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RESEARCH REPORT

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Biased emotional attention in patients with dental phobia

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Abstract

Biased motivated attention towards phobia-relevant pictures is a typical finding in specific phobia. In the visual system, the allocation of motivated attention is indexed by two event-related potential components – the Early Posterior Negativity and the Late Positive Potential. Enhanced Early Posterior Negativity and Late Positive Potential amplitudes are reliably observed in specific phobia such as, for instance, snake, spider, or blood-injection-injury phobia and to some extent also in dental phobia. However, regarding dental phobia results are sparse and its theoretical concept is not undisputed. To further elucidate the electrophysiological characteristics of dental phobia, we investigated visual emotional processing in dental phobia patients and controls. Subjects viewed neutral, phobia-irrelevant and phobia-relevant pictures while magnetoencephalographic and behavioural measures were recorded. All patients reported a history of traumatic experiences and depressive and anxiety symptoms, as well as dissociative and posttraumatic symptoms. In the magnetoencephalography, patients showed generally less evoked neural activation at parietal and temporal regions and a reduced differentiation between picture categories compared to controls. At the behavioural level, patients rated phobia-relevant pictures as clearly more negative as did controls. In contrast to previous reports, our results suggest that dental phobia cannot be associated with the typical effects of biased motivated attention seen in other specific phobias. Instead, results indicate that dental phobia shares typical characteristics with mild forms of posttraumatic stress disorder.

KEYWORDS

attention, dental phobia, emotion, MEG, vision

1 | INTRODUCTION

Biased attention to threat is one of the best-replicated findings in individuals with anxiety disorders (Mogg & Bradley, 1998). Fear promotes the detection of danger in the environment and ensures a fast response to threatening situations. Threat-related cues can be detected faster, ambiguous stimuli are more likely evaluated as being threatening (or at least more negative) and in the presence of fear-relevant information, maintenance of attention is altered in a maladaptive way. Thus, it has been argued that the attentional

Abbreviations: B-I-I, Blood-Injection-Injury; DSM, Diagnostic and Statistical Manual of Mental Disorders; EPN, Early Posterior Negativity; HADS, Hospital Anxiety and the Depression Scale; IAPS, International Affective Picture System; LPP, Late Positive Potential; MEG, Magnetoencephalography; PTSD, Posttraumatic Stress Disorder.

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bias to threat might account for the maintenance and even etiology of anxiety disorder (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007; Bishop, 2007; but see Van Bockstaele et al., 2014 for a bidirectional model regarding the causal relation of fear, anxiety, and attentional bias).

Depending on the focus of fear, the current version of the Diagnostic and Statistical Manual of Mental Disorders (DSM 5; American Psychiatric Association, 2013) distinguishes five types of specific phobia (animals, natural environment, blood-injection-injury, situation, and other cues). The Blood-Injection-Injury Type (B-I-I) is characterised by a high level of irrational fear and avoidance of seeing blood or injuries, medical instruments, receiving a transfusion or injection as well as undergoing an invasive medical procedure (American Psychiatric Association, 2013). Within the B-I-I type, dental phobia is the most prevalent specific phobia with a prevalence rate between 2.1% and 3.7% (Fredrikson, Annas, Fischer, & Wik, 1996; Oosterink, de Jongh, & Hoogstraten, 2009; Stinson et al., 2007). Dental phobia is associated with an extreme fear and pronounced avoidance behaviour of receiving dental care, in combination with continuously deteriorating oral health. However, though dental treatment can be considered an invasive medical procedure, and thus as part of the B-I-I type, some authors argue that dental phobia should be considered as a distinct type of specific phobia (De Jongh et al., 1998; van Houtem et al., 2013).

Psychophysiological reactions in B-I-I are typically described as a biphasic response pattern with an initial acceleration followed by a subsequent deceleration in heart rate and blood pressure, eventually leading to an increased likelihood of fainting. However, in a large population-based sample, only a small overlap between fainting and dental phobia could be observed: subjects with dental phobia reported fainting episodes in the past, but none of these actually fainted during treatment (De Jongh et al., 1998). Likewise, a passive viewing task with phobia-relevant pictures did not provoke fainting in dental phobic patients, nor led to a heart rate deceleration (Leutgeb, Schafer, & Schienle, 2011). Furthermore, dental phobia is as common in men as in women, whereas the prevalence of blood and injury phobia is much higher in women (Berggren, Carlsson, Gustafsson, & Hakeberg, 1995; Fredrikson et al., 1996; Öst, Sterner, & Lindahl, 1984). Thus, characteristic physiological responses and gender differences argue for a distinction between B-I-I and dental phobia.

Further evidence in favour of a more separated position of dental phobia among the B-I-I concept is provided by studies investigating attentional biases in individuals with different types of phobia. Stimuli with motivational significance capture attention. Compared to neutral pictures, viewing of emotional arousing, pleasant, or unpleasant pictures is associated with increased cortical responses in the visual system (Lang et al., 1998). Studies using event-related potentials typically report distinctions between motivationally significant and neutral visual stimuli within mid-latency and late time-intervals. Strongest differences are usually found within the so called Late Positive Potential (LPP) starting around 300 ms after picture onset with a widely distributed positive deflection at centro-parietal sensors (e.g. see Schupp, Flaisch, Stockburger, & Junghöfer, 2006; Olofsson, Nordin, Sequeira, & Polich, 2008 for reviews). The LPP is preceded by a negative event-related potential deflection (Early Posterior Negativity, EPN) over temporal-occipital regions and has been described in response to various visual emotional stimuli such as scenes (e.g. Junghöfer, Bradley, Elbert, & Lang, 2001), faces (e.g. Schupp et al., 2004), or words (Kissler, Herbert, Peyk, & Junghofer, 2007). EPN onset depends on paradigm and stimulus material and can vary between 130 and 200 ms.

