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Do not look away! Spontaneous frontal EEG theta/beta ratio as a marker for cognitive control over attention to mild and high threat

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ABSTRACT

Background: Low spontaneous EEG theta/beta ratio (TBR) is associated with greater executive control. Their role in regulation of attentional bias for stimuli of different threat-levels is unknown.
Objectives: To provide the first relations between frontal TBR, trait anxiety and attentional bias to mildly and highly threatening stimuli at different processing-stages.
Methods: Seventy-four healthy volunteers completed spontaneous EEG measurement, a self-report trait anxiety questionnaire and a dot-probe task with stimuli of different threat-level and 200 and 500 ms cue-target delays.
Results: Participants with high TBR directed attention towards mildly threatening and avoided highly threatening pictures. Moreover, the most resilient participants, (low TBR and low trait anxiety) showed attention towards highly threatening stimuli. There were no effects of delay.
Conclusions: These data confirm that executive control is crucial for the study of threat-related attentional bias and further support the notion that TBR is a marker of cognitive control over emotional information.

1. Introduction

Spontaneous (or resting-state) electroencephalographic (EEG) signal can be decomposed into power of different frequency bands. Theta/beta ratio (TBR) is the ratio of slow wave theta power (4–7 Hz) and fast wave beta power (13–30 Hz), that is found to have a very high one-week test-retest reliability (r = 0.93; Angelidis, van der Does, Schakel, & Putman, 2016). It has been suggested that low TBR might reflect enhanced prefrontal cortical (PFC) regulation over emotion-driven bottom-up tendencies (Knyazev, 2007; Schutter & Knyazev, 2012). Relatively greater theta compared to beta power (high TBR) has been reported many times for patients with attention deficit disorder or attention deficit/hyperactivity disorder (ADHD; Arns, Conners, & Kraemer, 2013; Barry, Clarke, & Johnstone, 2003). In line with this relationship, administration of psychostimulants that are commonly used to treat ADHD symptomatology and enhance PFC-network integrity, decrease TBR (Arnsten, 2006; Clarke, Barry, McCarthy, Selikowitz, & Brown, 2002; Clarke, Barry, McCarthy, Selikowitz, & Johnstone, 2007; Loo et al., 2016).

During the last decade, there has been increasing interest in TBR in healthy individuals, in particular in its association with cognitive control and specifically cognitive-affect regulation. Training of working memory capacity in high trait anxious individuals (working memory capacity is reduced in anxious people; Eysenck, Derakshan, Santos, & Calvo, 2007) has been found to decrease frontal TBR (Sari, Koster, Pourtois, & Derakshan, 2015). Theta band transcranial alternating current stimulation (tACS), a method that has sometimes been found to enhance working memory capacity (Jausovec & Jausovec, 2014), reduced spontaneous frontal TBR and improved flexible contingency-based learning in a motivated decision task (Wischnewski, Zerr, & Schutter, 2016). Moreover, frontal TBR has repeatedly been found to be correlated negatively to self-reported attentional control, cross-sectionally and with a one-week predictive interval (Angelidis et al., 2016; Putman, van Peer, Maimari, & van der Werff, 2010; Putman, Verkuil, Arias-Garcia, Pantazi, & van Schie, 2014). In addition, frontal TBR was found to predict the negative impact of a psychosocial stressor on self-reported state attentional control (Putman et al., 2014). All in all, and as we shall see below, accumulating evidence confirms that (frontal) TBR is negatively related to executive, most notably attentional, control. Ontogenetic and phylogenetical development of the brain towards more cortical control is related to decreasing theta and increasing beta activity (Knyazev, 2007). Theta oscillations are likely mostly generated

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in anterior cingulate cortex (ACC) and subcortical limbic structures (most importantly hippocampus; Mitchell, McNaughton, Flanagan, & Kirk, 2008). ACC-generated theta might signal necessity for increased cognitive control (Cavanagh and Frank, 2014; Cavanagh and Shackman, 2015). Beta EEG activity is of cortical origin and has been related to motoric and cognitive control, including attentional inhibition, cognitive set-maintenance and cognitive effort (Braboszcz and Delorme, 2011; Buschman and Miller, 2007, 2009; Engel and Fries, 2010; Huster, Enriquez-Geppert, Lavallee, Falkenstein, & Herrmann; Waldhauser, Johansson, & Hanslmayr, 2012) and has also been implicated in regulation of anxiety (Knyazev & Slobodskaya, 2003; Schutter & Knyazev, 2012; Schutter & Van Honk, 2005). However, it is not clear how such evoked-related theta and beta activity is related to spontaneous EEG.

Attentional control, a key function of executive control, regulates goal-directed processing of emotional information (Bishop, Jenkins, & Lawrence, 2007; Derryberry & Reed, 2002; Peers & Lawrence, 2009; Peers, Simons, & Lawrence, 2013; Putman, Arias-Garcia, Pantazi, & van Schie, 2012; Reinholdt-Dunne, Mogg, & Bradley, 2009; Schoorl, Putman, Van Der Werff, & Van Der Does, 2014; Taylor, Cross, & Amir, 2016). Evidence suggests that attentional control is reciprocally regulated by two systems; i) voluntary top-down processes, accountable for sustained attention to task-relevant information, which are mainly dependent on the dorsolateral PFC (Bishop, 2008; Fani et al., 2012; Gregoriou, Rossi, Ungerleider, & Desimone, 2014), and ii) automatic bottom-up processes, engaging attention to salient (e.g. emotionally arousing) information which is mediated by limbic, mostly subcortical areas (Bishop, 2008; Hermans, Henckens, Joels, & Fernandez, 2014; Ledoux, 1995). TBR is suggested to reflect cortical-subcortical interactions between such networks (Knyazev, 2007; Schutter & Knyazev, 2012). Consistent with this notion, low frontal TBR predicts resilience against stress-induced reductions of attentional control (Putman et al., 2014) and low frontal TBR was associated with better modulation by emotionally relevant stimuli of response inhibition (Putman et al., 2010), which is a key function of executive control (e.g. Derakshan & Eysenck, 2009; Miyake & Friedman, 2012). Additionally, low frontal/parietal TBR was linked to facilitated spontaneous emotion regulation (Tortella-Feliu et al., 2014). Other studies found that low frontal/central TBR (Massar, Kenemans, & Schutter, 2014; Massar, Rossi, Schutter, & Kenemans, 2012) and low frontal/parietal TBR (Schutter & Van Honk, 2005) were related to flexible goal-directed control over motivated decision-making and that lower frontal TBR was related to greater flexibility in contingency-learning in a motivated decision task (Schutte, Kenemans, & Schutter, 2017).

