed in patients with post-traumatic stress disorder (PTSD) who also reported low attentional control, suggesting that avoidance was the more automatic response (Schoorl et al., 2014). Also, the time course of such a supposedly secondary avoidant response is far from clear and it may occur even earlier than 200 ms after cue presentation (Koster, Crombez, Verschuere, Vanvolsem & De Houwer, 2007; Mackintosh & Mathews, 2003).

Consequently, individual differences in trait attentional control (AC) may be of crucial importance in the manifestation of attentional bias to threat. Trait AC may be measured by self-report (attentional control scale, ACS; Derryberry & Reed, 2002). Most studies on trait AC and attentional bias used the ACS (e.g., Bardeen & Orcutt, 2011; Derryberry & Reed, 2002; Putman, Arias-Garcia, Pantazi, & van Schie, 2012; Schoorl et al., 2014; Taylor, Cross, and Amir., 2016; Peers & Lawrence, 2009) and three studies used an objective (performance-based) measure of AC (Hou, Moss-Morris, Risdale, Lynch, Jeevaratnam, Bradley & Mogg, 2014; Reinholdt-Dunne, Mogg, & Bradley, 2009; Bardeen & Daniel, 2017). Research into the role of trait AC in attentional threat bias may benefit from using self-report as well as objective markers of trait AC to obtain converging evidence for different methods (see also Bardeen & Daniel, 2017).

A potential objective electrophysiological measure for trait AC can be derived from spontaneous (also known as "resting-state") activity in electroencephalography (EEG). Frontal theta/beta ratio (TBR) reflects the ratio between power in the slow (theta) frequency band and the fast (beta) frequency band. High TBR is related to poor prefrontal cortex (PFC) mediated attentional and inhibitory functions, as seen in attention deficit/hyperactivity disorder (ADHD; for reviews and meta-analyses see Arns, Conners, & Kraemer, 2013; Barry,

Clarke, & Johnstone, 2003). TBR has been suggested to reflect functional reciprocal cortical-subcortical interactions in healthy as well as clinical populations (Knyazev, 2007; Schutter & Knyazev, 2012) and it might reflect voluntary top-down processes of executive control (including AC), mediated by (dorso-lateral) PFC, over bottom-up processes from limbic areas (such as the anterior cingulate cortex, hippocampus and amygdala; Bishop, 2008; Gregoriou, Rossi, Ungerleider, Desimone, 2014; Knyazev, 2007; Schutter & Knyazev, 2012; Hermans, Henckens, Joels, & Fernandez, 2014). Besides TBR's association with ADHD, its status as an index of AC is based on repeated observations that frontal TBR is associated with PFC-mediated cognitive and cognitive-emotional processes (Angelidis, van der Does, Schakel, & Putman, 2016; Putman, van Peer, Maimari, & van der Werff, 2010; Putman, Verkuil, Arias-Garcia, Pantazi, & van Schie, 2014; Angelidis, Hagenaaers, van Son, van der Does, & Putman, 2018; Keune, Hansen, Weber, Zapf, Habich, Muenssinger & Wolf et al., 2017; Schutter & van Honk, 2005a; Massar, Kenemans, & Schutter, 2014; Schutte, Kenemans, & Schutter, 2017; Sari, Koster, Pourtois, & Derakshan, 2015). PFC-mediated cognitive control seems to play an important role in the attentional processing of threatening information (see also Mogg & Bradley, 2016; Shechner & Bar-Haim, 2016).

Accordingly, TBR was positively correlated with attention toward mild threat and negatively correlated with attention toward high threat, as measured with a dot-probe task (Angelidis et al., 2018). The latter correlation was mostly evident for low anxious people. Those data confirmed that adaptive attentional responding to varying threat levels depends on cognitive control and that TBR can be used to study these processes. The *first aim* of the present study was to replicate these novel findings for TBR and trait anxiety in relation to threat-level dependent attentional bias, using the same dot probe task as Angelidis et al. Because of the theoretical assumption that processes of trait AC in attentional threat-bias need some time to develop as they might rely on secondary PFC-mediated control over fast and automatic initial bottom-up processes (Ohman, 1993, 1994; Whalen, 1998; Derryberry & Reed, 2002; Mogg & Bradley, 1998; 2016; Bardeen & Orcutt, 2011; Koster et al., 2007), Angelidis et al. (2018) tested if effects of TBR would be different in early and late processing stages. However, contrary to expectations, the results of Angelidis et al. were independent of processing stage: a 200 ms cue-target delay (intended to capture the early attentional processes) showed no different results than a 500 ms cue-target delay (late attentional processes). We concluded that 200 ms delay may have been too long to capture early attentional processes and that the delay-hypothesis should be revisited. The *second aim* of the present study was therefore to revisit the hypothesis that AC should influence attentional bias more in later and controlled than in earlier and automatic processing stages, using shorter cue-target delays than in Angelidis et al.: a short delay of 80 ms and a long delay of 200 ms.