Taken together, these findings suggest that frontal TBR is a reliable electrophysiological marker of the neural dynamics involved in executive control over cortical and subcortical processes. This may in particular be the case during the processing of emotional information (Morillas-Romero, Tortella-Feliu, Bornas, & Putman, 2015), rendering it a promising tool to investigate cognitive-affect regulation. It would therefore be of value to investigate relations between TBR and the control of attentional bias to threat.

Attentional bias toward threat is a cognitive mechanism enhancing the processing of threatening stimuli in order to take the necessary actions (e.g., Ledoux, 1995; Mogg & Bradley, 1998; Oatley & Johnson-laird, 1987). Neurocognitive evidence suggests that attentional bias is a manifestation of cortical-subcortical interactions. As noted above, the salience network augments the automatic processing of salient information whereas top-down executive control advances higher order goal-directed cognition and behaviours (Bishop et al., 2007; Eysenck et al., 2007; Hermans et al., 2014; Mogg & Bradley, 2016; Monk, Trafton, & Boehm-Davis, 2008; Monk et al., 2006). Attentional bias to threat has been studied extensively for several decades as it is considered to play a key role in the development and/or maintenance of affective disorders when its regulation fails (e.g., Beck, 1967; Mathews & Mackintosh, 1998; Mogg & Bradley, 1998; for a recent review see, Van Bockstaele et al., 2014). A vast body of research suggests that anxious individuals exhibit excessive attentional bias to mild threatening information (for meta-analyses see, Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007; Armstrong & Olatunji, 2012; for theoretical reviews see, Cisler & Koster, 2010; Van Bockstaele et al., 2014).

According to several theoretical models (e.g., Mogg & Bradley, 1998; Mathews & Mackintosh, 1998; see Mogg & Bradley, 2016, for an overview and integrative framework) the subjectively perceived threat-level is a crucial feature in the investigation of attentional bias to threat. Subjectively perceived threat is determined not only by individual differences in threat evaluation but also by characteristics of the stimuli (the latter will be referred to as the stimulus threat-level from hereon in). Yet, the influence of stimulus threat-level has received limited systematic empirical study. Most studies have been performed using only a single class of threat stimuli, such as threatening words or pictures of threat-related facial expressions (for overviews see e.g., Bar-Haim et al., 2007; Cisler & Koster, 2010; Bradley, 1998, 2016;), which are defensibly of limited threat intensity, also for highly anxious people. The cognitive-motivational analysis (Bradley, 1998, 2016;) hypothesizes a curvilinear relationship between subjectively perceived threat and attentional bias and postulates the cognitive and emotional efficiency of avoiding mild threatening information and attending high threatening information. According to this framework, low anxious people would avoid unduly processing of goal-irrelevant mild threat in order to focus attention and allocate executive resources to goal-relevant information and to prevent unduly habituation to threat. Indeed, many studies have reported such avoidance of mild threat in low anxious participants (i.e. threatening faces or words, and mild threatening scenes; Bradley, Mogg, Falla, & Hamilton, 1998; Bradley et al., 1997; Koster, Verschuere, Crombez, & Van Damme, 2005; Koster, Crombez, Verschuere, & De Houwer, 2006; MacLeod, Mathews, & Tata, 1986; Mogg & Bradley, 2002; Mogg et al., 2000; Wilson & MacLeod, 2003). In addition, low anxious people would attend towards information which is so highly threatening that its attentional processing is essential for adequate coping with environmental demands (e.g., Mogg et al., 2000; Wilson & MacLeod, 2003). This functional differential responding is accomplished by (prefrontal cortical) cognitive control functions that regulate the attentional response after bottom-up input from automatic threat-appraisal (Mogg & Bradley, 2016). In contrast to this adequate, non-anxious response style, high trait anxious people would attend excessively toward mild threats (for reviews see, Bar-Haim et al., 2007; Armstrong & Olatunji, 2012) as their automatic threat appraisal is biased to overrate danger and anxiety is associated with limited prefrontal cognitive control (Arnsten, 2011, 2015; Derakshan & Eysenck, 2009; Hermans et al., 2014). It is also suggested that high anxious people will avoid high threat stimuli (Amir, Foa, & Coles, 1998; Chen, Ehlers, Clark, & Mansell, 2002; Koster et al., 2005; Koster, Crombez, Verschuere, Van Damme, & Wiersema, 2006; Mackintosh & Mathews, 2003; Mathews, May, Mogg, & Eysenck, 1990; Mogg, Bradley, Miles, & Dixon, 2004; Mogg, Weinman, & Mathews, 1987; Monk et al., 2006; Pine et al., 2005; Price et al., 2014; Putman, 2011; Rohner, 2002, 2004; Schoorl et al., 2014; Wald et al., 2013; Wald, Lubin et al., 2011; Wald, Shechner et al., 2011). This latter anxious avoidance of high threat would be a more controlled and motivated attempt to relieve the short term distress that processing of high threat induces (Bradley, 1998, 2016;). Because such avoidance would require top-down executive control over the attentional bias (i.e., PFC control over a ventral salience network), anxious threat avoidance might become more evident in later stages of attention. However, findings concerning this time-course of vigilance versus avoidance have been inconsistent (Cisler & Koster, 2010; Mogg & Bradley, 2016), which might in part be due to a less then systematic regard for stimulus threat-level or cue-target delay.

In sum, the occurrence of attentional bias toward or away from threat in experimental methods to measure attentional bias is presumably dependent on at least four (often interacting) factors:

participants' anxiety level, participants' attentional control level, stimulus threat-level, and temporal stage of processing.

Besides anxiety, voluntary cognitive control is thus suggested to have an important role in the attentional processing of threatening information (see, Corbetta & Shulman, 2002; Derakshan & Eysenck, 2009; Derryberry & Reed, 2002; Mogg & Bradley, 2016). By far most studies have addressed relationships between attentional threat bias and anxiety, but more recently, accumulating evidence shows that trait attentional control as assessed with the self-report attentional control scale (ACS; Derryberry & Reed, 2002), is indeed associated with regulation of attentional processing of threat (e.g., Bardeen & Orcutt, 2011; Bishop et al., 2007; Derryberry & Reed, 2002; Putman et al., 2012; Schoorl et al., 2014; Peers & Lawrence, 2009; Taylor et al., 2016). To the best of our knowledge, only two studies have addressed relationships between attention to threat and objective measures of attentional control (Hou et al., 2014; Reinholdt-Dunne et al., 2009). In such studies assessing the role of attentional control, it was sometimes found to be related to vigilance and sometimes to avoidance, which might be due to a variety of methodological differences between these studies, ranging from the stimuli and temporal intervals to the methods used to asses attentional bias (e.g., visuospatial attention versus cognitive interference). Since according to the cognitive-motivational analysis the manifested attentional bias is determined by an interplay between automatically perceived threat and cognitive control, we should expect to see that individual differences in attentional control moderate effects of threat level on attentional bias, with more control being associated with greater differential responding to various (perceived) threat intensities.