Another unexpected finding in Angelidis et al. (2018) was that self-reported trait AC was not related to threat-bias or to TBR. To show the role of trait AC in attentional processing of threat using converging methods (EEG and self-report) would strengthen the interpretation of these findings. Therefore, the *third aim* of the current study was to re-examine the relationship between attentional bias and trait AC, using ACS scores as well as TBR as indices of trait AC. We hypothesized that TBR and ACS would be negatively correlated – when controlling for trait anxiety (c.f., Putman et al., 2010; 2014; Angelidis et al., 2016) and that both indices would show similar relations with anxious attentional bias to threat.

In summary, building on the findings of Angelidis et al. (2018) and theoretical frameworks on the effects of threat-level and processing stages in relation to anxiety as outlined above (e.g. Mogg & Bradley, 1998; 2016), we aimed to investigate whether frontal EEG TBR is related to attentional bias in response to mild and high threatening stimuli (also in interaction with trait anxiety), if these effects are more pronounced in later (controlled) than earlier (automatic) processing stages and if self-reported trait AC and TBR (which are expected to correlate negatively) show converging effects. We used the same design as in Angelidis et al., (2018), but the dot-probe task contained a similar but new set of stimuli and shorter cue-target delays (80 and 200 ms). We tested the following hypotheses:

Hypothesis 1a: Frontal TBR moderates attentional responding to threat-level dependent bias in a dot-probe task, and high frontal TBR will be related to relatively more attention toward mild threatening pictures and relatively more attention away from high threatening pictures.

Hypothesis 1b: Self-reported trait anxiety moderates the relationship of hypothesis 1a between frontal TBR and effect of threat-level.

Hypothesis 2: These effects of hypothesis 1a and 1b should be more pronounced after a long cue-target delay (200 ms) than after a short cue-target delay (80 ms).

Hypothesis 3: Self-reported trait AC correlates negatively to TBR when controlling for trait anxiety.

Hypothesis 4a: Self-reported trait AC moderates attentional responding to threat-level dependent bias in a dot-probe task, and low trait AC will be related to relatively more attention toward mild threatening pictures and relatively more attention away from high threatening pictures.

Hypothesis 4b: Self-reported trait anxiety moderates the relationship of hypothesis 4a between self-reported trait AC and effect of threat-level.

Hypothesis 5: These effects of hypothesis 4a and 4b should be more pronounced after a long cue-target delay (200 ms) than after a short cue-target delay (80 ms).

These hypotheses were tested in a sample of healthy students, unselected for anxiety levels, looking at the average TBR of the frontal electrodes F3, Fz and F4 as in almost all relevant previous studies in healthy participants.

Methods

Participants

Fifty-three students (47 women) took part in this study. All participants signed informed consent. Participants had to be between 18 and 30 years old. Exclusion criteria were: presence of a mood, anxiety, or attention disorder; frequent use of psychoactive substances; and (history of) a neurological disorder. The study was approved by the local ethics review board (CEP#5927902162).

Materials

Questionnaires. Participants completed the trait version of the State-Trait Anxiety Inventory (STAI-t; Spielberger, 1983; Van der Ploeg, Defares & Spielberger, 1980) and the Attentional Control Scale (ACS; Derryberry & Reed, 2002; Verwoerd, de Jong, & Wessel, 2006). The STAI-t assesses trait anxiety (20 items, range 20-80;

Cronbach's alpha in the current study = 0.89) and the ACS assesses self-reported attentional control in terms of attentional focus, attentional switching and the capacity to quickly generate new thoughts (20 items, range 20-80; Cronbach's alpha in the current study = 0.85).