Based on above notions concerning the role of anxiety on automatic threat-appraisal and the negative relation between anxiety and attentional control, one would also expect that attentional control interacts with anxiety in the processing of threatening information in healthy as well as in clinical samples. This has been reported several times now (e.g., Bardeen & Orcutt, 2011; Derryberry & Reed, 2002; Hou et al., 2014; Reinholdt-Dunne et al., 2009; Schoorl et al., 2014; Taylor et al., 2016). Derryberry and Reed showed that such an interaction between attentional control and anxiety moderated threat bias only in later stages of attention, in line with the assumption that cognitive control is a voluntary and slower process. However, contrary to those findings, Bardeen and Orcutt reported a relationship between attentional control and attentional bias only for a short (150 ms) but not for a long (500 ms) cue-target interval. Schoorl et al. did find an anxiety-attentional control interaction for the latter longer delay with a similar dot probe task.

In sum, for a fuller understanding of attentional bias to threat, we need to consider not only anxiety levels, but also attentional control levels, stimulus threat-levels and possibly also temporal stages of attentional processing. As of yet, to the best of our knowledge, not one study has addressed all of these factors simultaneously. In addition, the almost exclusive reliance on self-reported attentional control might be considered a limitation, as one study that used an objective measure of attentional control as well as the self-reported ACS reported divergent findings for these measures with respect to attentional threat bias (Reinholdt-Dunne et al., 2009). Therefore, the aim of the present study was to investigate the relationship between frontal TBR, trait anxiety and attentional processing of threatening information of various threat-levels.

Considering TBR as an objective marker for executive control (e.g., Angelidis et al., 2016; Putman et al., 2010; Putman et al., 2014; Tortella-Feliu et al., 2014), and based on the cognitive-motivational analysis (Bradley, 1998, 2016;), we hypothesized firstly that TBR is related to differential attentional responses to stimuli of different threat-level. Specifically, in a non-selected sample with mostly limited trait anxiety levels and thus likely moderate threat-perception of mild threat stimuli, we would expect that participants with high cognitive control (low TBR) would show little attentional bias toward mild threat on a dot-probe task. For highly threatening stimuli the opposite was expected: people with low TBR should show large bias toward high threat. Secondly, as anxiety is considered to determine the automatic perception of threat intensity (Bradley, 1998, 2016;) and due to previous findings suggesting the interacting role of attentional control and anxiety on attentional bias (e.g., Bardeen & Orcutt, 2011; Derryberry & Reed, 2002; Reinholdt-Dunne et al., 2009; Schoorl et al., 2014; Taylor et al., 2016) we hypothesized that the relation between TBR and the effect of threat-level would interact with levels of trait anxiety. A more specific prediction seems premature given the scarcity of evidence on how participants' anxiety levels interact with stimulus threat-level, but given the theoretical frameworks outlined above, the assumption of moderation by anxiety seems most likely and must be tested. Thirdly, we expected that relationships between TBR and threat level-dependent attentional bias (and trait anxiety) would interact with the time-stages of attentional processing. It was specifically expected that direct or anxiety-dependent relations between TBR and dot-probe performance would be most evident in later stages of attention. Finally, as secondary research questions, we sought to replicate the negative association between TBR and self-reported attentional control using the ACS (Putman et al., 2010; Putman et al., 2014; Angelidis et al., 2016) and assess the relationship between ACS score and dot-probe performance, expecting a similar (but opposite) pattern of results as for TBR.

2. Methods

2.1. Participants

Seventy four Dutch-speaking participants (36 males) were recruited on Leiden University campus. Exclusion criteria were: diagnosis of mood, anxiety, or attention disorders, frequent use of psychoactive substances and (history of) a neurological disorder. All participants signed informed consent. Due to ethical considerations, participants were informed in advance about the potentially disturbing nature of some of the images that were used in the dot probe task. The study was approved by the local review board.

2.2. Apparatus and materials

2.2.1. EEG recording

Eight-minutes resting-state EEG data (in alternating 1-min blocks of closed and open eyes) were acquired with Biosemi ActiveTwo system following the same method as Putman et al. (2014) and Angelidis et al. (2016). The sampling rate was set at 256 Hz (Allen, Coan, & Nazarian, 2004). Ag/AgCl electrodes were used on the F3, Fz, F4, C3, Cz, C4, P3, Pz, P4 10/20 positions. The present research questions concerned the frontal electrodes (Angelidis et al., 2016; Putman et al., 2010; Putman et al., 2014; Schutter & van Honk, 2004; Schutter & Van Honk, 2005). Common mode sense (CMS) and driven right leg (DRL) electrodes served as ground. Ag/AgCl electrodes were applied on the supra- and suborbital ridge of the right eye and on the external canthi of each eye to record electro-oculogram (EOG).

Data preparation. The same procedure as in Putman et al. (2014) and Angelidis et al. (2016) was used. Scalp signals were offline re-referenced to the average of the left and right mastoid electrodes. A 50 Hz notch filter, a low-pass filter of 100 Hz, and a high-pass filter of 0.1 Hz were applied to the re-referenced data. (Angelidis et al., 2016)Then, data were segmented into segments of 4 s with 50% overlap. After rejecting segments with artifacts, data were corrected for ocular movements (Gratton, Coles, & Donchin, 1983). The remaining segments were averaged for further analysis. A fast Fourier transformation (10% hamming window, using a resolution of 0.25 Hz) was then used to estimate area power density ($\mu V^2/Hz$) in the theta (4–7 Hz) and beta (13–30 Hz) frequency bands. Then the ratio of the average three frontal power densities (F3, Fz, F4) of theta divided by beta was calculated in order to obtain frontal TBR (cf. Putman et al., 2010, 2014; Angelidis et al., 2016). Natural log-normalization (Ln) was applied to average frontal TBR due to typical skewed distribution. Higher TBR reflects relatively greater theta compared to beta power (lower attentional control). Data processing was performed in Brain Vision Analyzer V2.04 (Brain Products GmbH, Germany).

2.3. Dot-probe task

Attentional bias was assessed by with a dot-probe task (c.f. Arguedas, Green, Langdon, & Coltheart, 2006; Koster, Crombez, Verschuere, Van Damme et al., 2006; Pourtois, Grandjean, Sander, & Vuilleumier, 2004). The present task consisted of 206 trials (12 practice trials and 2 buffer trials immediately followed by 192 test trials). Each trial started with an inter-trial interval (ITI) that varied randomly between 500 and 1500 ms. The ITI was followed by a black fixation cross that was presented for 1000 ms in the middle of a grey screen. Then, a pair of pictures appeared simultaneously, 2.2 cm left and right of the centre of the screen. After the offset of the pictures after a cue-target delay of either 200 or 500 ms, a probe (black dot with 5 mm diameter) appeared directly below the central position of a threat picture (congruent trial) or a neutral picture (incongruent trial). The probe remained on the screen until participant's response. The participants were asked to indicate the position of the probe by pressing either the right or the left labeled button on the response box (SRBOX; Psychology Software Tools, PST) with their index fingers. Attentional bias was calculated by subtracting RTs in congruent trials from RTs in incongruent trials. Positive scores are considered an indication of selective attention towards threat (vigilance) while negative scores reflect avoidance of threatening stimuli.