Dot-Probe task pictures and IAPS ratings. For the dot-probe task, 60 pictures were used from the International Affective Picture System (IAPS; Center for the Study of Emotion and Attention, 1999), a standardized set of emotion eliciting color pictures with normative ratings on valence and arousal. The pictures (stimuli) were selected according to the ratings for valence and arousal (scale 1-9; valence 1: very unpleasant to 9: very pleasant and arousal scales; 1: not arousing at all to 9: very arousing) provided by Lang et al (2005)¹. The mean valence score for mild threatening (MT) stimuli was $M = 2.52$ ($SD = 0.66$) and for high threatening (HT) stimuli $M = 1.63$ ($SD = 0.33$); the mean arousal scores were $M = 5.98$ ($SD = 0.91$) and $M = 6.79$ ($SD = 0.55$), respectively.

Of the 48 stimuli that were used in the main task, 32 were neutral (N; e.g. shoes), eight were high threatening (e.g. mutilated body), and eight were mild threatening (e.g. angry dog) in content. Three types of stimulus pairs were created: N-N, MT-N and HT-N. N-N trials were included to avoid habituation to threatening stimuli; the results on these trials are not reported here. A total of 8 N-N, 8 HT-N and 8 MT-N stimulus pairs were created. The remaining 12 neutral stimuli were selected for twelve N-N practice trials. Each pair of stimuli was subjectively matched on color and composition. We tested whether the average valence and arousal ratings reported by Center for the Study of Emotion and Attention (1999) differed between the categories. HT stimuli had lower valence ratings than MT ($t(31) = 3.42, p = 0.004$), and neutral stimuli ($t(31) = 13.20, p < 0.001$). MT stimuli also had more unpleasant ratings than neutral stimuli ($t(31) = 10.40, p < 0.001$). No difference was found between arousal ratings of HT stimuli and MT stimuli ($t(31) = -2.16, p = 0.53$), HT and MT pictures were both more arousing than neutral pictures (HT-N: $t(31) = -7.15, p < 0.001$; MT-N: $t(31) = -4.68, p < 0.001$).

EEG recording and software. EEG recording was done using 32 Ag/AgCl electrodes placed in an extended 10-20 montage using the ActiveTwo BioSemi system (BioSemi, The Netherlands). Electrodes placed on the left and right mastoids were used for offline re-referencing of the scalp signals to the mastoid signals. The dot-probe task and questionnaires were programmed and presented using E-Prime V2.0 (Psychology Software Tools, Pittsburgh, PA).

Procedure

General Procedure. After informed consent had been obtained, participants completed the STAI-t and the ACS. This was followed by the measurement of resting state EEG in eight alternating one-minute blocks of eyes open/closed recording. The dot-probe task was performed afterwards. The study took approximately 1 hour to complete.

Attentional bias. The dot-probe task was as in Angelidis et al. (2018), however we used a largely different stimulus set and different intervals for short and long probe-delays. During the task, participants sat at a distance of 80 cm away from the screen. The task consisted of 12 practice and 192 test trials, consisting of 64 HT-N, 64 MT-N and 64 N-N trials. In test trials, all stimulus pairs were presented eight times in random order, fully

counterbalanced for cue-target delay (80 or 200 ms), probe position (left/right), and congruency. Each trial started with a random inter-trial interval (ITI) between 500 and 1500 ms. The ITI was followed by a black fixation cross that was presented for 1000 ms in the center of a grey screen, and participants were instructed to look at this cross. The fixation cross was followed by two pictures that appeared vertically centered, 2.2 cm left and right from the screen. Pictures were presented with a height of 7.6 cm and width of 10.7 cm. Immediately after offset of the pictures, a probe (black dot; 5 mm diameter) appeared below the left or right picture location. The participants were asked to indicate the probe location as fast and accurately as possible by pressing response boxes attached to the left and right arm of their chair with their index fingers.