Forty eight pictures were selected from the International Affective Picture System (IAPS; Center for the Study of Emotion and Attention). Pictures with black borders were size-adjusted to fit the file format after deleting the black borders. The neutral pictures were pictures of household objects or scenes; the mildly threatening pictures (MT) depicted scenes of human or animal attack; and the highly threatening (HT) pictures depicted scenes of physical injury. Three categories of stimulus pairs[1] were developed; highly threatening pictures presented together with neutral pictures (HT-N), mildly threatening pictures paired with neutral pictures (MT-N) and pairs of two neutral pictures (N-N). Stimuli in each pair were subjectively matched for complexity, brightness and color. Each category of picture-pairs (N-N, MT-N, HT-N) consisted of eight pairs and each pair was presented eight times equally divided across 200 and 500 ms presentation time, localization of threatening pictures on the right and left side of the screen, and congruency. The eight trials of each stimulus-pair were presented in a random order while, in order to avoid sequential presentations of the same stimulus-pair, each stimulus-pair was randomly presented within 8 cycle-presentations. Pictures were presented with a height of 7.6 cm and width of 10.7 cm. The dot-probe task was programmed in E-Prime 2 (Psychology Software Tools, PST) and presented on a 19" CRT monitor (resolution at 1024 × 768). Participants were seated in a chair maintaining an approximately 80 cm viewing distance from the screen.

Data preparation. First, all error trials were removed (on average 0.65%). Then, trials with an RT < 200 or > 1000 ms were removed as premature responses or extremely long RTs. A second filter was also applied in order to remove individual outliers which were defined as RTs that deviated more than three standard deviations from the individual RT mean. These filters resulted in the removal of 1.66% of the total trials. Individual mean RTs for congruent and incongruent threatening trial types were calculated. Then, attentional bias was calculated by subtracting the mean RT for congruent trials from the mean RT for the incongruent trials, separately for short and long delays, and mild and high threat stimuli. Positive congruency scores indicate selective attention towards threat whereas negative scores indicate attentional avoidance.

2.4. Picture-rating

The 9-point self-assessment manikin (SAM) scales (Lang, 1980) was used to verify ratings for valence and arousal of the IAPS stimuli. Participants were asked, with written instructions, to rate the pictures for valence and arousal. Examples of both valence (1: very unpleasant to 9: very pleasant) and arousal scales (1: not arousing at all 9: very arousing) were provided. Each trial started with a 3 s presentation of a picture which was followed by the SAM scales for valence and arousal until participant's response. All pictures appeared in the same size in which they had been presented in the task and in a random order. Due to the great number of pictures in total, they were divided into three groups and each group was rated by a roughly equal number of participants (half males) in order to limit the duration of the test session. The groups of pictures were approximately equally composed of neutral, MT and HT pictures. The total number of pictures per category was even, so even distribution across the three groups of participants was not possible (of twenty threat pictures, two groups rated seven pictures and one group rated six pictures).

2.5. Questionnaires

Trait anxiety was assessed with Spielberger's State-Trait Anxiety Inventory (STAI-t; Spielberger, 1983; Van der Ploeg, Defares, & Spielberger, 1980). The questionnaire consists of 20 four-point Likert items. An example of an item is "I worry too much over something that really doesn't matter". As commonly reported, the internal consistency of STAI-t was high in the present study (Cronbach's alpha was 0.88).

The Attentional Control Scale (ACS; Derryberry & Reed, 2002; Verwoerd, de Jong, & Wessel, 2006) consists of 20 items, rated on a 4-point Likert-scale, assessing attentional focus, attentional shift and cognitive flexibility. Examples of items are "When I'm working hard on something, I still get distracted by events around me" and "After being interrupted or distracted, I can easily shift my attention back to what I was doing before". Internal consistency of the total ACS score in this study was good (Cronbach's alpha 0.79).

2.6. Procedure

After a brief screening procedure, spontaneous EEG was recorded in a room with dim light. Participants were then asked to complete some questionnaires and perform the dot-probe task and other tests that are not relevant to the present research question. Finally, participants were asked to rate the pictorial stimuli that were used in the dot probe tasks for valence and arousal.

3. Results

3.1. Data quality check

Four participants were excluded for recent use of drugs. One participant was removed from the analyses as he did not comply with the procedures. For the remaining 69 participants, data were checked for univariate (mean ± 2.5 SDs), bivariate ($D^2 > 9.9$, $p < .001$) and multivariate outliers (standardized residuals ± 3; Stevens, 2002) resulting in the exclusion of four cases and thus a final sample of 65 participants. Post-hoc re-analyses were performed for all crucial hypotheses with these four outliers retained, which overall yielded similar

[1] The pairs of pictures that were used: **HT-N**: 5130-3120, 5390-3130, 5520-3064, 5530-3110, 5731-3400, 5740-3069, 7161-3080, 7234-3060; **MT-N**: 7031-6211, 7042-2692, 7057-7361, 7110-6800, 7179-6940, 7192-3280, 7217-2710, 7283-9230; **N-N**: 5471-7490, 7020-7056, 7080-7090, 7190-7170, 7205-7041, 7233-7100, 7491-5510, 7705-7224. Current ratings on valence and arousal are presented in the results section.
[2] N-N trials were included to avoid habituation to threatening pictures and exploratively look at a different research question, not relevant to the goal of the current paper. Thus we do not further report data from these trials.

Table 1
Means and standard deviations for background characteristics, self-report, and frontal EEG data for the total sample (N = 65).

	M	SD
Age	21.8	2.1
STAI-t	35.9	7.1
ACS	53.7	7.3
TBR	1.176	0.553
Theta	11.728	5.814
Beta	11.148	6.015

Note: reported descriptives of frontal TBR, theta power, and beta power are not Ln-normalized for more intuitive appreciation and comparability with other studies. STAI-t = Spielberger's state trait anxiety inventory − trait subscale, ACS = attentional control scale.

results.

3.2. Participants

The characteristics of the sample are presented in Table 1.

3.3. TBR and threat level-dependent attentional bias

A repeated measures (rm) ANOVA was performed on bias scores with Cue-target delay (2; 200 and 500 ms) and Threat level (2; MT and HT) as within-subjects factors, and centered TBR as a covariate. Analysis revealed a significant Threat level × TBR interaction (F(1, 63) = 19.19, $p < .001$, $\eta_p^2 = 0.23$). No other interactions or main effects were significant.

In order to facilitate interpretation of the Threat level × TBR interaction a contrast score was computed between bias scores for MT pictures and HT pictures (ΔThreat; bias score for MT Pictures − bias score for HT pictures) with positive scores indicating greater bias score for MT stimuli relative to HT stimuli. Post-hoc correlational analyses revealed that the significant Threat level × TBR interaction reflected a positive relationship between TBR and ΔThreat (r = 0.48, $p < .001$; see Fig. 1a) indicating that participants with higher TBR showed stronger difference in bias scores between MT and HT pictures, by being more attentive for MT pictures (r = 0.24, p = .057; see Fig. 1b) and avoidant of HT pictures ($r = -0.37$, p = 0.003; see Fig. 1c). The Threat level × TBR interaction remained highly significant after controlling for STAI-t (F(1, 62) = 20.77, $p < .001$, $\eta_p^2 = 0.251$). In sum, the first hypothesis was confirmed: TBR (attentional control) moderates effects of threat level on attentional bias, also independent of trait anxiety: low TBR is related to less bias toward mild threat and more bias toward high threat.[2]

3.4. TBR, trait anxiety and threat-level dependent attentional bias

The second hypothesis was tested by conducting the same rm ANOVA with STAI-t and TBR, and the STAI-t × TBR interaction term as co-variates to test for a crucial three-way Threat level × TBR × STAI-t interaction. Analysis revealed a significant Threat level × TBR (F(1, 61) = 23.68, $p < .001$, $\eta_p^2 = 0.28$) and a significant Threat level × TBR × STAI-t interaction (F(1, 61) = 7.375, p = .009, $\eta_p^2 = 0.11$).

In order to unravel the nature of the three-way interaction, simple slopes analyses were conducted (Aiken & West, 1991). The above mentioned significant lower-level interaction between Threat-level and TBR is visible as a general positive relationship between TBR and ΔThreat (collapsed for Cue-target delay). This relationship was

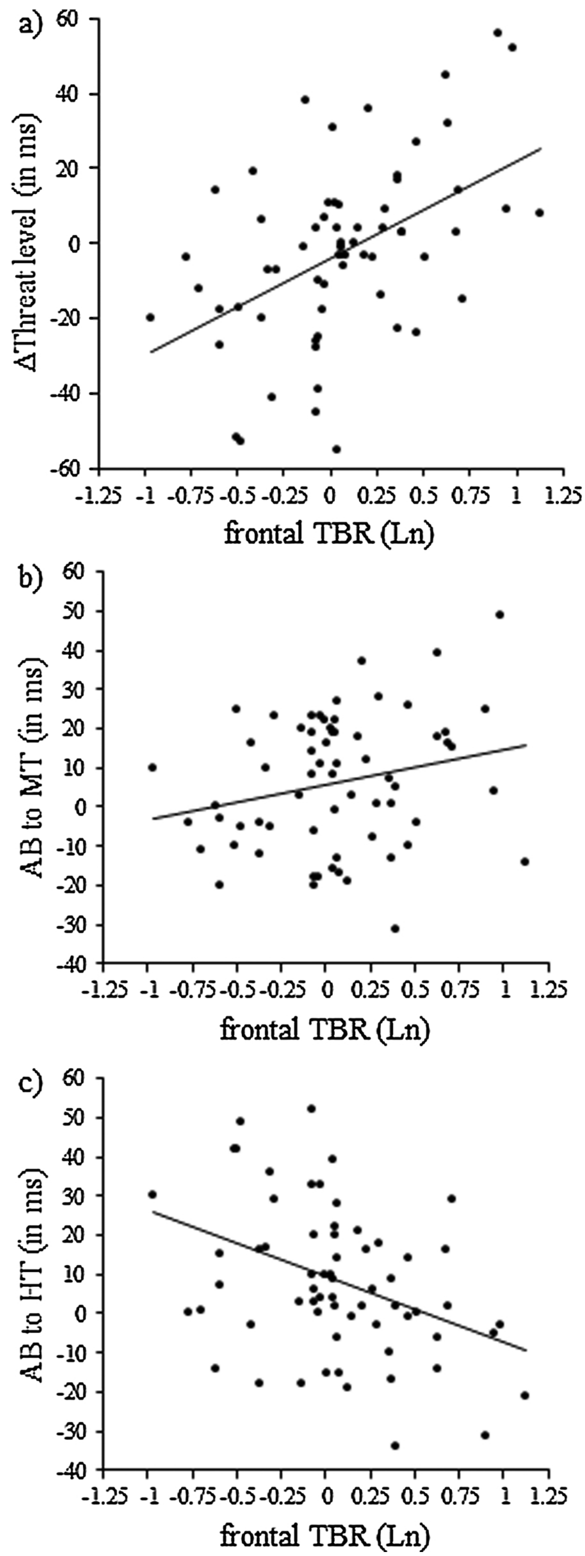

Fig. 1. Scatterplot for the relationship between Ln-normalized frontal EEG TBR and a) ΔThreat level (Bias for MT stimuli − Bias for HT stimuli) b) attentional bias to HT pictures and c) attentional bias to MT pictures. a) Participants with lower TBR display relatively increased attentional bias towards high threat compared to reduced attentional bias towards/or avoidance to mild threat, while participants with higher TBR show the reverse pattern. b) Participants with lower TBR show attentional bias towards HT while high TBR participants are more avoidant of HT. c) Participants with lower TBR are more avoidant/less attentive of MT while high TBR individuals show greater attentional bias towards MT.

[2] To assess the added value of using TBR as predictor over the self-report ACS, we performed a hierarchical regression (Stevens, 2002), which showed that TBR uniquely explained 23.1% of the variance after controlling for ACS.