Data Processing

Dot-Probe data. Incorrect responses were excluded from analyses. One participant made 27 errors (more than five standard deviations above mean) and was excluded from further dot-probe task analyses. The average number of errors of the remaining participants was 3.57 ($SD = 2.5$) with a range from 0 to 11. Probe detection was measured in milliseconds and reaction times (RTs) that were shorter than 300 ms or longer than 1000 ms were defined as outliers and removed from the data. After applying this first filter, RTs that deviated more than three standard deviations from the individual mean RT were also removed as outliers (mean total number of removed outliers per participant was 4.27 ($SD = 2.61$)). The number of outliers per participant ranged from 0 to 14. An average of 2.1% of the data were removed in total; mean RT of remaining data was 335 ms ($SD = 36$). Bias scores were calculated for HT-N and MT-N trials separately in short cue-target delay trials (80 ms) and long cue-target delay trials (200 ms) by subtracting the average response time on congruent trials from incongruent trials. Positive bias scores indicate selective attention towards threat whereas negative scores indicate attentional avoidance. Mean RTs and SDs per stimulus-pair per condition and bias scores are presented in **Table 1**. Finally, Δ threat-level contrast scores were calculated separately for short and long delay conditions by subtracting average bias scores of HT-N trials from average bias scores of MT-N trials (a higher score reflecting a relatively stronger attentional bias toward mild compared to high threatening stimuli).

EEG processing. Offline data processing was done using Brain Vision Analyzer V2.0.4 (Brain Products GmbH, Germany). Data was high-pass filtered at 0.1 Hz, low-pass filtered at 100-Hz and a 50-Hz notch filter was applied. The data were automatically corrected for ocular artifacts (Gratton, Coles & Donchin, 1983) in segments of 4 seconds. Remaining segments containing muscle movements, amplitudes above 200 μV or other artifacts were removed. Fast Fourier transformation (Hamming window length 10%) was applied to calculate power density for the beta (13-30 Hz) and theta (4-7 Hz) band. The present research questions concerned the average of the frontal electrodes (F3, Fz and F4, as in Angelidis et al., 2018; see also Angelidis et al., 2016; Putman et al., 2010; Putman et al., 2014; Schutter & Van Honk, 2005). These frontal averages were therefore calculated for both the beta and theta band, other electrodes were used for exploratory purposes that were not meant to be reported. One participant had extremely high theta activity (more than four standard deviations above the mean) and was excluded from further EEG analyses. Frontal theta/beta ratio was calculated by dividing the frontal theta by frontal

beta power density. Frontal theta/beta ratio was non-normally distributed and therefore log10-normalized.

Statistical analyses. The mean bias scores were analyzed using a cue-target delay x threat-level (2 x 2) repeated measures analysis of variance (rm ANOVA). To test if TBR moderated the effect of threat-level on bias score (hypothesis 1a), a 2 level (threat-level) repeated measures ANOVA was performed, this time with frontal TBR added as a covariate to the model. This concerns a directional planned replication hypothesis, so a one-sided test was performed. Mahalanobis distance tests were used to check for bivariate outliers. To test hypothesis 1b and 2, the 2 level (threat-level) rm ANOVA was repeated, followed by a cue-target delay (2) x threat-level (2) rm ANOVA with centered frontal TBR, centered STAI-t, and their interaction term added as covariates to both models. Centered variables were used as predictor variables in the model to control for multicollinearity. Partial correlation testing was done to test hypothesis 3 for the association between TBR and ACS, and to control for confounding by STAI-t (see Putman et al., 2010; 2014; Angelidis et al., 2016). The same analyses that were done for hypotheses 1a, 1b and 2 were repeated for hypotheses 4a, 4b, and 5 but centered frontal TBR was replaced by centered ACS.

Results

Participants

Participants ($N = 53$) had a mean age of 21.7 years; ($SD = 2.6$), mean STAI-t score of 37.7 ($SD = 9.9$) and mean ACS score of 51 ($SD = 8.4$). The mean frontal TBR that was measured during resting state was 1.26 ($SD = 0.54$).

Dot-Probe

Mean RTs and bias scores are presented in Table 1 (see **Table 1**). No significant main effect or interaction effects were observed: cue-target delay ($F(1,51) = 0.067, p = 0.798, \eta_p^2 = 0.001$); threat-level ($F(1,51) = 0.504, p = 0.481, \eta_p^2 = 0.01$) cue-target delay x threat-level ($F(1,51) = 3.283, p = 0.076, \eta_p^2 = 0.06$). Overall bias score compared to zero was also not significant, $t(51) = -0.169, p = 0.866$. In sum, without taking into account variables of individual differences, no clear pattern of biases occurred for the dot-probe task; see **Table 1**.

Footnotes:

¹The following pairs of pictures numbers were used: **HT-N**: 3010-1616, 5661-3130, 3000-7195, 3053-7200, 7496-3064, 7291-3080, 3051-7482, 7110-3068; **MT-N**: 7330-1300, 6570-5890, 3350-5532, 5480-8485, 9265-1590, 5622-9584, 5470-3530, 5830-9921; **N-N**: 2514-1540, 5471-5593, 1731-7490, 2388-2594, 5833-2398, 5010-5201, 5731-2515, 5250-7031.

Table 1. Mean RTs and bias scores (and standard deviations) in ms for the two probe-delays and threat-levels in the dot-probe task ($n = 53$).

<u>Probe-target delay</u>	<u>Threat-level</u>	<u>Congruent</u>	<u>Incongruent</u>	<u>Bias score</u>
80 ms	MT-N	339 (36)	341 (41)	2 (20)
	HT-N	340 (35)	337 (38)	-3 (16)
200 ms	MT-N	330 (39)	326 (39)	-4 (16)
	HT-N	330 (38)	333 (38)	3 (21)
Total	MT-N	334 (41)	333 (39)	-1 (10)
	HT-N	335 (35)	335 (37)	-0.4 (14)

Hypothesis 1a; Frontal TBR moderates attentional responding to threat-level dependent bias in a dot-probe task

Mahalanobis distance tests revealed a significant bivariate outlier case for the relationship between frontal TBR and threat-bias ($D^2 = 7.46$; $p < 0.05$ for MT bias and $D^2 = 14.06$; $p < 0.001$ for HT bias). This case was removed for analyses on TBR and dot-probe task data. The main effect of threat-level was non-significant ($F(1,48) = 0.142$, $p = 0.708$, $\eta_p^2 = 0.003$), but interaction effect of frontal TBR x threat-level was significant (one-tailed) ($F(1,48) = 3.038$, $p = 0.044$, $\eta_p^2 = 0.06$). The effect remained significant (one-tailed) when controlling for STAI-t ($F(1,47) = 3.831$, $p = 0.028$, $\eta_p^2 = 0.075$). **Figure 1.1** depicts this interaction as the relation between TBR and Δ threat-level. It can be seen that high frontal TBR is associated with relatively more attention toward mild threat than toward high threat. Follow-up tests showed no significant correlation between frontal TBR and bias for MT ($r = -0.19$, $p = 0.19$) but a significant negative correlation between frontal TBR and bias for HT ($r = -0.41$, $p = 0.003$). Hypothesis 1a was therefore confirmed.

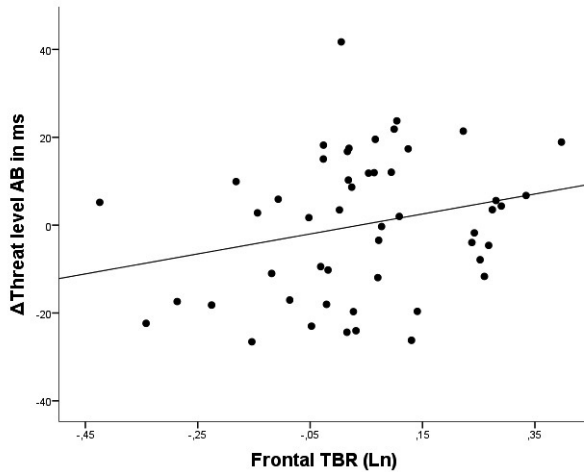


Figure 1.1 The relation between Ln-normalized frontal EEG TBR and Δ Threat level (Bias for MT stimuli – Bias for HT stimuli).

Hypothesis 1b; Self-reported trait anxiety moderates the relationship between frontal TBR and effect of threat-level

The crucial interaction effect between frontal TBR, STAI-t and threat-level was not significant, $F(1,46) = 0.046$, $p = 0.831$, $\eta_p^2 = 0.001$. Hypothesis 1b was therefore rejected.

Hypothesis 2; Cue-target delay related to TBR and TBR x trait anxiety in threat-level dependent dot-probe performance

The crucial interaction effect between frontal TBR x cue-target delay x threat-level was not significant, $F(1,48) = 0.016$, $p = 0.898$, $\eta_p^2 < 0.001$. When we added STAI-t and the frontal TBR x STAI-t interaction term, there was no significant crucial STAI-t x TBR x cue-target delay x threat-level interaction, $F(1,46) = 1.005$, $p = 0.321$, $\eta_p^2 = 0.021$. Thus, hypothesis 2 was rejected.