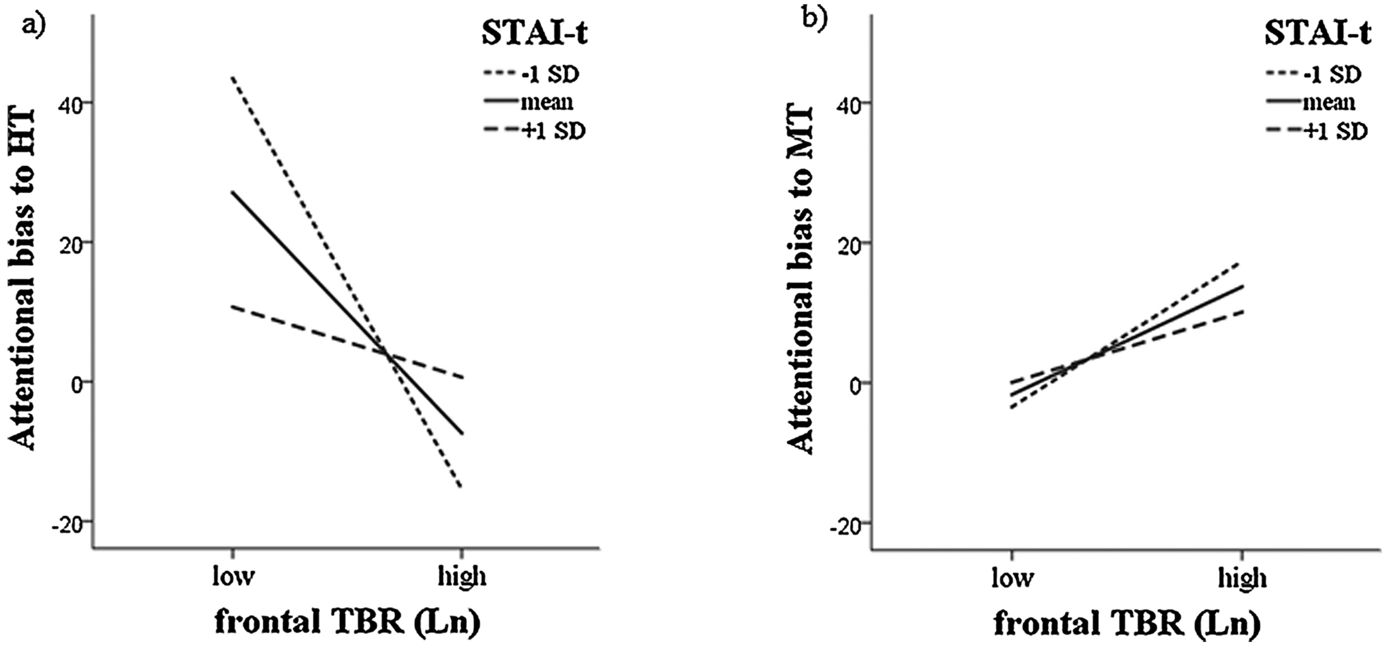

Fig. 2. Simple slopes for the moderation of STAI-t on the relationship between Ln-normalized frontal EEG TBR (low = 2 SDs below the mean; high = 2 SDs above the mean) and attentional bias to a) HT and b) MT pictures. Frontal TBR (Ln) = Ln-normalized frontal theta/beta ratio, STAI-t = trait anxiety. a) High TBR is associated with HT-avoidance; an effect which is not significant for high STAI-t, which is associated with low attentional bias to HT regardless of TBR. b) A higher TBR is associated with attentional bias towards MT, regardless of STAI-t.

significant for low and mean STAI-t, somewhat stronger for low STAI-t (1 SD below the mean; $\beta = 0.844$, $t = 5.184$, $p < .001$) compared to mean STAI-t ($\beta = 0.529$, $t = 4.916$, $p < .001$), while it was not significant for high STAI-t (1 SD above the mean; $\beta = 0.214$, $t = 1.392$, $p = .169$).

Further simple slopes analyses were conducted separately for bias scores for MT and HT pictures, in order to further investigate the nature of the above mentioned complex interaction (see Fig. 2). These analyses revealed that the TBR × STAI-t interaction was significant ($\Delta R^2 = 0.075$, $p = .016$) for attentional bias to HT pictures (see Fig. 2a) but not to MT pictures ($\Delta R^2 = 0.005$ $p = .563$; see Fig. 2b). In general, a negative relationship was observed between TBR and attentional bias to HT pictures ($r = -0.367$, $p = .003$). This relationship is significant for low ($\beta = -0.734$, $t = 4.257$, $p < .001$) and average ($\beta = -0.429$, $t = -3.769$, $p < .001$) STAI-t scores but not for high STAI-t score ($\beta = -0.125$, $t = -0.769$, $p = .445$). As can be seen in Fig. 2a, a combination of low TBR and low STAI-t is related to vigilance to high threat, compared to low TBR high STAI-t, while for high TBR there is no relationship between STAI-t and high threat bias. A general positive relationship is observed between TBR and attentional bias for MT pictures indicating that regardless of STAI-t, higher TBR is related to vigilance to MT pictures and low TBR is related to low vigilance (see Fig. 2b). In sum, the second hypothesis was confirmed: trait anxiety and TBR (attentional control) are interactively related to differential attentional responding to stimuli of low and high threat level.

3.5. The role of cue-target delay

In above reported Threat level × Cue-target delay × TBR rm ANOVA, there were no main effect or interactions for Delay analyses (for the crucial Threat level × TBR × Cue-target delay interaction: $F(1, 63) = 1.96$, $p = .166$, $\eta_p^2 = 0.03$). Also in the Threat level × Cue target delay × TBR × STAI-t model, no significant main effect or interactions were observed for Cue-target delay (for the crucial Threat level × TBR × STAI-t × Cue-target delay interaction: $F(1, 63) = 0.13$, $p = .724$, $\eta_p^2 < 0.01$). Hence, the third hypothesis is rejected: the observed relationships between TBR and attentional bias, and interactive relations between TBR, trait anxiety, and attentional bias are not dependent on cue-target delay.

3.6. Secondary analyses; self-reported attentional control, trait anxiety and TBR

As TBR was expected to correlate negatively with both ACS and STAI-t, which are themselves negatively related ($r = -0.347$, $p = .004$), partial correlations for TBR and ACS as well as STAI-t were performed with the two scales as each other's control variable in order to prevent obfuscating confounding (cf. Putman et al., 2010, 2014; Angelidis et al., 2016). TBR was not associated with ACS after controlling for STAI-t (partial $r = -0.146$, $p = .241$), whereas the negative association between TBR and STAI-t was significant after controlling for ACS (partial $r = -0.352$, $p = .004$; as previously reported in Putman et al., 2010). Thus, a negative relation between TBR and self-reported attentional control was not replicated. A negative relation between TBR and trait anxiety was replicated.

3.7. Secondary analyses; self-reported attentional control and attentional bias

The Cue-target delay × Threat level rm ANOVA was conducted again with ACS as a covariate. Analyses did not reveal significant effect of ACS, indicating that ACS was not related to attentional bias to threat or effects of threat level thereon. Similarly, there were not any significant effects when attentional control and its interaction with STAI-t were included in the model. Thus, self-reported attentional control as measured with the ACS was unrelated to dot-probe task performance.

3.8. Secondary analyses; central and parietal EEG TBR

Although the main interest of this study was on frontal EEG TBR, we performed the same analyses with TBR in central and parietal regions for exploratory reasons. The correlations between frontal and central TBR, frontal and parietal TBR, and central and parietal TBR were significant and very strong ($r = 0.837$, $p < .001$; $r = 0.713$, $p < .001$;

$r = 0.920$, $p < .001$, respectively).Analyses revealed the same TBR × Threat level and TBR × STAI-t × Threat level interactions (weaker for parietal TBR as it would be expected based on Putman et al. (2010, 2014)) with the same direction. No other interactions were found.