Hypothesis 3: The relation between TBR and trait-AC

TBR was significantly negatively correlated to trait AC (as measured by the ACS; when controlling for STAI-t, the partial correlation was $r = -0.32$; $p = 0.024$). Frontal TBR also correlated significantly negatively to STAI-t when controlling for ACS (partial $r = -0.336$; $p = 0.016$). Hypothesis 3 was thus confirmed.

Hypothesis 4a and 4b; The effect of trait AC and trait AC x trait anxiety in threat-level dependent dot-probe performance

We performed the same moderation analyses for trait AC (as measured by the ACS), as we did for TBR using the 2 level (threat-level) repeated measures ANOVA with ACS as covariate. This showed no significant ACS x

threat-level interaction, $F(1,50) = 0.149, p = 0.701, \eta_p^2 = 0.003$. To test if the interaction of ACS x STAI-t moderated effect of threat-level, the model was repeated using ACS, STAI-t and their interaction in the model. This revealed no significant ACS x STAI-t x threat-level interaction, $F(1,48) = 0.167, p = 0.685, \eta_p^2 = 0.003$. Hypotheses 4a and 4b are therefore rejected.

Hypothesis 5; Cue-target delay related to trait AC x trait anxiety in threat-level dependent dot-probe performance

A significant ACS x cue-target delay x threat-level interaction was found, $F(1,50) = 7.339, p = 0.009, \eta_p^2 = 0.128$. This interaction remained significant when we controlled for STAI-t, $F(1,49) = 7.863, p = 0.007, \eta_p^2 = 0.138$. This confirms hypothesis 5. Follow-up analyses showed a trend-level ACS x threat-level interaction in the short delay condition, $F(1,50) = 3.174, p = 0.08, \eta_p^2 = 0.06$. **Figure 1.2, left panel**, depicting this interaction as the correlation between ACS and Δ threat-level, clarifies the nature of this interaction; higher ACS scores were associated with a tendency toward higher difference scores for bias for mild minus high threat. ACS was negatively associated with bias toward HT ($r = -0.29, p = 0.04$) and not with bias for MT ($r = 0.09, p = 0.53$) in the short delay condition.

In the long delay condition, there was a significant ACS x threat-level interaction, $F(1,50) = 5.046, p = 0.03, \eta_p^2 = 0.092$, which remained significant when controlling for STAI-t, $F(1,50) = 5.696, p = 0.02, \eta_p^2 = 0.104$. **Figure 1.2** clarifies the nature of this interaction; lower ACS scores were associated with a tendency toward higher difference scores for bias for mild minus high threat. ACS was significantly negatively correlated to bias to MT ($r = -0.28, p = 0.04$) and non-significantly positively correlated with bias to HT ($r = 0.20, p = 0.15$).

To test if ACS and STAI-t interactively moderated a cue-target delay x threat-level effect on bias scores, the cue-target delay (2) x threat-level (2) ANOVA was run with ACS, STAI-t and their interaction term in the model. This showed no significant STAI-t x ACS x cue-target delay x threat-level interaction, $F(1,48) = 0.001, p = 0.973, \eta_p^2 < 0.001$. Hypotheses 5 is thus partially confirmed.