3.9. IAPS ratings

Separate rm ANOVAs for valence and arousal ratings were performed, with Threat level (3; Neutral, MT, and HT) as a within-subjects factor. Regarding valence, analyses revealed a main effect of Threat level ($F(2, 63) = 189.79$, $p < .001$, $\eta_p^2 = 0.86$) indicating that participants perceived HT ($M = 2.28$, $SD = 1.07$) pictures as more unpleasant than the MT ($M = 4.08$, $SD = 0.99$; $t = 13.753$, $p < .001$) and neutral pictures ($M = 5.32$, $SD = 0.70$; $t = 19.290$, $p < .001$), and the MT pictures were scored as more unpleasant than the neutral pictures ($t = 7.722$, $p < .001$). For arousal, a main effect of Threat level ($F(2, 63) = 113.59$, $p < .001$, $\eta_p^2 = 0.783$) was found. Post-hoc *t*-tests confirmed that HT stimuli ($M = 5.73$, $SD = 2.05$) were perceived as more arousing than MT ($M = 3.69$, $SD = 1.8$; $t = 10.122$, $p < .001$) and neutral stimuli ($M = 1.86$, $SD = 0.88$; $t = 15.169$, $p < .001$). Finally, MT pictures were more arousing than neutral ($t = 9.040$, $p < .001$).

4. Discussion

The main goal of this study was to investigate spontaneous frontal EEG TBR in relation to attentional responses to mild and high threat. Results demonstrated that TBR moderated attentional bias to different threat-levels, as expected. Specifically higher TBR predicted increased attentional bias towards mild threat and attentional avoidance of high threat, irrespective of trait anxiety. In addition, trait anxiety interacted with this moderation between TBR and threat-level, such that the participants with low TBR and low trait anxiety were more attendant to HT stimuli compared to the rest of the participants who showed avoidance or reduced attentional bias towards HT stimuli. These associations were not more pronounced in later (500 ms cue-target delay) compared to earlier stages of attention (200 ms cue-target delay). These findings are further discussed below.

This is the first study showing that the influence of differential threat-level on attentional bias is related to electrophysiological correlate of cognitive control. Importantly, although the current data showed a negative correlation between TBR and trait anxiety, this did not confound the finding: our results clearly show that the TBR relation to attentional biases is independent of trait anxiety. Our findings of a negative relation between TBR and bias toward high threat and a positive relation between TBR and bias toward mild threat are in line with the cognitive-motivational analysis of attentional threat-bias and its updated integration with recent literature on attentional control (Bradley, 1998, 2016;). These models stress the functional value of differential attentional responding as a function of perceived estimation of threat and attentional control functions (Bradley, 1998, 2016; ; Shechner & Bar-Haim, 2016). Specifically, this framework postulates the cognitive and emotional efficiency of avoiding mildly threatening information and attending highly threatening stimuli, which is thought to be absent in people with high levels of (trait) anxiety or low cognitive control. The current data confirm this prediction by demonstrating a negative relationship between TBR and attentional preference for high versus low threat, in line with studies assessing attentional control with the self-report ACS (Derryberry & Reed, 2002; Taylor et al., 2016) or objective measures of attentional control (Hou et al., 2014; Reinholdt-Dunne et al., 2009). These latter two studies assessed momentary attentional control by means of computer tasks measuring, most importantly, attentional inhibition (Miyake & Friedman, 2012). The current findings for TBR extend these findings as they likely reflect influence of trait as well as state attentional control: TBR is very stable in healthy participants (Angelidis et al., 2016) as well as in patients with neurological deficits (Keune et al., 2017), although pharmacological improvement of PFC function can acutely reduce TBR (Loo et al., 2016).

The present data are the first to our knowledge relating TBR to task-based attentional processing of emotional stimuli and further reinforce the notion that frontal TBR is a marker for executive function over emotional responses. TBR uniquely explained 23% additional variance over ACS for predicting threat-level dependent bias, demonstrating that TBR has unique and independent predictive value in the study of emotion-attention interaction. Moreover, the current evidence further fortifies the notion that PFC-mediated cognitive control plays a more critical role in threat-related attentional processing (e.g., Mogg & Bradley, 2016; Pessoa & Adolphs, 2010) than traditionally emphasized.

Low attentional control has been reported to predict PTSD development (Bardeen, Fergus, & Orcutt, 2015). It is tempting to speculate that low attentional control plays an etiologic and maintaining role in PTSD and other anxiety disorders due to its relationship with attentional avoidance for trauma-related information (Mogg & Bradley, 2016; Pine et al., 2005; Wald, Shechner et al., 2011) as avoidance might impede sufficient threat-processing for normalization of fear-responses (Mathews et al., 1990; Mogg et al., 1987). Maladaptive avoidant behavior is a prominent feature in various types of psychopathology (e.g., American Psychiatric Association, 2013; Bogels et al., 2010; Brewin & Holmes, 2003; Rachman, 2004; Williams & Moulds, 2007). Accordingly, previous evidence from our lab has shown that highly anxious PTSD patients who also displayed low self-reported attentional control were avoidant of trauma-related threatening stimuli (Schoorl et al., 2014). The role of attentional control and its relation with aberrant attentional threat-processing in the etiology, maintenance and treatment of anxiety disorders must not be underestimated (Mogg & Bradley, 2016). TBR seems to provide a promising variable of interest for such research.

As expected, frontal TBR interacted with trait anxiety in its association with threat-level modulated attentional bias, but only for high threat. Specifically, the likely most resilient participants of the present sample, individuals with higher cognitive control (as reflected by low TBR), and medium and low anxiety were the participants who most clearly attended highly threatening stimuli. The current data for high threat (i.e., a negative relation between trait anxiety and bias toward high threat for low TBR) support the notion that attention toward high threat should not be dependent on high levels of anxiety (Bradley, 1998, 2016;). This particular prediction from the cognitive-motivational framework had so far perhaps received the least direct empirical support (e.g., Mogg & Bradley, 2016; Mogg et al., 2000; Wilson & MacLeod, 2003; Koster, Crombez, Van Damme, Verschuere, & De Houwer, 2004). Interestingly, accumulating evidence suggests that individuals who attend threat in stressful situations, as measured with a dot-probe task, are more resilient in the development of PTSD symptomatology compared to those who avoid processing of threat (e.g. for a review see, Shechner & Bar-Haim, 2016). In line with this notion, Wald et al. (2016) found that training attention towards threat before combat exposure prevented later development of PTSD symptoms. All in all, evidence for the predicted ubiquity and functionality of attention toward high threat is accumulating. Our current findings suggest that this potentially more resilient attentional response to high threat might crucially depend on adequate attentional control.

Although it is often reported that trait anxiety is solely predictive of attentional bias to threat (e.g., Bar-Haim et al., 2007), this was not the case in our study. This is not wholly unexpected based on a recent meta-analysis indicating that the relationship between trait anxiety and attentional bias towards threat is not as consistent as previously suggested (Van Bockstaele et al., 2014). This inconsistency is possibly accounted for by other individual differences or methodological differences that are not taken into account, such as cognitive control and the variation of attentional patterns across threat intensity, as demonstrated in the current study.

Previous studies have shown that the interacting attentional control and trait anxiety were predictive of attentional processing of threat (Bardeen & Orcutt, 2011; Derryberry & Reed, 2002; Reinholdt-Dunne et al., 2009; Schoorl et al., 2014; Taylor et al., 2016). Specifically for threat-level dependent responding, an interaction with trait anxiety is likely because of its theorized influence in automatic threat-appraisal (Bradley, 1998, 2016;). Although we dared not make too specific predictions for this relationship, it is noteworthy that interactive influences of trait anxiety and TBR were only observed for high threatening stimuli: it would make sense if anxiety were related to hypervalenced processing of mild threat stimuli. One could argue that hypervalenced appraisal in our non-clinical sample does not occur for the mildly threatening stimuli as they were simply not arousing enough for such a healthy sample. The current finding that for low TBR there is a negative relation between trait anxiety and attentional bias toward high threat fits the notion that subjective threat value (as a joint function of differences in subjective threat-appraisal as well as stimulus threat-level) primes the attentional processing of threat.

Our third research question concerned early versus late processing. The top-down cognitive control mechanisms that interact with bottom-up influences of threat-appraisal in the regulation of attention to threat, are thought to be of greater influence in later stages of attention, specifically for the regulation of attentional avoidance (e.g., Cisler & Koster, 2010). Even though, as already mentioned in our introduction, present evidence concerning this time-course of attentional control seems rather contradictory (e.g., Bardeen & Orcutt, 2011; Derryberry & Reed, 2002; Schoorl et al., 2014), it seems a likely prediction from most psychological and neurological views on attentional threat processing (see e.g., Cisler & Koster, 2010; Hermans et al., 2014; Ledoux, 1995; Öhman, 1993,1994). Because of the strong theoretical basis of this hypothesis we are inclined to interpret the current data that seem at odds with this notion to rely on methodological issues. Specifically, we used a 500 ms cue-target delay for late and a 200 ms cue-target delay for early processing. There is ample evidence suggesting that a delay of 500 ms captures a relatively late time window, which likely allows multiple shifts of visual attention after initial attentional deployment (e.g., Buodo, Sarlo, & Munafò, 2010; Klein, 2000; Koster, Crombez, Verschuere, Vanvolsem, & De Houwer, 2007). We found no effect of cue-target delay on any of the results for bias scores, though post-hoc inspection (unreported) revealed that the results for the moderating role of TBR on threat-level were non-significantly stronger in the 200 ms condition. Since the overall results are what one would expect for late processing and because there is evidence suggesting that secondary visual attentional responses to threat might already occur before 200 ms (e.g., Bardeen & Orcutt, 2011; Koster et al., 2007), we conclude that our 200 ms cue-target delay was likely too long to capture truly early attentional bias.

A negative association between spontaneous TBR and trait anxiety was found which remained significant after controlling for ACS, an analysis that was applied due to the typical (and current) ACS-STAI-t relation (e.g., Angelidis et al., 2016; Derryberry & Reed, 2002). The negative association between TBR and trait anxiety after controlling for ACS has been reported once previously (Putman et al., 2010). As another secondary interest for the current study, we also assessed relationships with ACS and attentional bias. Unexpectedly, and surprising in light of the results for our objective measure TBR, self-reported attentional control as measured with ACS was not related to attentional bias in any way (c.f., Reinholdt-Dunne et al., 2009). It is noticeable that TBR was also not associated with ACS in the current sample, contrary to our expectation based on consistent previous evidence from three replicating studies reporting negative associations between TBR and ACS (Putman et al., 2010, 2014; Angelidis et al., 2016; but see, Morillas-Romero et al., 2015), a recent study reporting a negative relation between TBR and objectively assessed attentional function in multiple sclerosis patients (Keune et al., 2017) and more in general the above cited studies reporting a negative relation between TBR and executive control. Distribution of ACS or TBR scores in the current sample were not substantially different from previous student samples on the basis of which one should expect relations between TBR and ACS or attentional bias. We cannot identify a likely cause for the current lack of relations between ACS and TBR or threat bias. Given the null-results for ACS for both constructs of interest, we consider the positive findings for TBR more informative but conclude that future studies should attempt a direct replication and re-assess associations with ACS.

Several potential limitations to this study affirm the necessity for further research. Firstly, as noted above, anxiety levels were limited in the present sample (healthy students), which may have limited sensitivity for our mild threat condition. It has been shown that state anxiety can affect emotional attentional processing (e.g. Carr, Scully, Webb, & Felmingham, 2016; Edwards, Burt, & Lipp, 2006), for instance in interaction with trait anxiety (Egloff & Hock, 2001). It would be very informative to investigate the currently studied processes and relations in more anxious samples or under acute stress. Secondly, although our high threat stimuli were clearly rated as more negative, we also selected them to be highly arousing, which was also confirmed by analysis of the rating data. However, since we did not include highly arousing positive stimuli in our study, we cannot exclude with certainty that the results for the high threat stimuli might be a result of valence-independent arousal. It should be noted that the available choice for stimuli that are as arousing as our high threat stimuli while being of positive valence is quite limited (though possibly erotic stimuli could serve such a purpose; c.f. Putman & Berling, 2011). Perhaps differential conditioning of stimuli as cues for potent positive or negative conditioning (as was done successfully for negative conditioning; Koster et al., 2004) could solve this problem. Moreover, future studies could investigate the relationship between spontaneous TBR and event-related oscillations during a dot-probe task with threatening pictures. Finally, we suggest that future studies should use less than 200 ms to probe early processing (and perhaps even less than 500 ms for late processing) when using a dot probe task to address the issue of time-course of threat-biased attention (see also, Mogg & Bradley, 2016).

In conclusion, the present data verify and further extend the aforementioned suggestion that spontaneous frontal EEG TBR is an electrophysiological marker for executive control over emotional processing in healthy individuals, and specifically attentional processing of threatening stimuli. In addition, the data support the longstanding but often ignored claim that threat-level is of pivotal influence in studies of threat-selective attention. This issue should be explicitly addressed in studies' design and interpretation of results. Finally, this study should add to the growing realization that consideration of individual differences in attentional control is a sine qua non for the future study of attentional bias in (the treatment of) anxiety disorders (Mogg & Bradley, 2016).

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