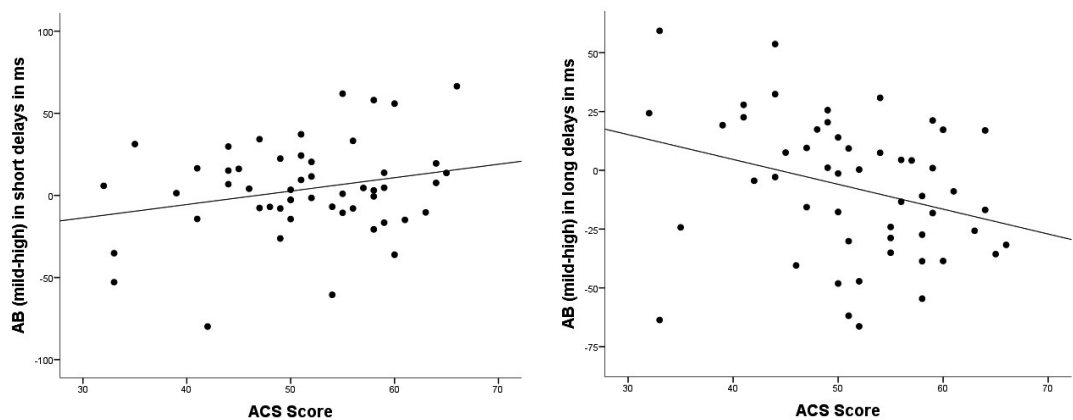


Figure 1.2. The relationship between Δ threat-level (bias score MT – bias score HT) in ms and attentional control in short (80 ms, left) and long (200 ms, right) cue-target delays.

Discussion

This study investigated whether frontal EEG TBR is related to threat-level dependent attentional bias, alone and in interaction with trait anxiety, if results were more pronounced after a longer cue-target delay than after a shorter delay and if findings for self-reported trait AC and for TBR converged, to further test the construct validity of TBR as a marker of trait AC and its role in attentional bias. Results showed that lower TBR was associated with more attention toward high than toward mild threat. Trait anxiety did not interact with TBR's relation to threat-level dependent bias, contrary to expectation. The TBR threat-level interaction was not affected by cue-target delay. As expected, TBR and ACS were negatively correlated, and ACS moderated attentional bias to different threat-levels in a similar manner as TBR did. ACS did not interact with trait anxiety either, but the association between ACS and threat-level was dependent on cue-target delay, as predicted: the ACS x threat-level interaction was specific to the longer cue-target delay. These results are further discussed below.

The finding that TBR moderates attentional bias to different threat-levels replicates our previous study (Angelidis et al., 2018). We tested this hypothesis one-sided since it concerns a planned replication hypothesis, but it should be noted that this was a statistical trend ($p=0.056$) when tested two-sided, likely due to our somewhat smaller sample size. Angelidis et al. (2018) reported that higher TBR (low cognitive control) was associated with relative avoidance of high threatening stimuli compared to mild threatening stimuli and the current data show the same interaction for TBR and threat-level. This is in line with the cognitive motivational model of attentional bias (Mogg & Bradley, 1998; 2016), indicating that attentional bias towards threat may be opposed by mechanisms of avoidance and that individual differences in cognitive control are crucial in the actual manifestation of threat-bias toward or away from threat (Mogg, Weinman & Mathews, 1987; Mogg & Bradley, 2016).

Our next hypothesis was that the moderation of TBR on threat-level would be different in early (80 ms cue-target delays) compared to later (200 ms cue-target delays) stages of attention. However, our data did not show this, similar as in Angelidis et al. (2018) where cue-target delays of 200 and 500 ms were used. The expectation that cue-target delay would affect the results originates from the assumption that the cognitive control mechanisms that regulate automatic attention away from threat (attentional avoidance) occur at later stages of attentional processing (Derryberry & Reed, 2002; Cisler & Koster, 2010; Mogg & Bradley, 1998; 2016). The current results for TBR and the results of Angelidis et al., (2018) do not support this notion. One methodological explanation of the current findings might be that the short cue target delay was too short for sufficient emotional-attentional processing so no bias might be measured at all. However, ACS scores were significantly associated with bias (toward high threat) in the short delay condition. This suggests that the short cue target delay condition was sufficient to allow measurement of attentional bias. An 80 ms delay is known to allow orienting of visuospatial attention (Posner & Cohen, 1984) and in dot-probe tasks, anxious selective attention toward threat has been observed already after 50 ms (Armony & Dolan, 2002) and even after 34 ms, using subliminal presentation (Fox, 2002). All in all, we do not think that the cue-target delay of 80 ms was too short. Another possible methodological explanation for the current data might be that the difference between 80 ms and 200 ms is not large enough to distinguish between early and late attentional processes. Importantly though, we did find a significant delay-dependent ACS moderation of threat-level, where the association was stronger in the longer cue-target condition, as expected. In conclusion, we do not have a ready explanation for the absence of a delay effect for TBR, especially considering the current positive finding for ACS. The latter finding is in line with two previous studies (Derryberry & Reed, 2002; Bardeen & Orcutt, 2011) that also measured visuospatial threat-biased attention, albeit with different cue-target delays. Considering a delay effect for one measure of trait AC (ACS) but no such effect for the other index of trait AC (TBR), we conclude that our results on this issue are inconclusive. Measuring the time-course of attention remains notoriously difficult (see also Mogg & Bradley, 2016). Different methods such as emotional cueing tasks (Koster et al., 2007), event-related potential tasks (Harrewijn, Schmidt, Westenberg, Tang, & van der Molen, 2017) or even non-spatial emotional-attention tasks such as interference tasks (Clarke et al., 2013) or serial presentation tasks (Peers & Lawrence, 2009) might be used in future studies to assess the time-course of selective attention, attentional avoidance and attentional control.

We hypothesized that the moderation of TBR on threat-level would interact with trait anxiety, but this was not observed. A possible explanation might be that we used different stimuli than in Angelidis et al. (2018). We cannot compare the sets because the ratings of the stimuli in Angelidis et al. (2018) were collected in a different sample and in a different experimental setting than the IAPS ratings. Perhaps pre-selecting participants on high trait anxiety and/or manipulation of state anxiety could be helpful in resolving this issue, as attentional threat bias might depend on interaction between trait and state anxiety (Egloff & Hock, 2001).

Contrary to Angelidis et al. (2018), a significant correlation between TBR and ACS scores (independent of trait anxiety) was found in the current sample, which is in line with previous studies from our lab (Putman et al., 2010; 2014; Angelidis et al., 2016) and with reported negative correlations between TBR and task-based objective measures of attention (Keune et al., 2017). Conceptualizing TBR as a marker of attentional control, we also

predicted that ACS scores (which indicate trait AC) would show a similar relation with dot-probe task performance as TBR. This was partially confirmed: lower ACS was related to relative avoidance of high threatening stimuli and also to attentional bias toward mild threatening stimuli. This conceptually replicates the TBR effect, but only when taking cue-target delay into consideration, which is largely consistent with our predictions. Although TBR was reported to have a very high one and two-week re-test reliability (Angelidis et al., 2016; Keune et al., 2017), little is known about transient state-fluctuations of TBR and operationally our TBR measure was done at a single point in time. Since acute fluctuations in trait AC may occur as a function of factors as diverse as fatigue (van der Linden, Frese & Meijman, 2003) or circadian rhythm (van Dongen & Dinges, 2000), results for trait and state measures of trait AC should not be expected to correlate perfectly. As such it is encouraging that results of the current study for trait ACS and TBR converged. This solidifies the interpretation of the current TBR results as well as the similar results of Angelidis et al., (2018), supporting the construct validity of TBR as a reflection of neural processes underlying trait AC.

Altogether, our findings that both TBR and ACS are related to attentional processing of cues with different threat-levels, indicate that executive control plays a critical role in threat processing. The current study emphasizes the importance of threat-level; different attentional responses were found for high versus mild threatening stimuli, moderated by frontal TBR and ACS. Schechner & Bar-Haim (2016) recently also emphasized the importance of subjective threat evaluation (influences of state anxiety) in the manifestation of threat-avoidant attentional bias. Their findings and ours carry possible implications for the currently popular attentional bias modification paradigm and its attempts to train attentional bias away from threat with the objective of effecting more adaptive and healthy attentional processing styles (Cristea, Kok & Cuijpers, 2015).

Potential limitations of this study include that we used a smaller sample and a lower number of males than the previous study (Angelidis et al., 2018). The stimulus set included eight high and eight mild threatening stimuli, which may be considered a fairly small set. The fact that our results for TBR and threat-level dependent attention partially replicate Angelidis et al. (2018) who used a largely different stimulus-set, is reassuring. Still, future research could consider using larger sets of stimuli to avoid possible artefacts resulting from narrow stimulus sampling.

To conclude, this study partially replicated previously reported relations between TBR and threat-level dependent dot probe bias and as such supports the notion of frontal TBR as an electrophysiological marker for executive control, i.e. regulation of attentional processing of threatening stimuli. The direction of attentional bias depends on individual differences in attentional control and threat level of the stimuli. The issue of early and automatic versus late and controlled attentional processing remains unresolved as only effects of self-reported trait AC, but not of TBR, were confined to a later stage of processing and requires further investigation. Finally, converging results were found for TBR and an often used and validated (Judah, Grant, Mills, & Lechner, 2014) self-report measure of trait AC, supporting construct validity.

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Chapter 1

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