In recent years, studies investigating the neural correlates of specific phobia mainly reported increased amplitudes of the EPN and LPP in subjects suffering from specific phobia when phobia-relevant vs. neutral pictures were compared (Moser, Huppert, Duval, & Simons, 2008; Muhlberger et al., 2009; Wieser, Pauli, Reicherts, & Muhlberger, 2010). In contrast, blood-fearful subjects did not process phobia-relevant pictures differently than did the healthy controls. However, a general hypervigilance has been observed in the group of blood-fearful subjects with a generally stronger brain activation in response to all examined picture categories (Buodo, Peyk, Junghofer, Palomba, & Rockstroh, 2007). To our knowledge, only one research group investigated attention allocation in subjects diagnosed with dental phobia and consistently reported an increase in the LPP amplitude when subjects passively viewed pictures depicting scenes of dental treatments (Leutgeb et al., 2011; Schienle, Kochel, & Leutgeb, 2011). Thus, regarding the attentional bias seen in most anxiety disorders, dental phobia seems to share more similarities with animal phobia than with the B-I-I phobia, again calling into question the classification as part of the B-I-I subtype. Given that severe forms of dental phobia share many characteristics (e.g. nightmares, flashbacks, loss of interest, avoidance) with posttraumatic stress disorder (PTSD), others even argue that dental phobia is more closely related to PTSD than to specific phobia. (Bracha, Vega, & Vega, 2006; de Jongh, Aartman, & Brand, 2003; de Jongh, Fransen, Oosterink-Wubbe, & Aartman, 2006). Regarding visual emotional processing, patients with PTSD generally do not display the hypervigilance found in patients with specific phobia. Patients diagnosed with PTSD (and even traumatised individuals, who do not meet criteria for current PTSD) displayed reduced cortical activity

TABLE 1 Participants' scores on the self report questionnaires. The two groups differed significantly throughout all questionnaires with $p < 0.001$

	Patient group		Control group	
	M	*SD*	*M*	*SD*
Brief symptom inventory	57.38	13.87	36.81	7.33
Hospital anxiety and depression				
Anxiety	7.44	3.67	2.44	1.46
Depression	4.13	3.42	0.81	0.91
Dental anxiety scale	18.13	1.63	7.06	1.57
Dental fear scale	82.88	9.19	28.38	6.54
Impact of event scale	−1.62	1.91	−4.30	0.25
Dissociative symptoms	7.84	6.07	0.88	1.31

when threat-related and pleasant pictures presented were presented (Catani, Adenauer, Keil, Aichinger, & Neuner, 2009). Kounios and colleagues found that mainly the well-adjusted veterans showed suppressed late positive potentials at parietal sites following the presentation of both, trauma and non-trauma words (Kounios et al., 1997). Another ERP study found reduced early and late negative potentials in patients with PTSD over the posterior temporo-occipital cortex and no differentiation between stimulus types (Felmingham, Bryant, & Gordon, 2003). Similar results were obtained by Adenauer and colleagues using MEG. Comparing trauma-exposed refugees with and without PTSD, they found reduced processing of pictures, irrespective of emotional content, only in individuals meeting criteria for a PTSD (Adenauer et al., 2010). Thus, an emotion-unspecific and reduced cortical visual processing can be found in patients suffering from PTSD.

Using Magnetoencephalography (MEG), we investigated visual emotional processing in patients diagnosed with dental phobia and controls while viewing pictures with neutral, phobia-irrelevant and phobia-relevant content in two consecutive sessions. In session one, subjects were presented pictures with neutral and negative valence to test basic visual emotional processing. In this session we expected no differences between patients and healthy controls except potentially hypervigilance driven stronger amplified evoked responses to stimuli of both valence categories in patients. In a second session, participants were confronted with negative pictures (phobia-irrelevant) and pictures of dental treatment (phobia-relevant).

In line with results from studies on specific phobia, we expected increased demand and allocation of attentional resources for pictures showing dental treatment compared to negative pictures as indicated by enhanced differential activity specifically withintheEPNandLPPtimeinterval.

2 | MATERIALS AND METHODS

2.1 | Subjects

Sixteen non-phobic individuals and 16 individuals suffering from dental phobia (according to DSM-5) with a history of traumatic experiences during a previous dental treatment participated in the study. Traumatic events often precede the manifestation of dental phobia (de Jongh et al., 2003); however, are not indispensable for its diagnosis according to the DSM-5, which is why the group of patients can be considered as quite heterogeneous. Therefore, to maximise homogeneity in the patient group, an aversive dental experience like high levels of pain during dental treatment was set as an additional inclusion criterion. Participants with dental phobia were recruited via an article in the local newspaper, a local television, and a local radio report. All participants underwent a clinical examination conducted by a clinical psychological and psychotherapist. Participants with severe mental or physical illness were excluded from the study. The control group was matched with regard to age, sex, and years of education and was recruited via a newspaper announcement. In all participants, dental anxiety was assessed using the German version of the Dental Anxiety Scale (Corah, 1969; Tönnies, Mehrstedt, & Eisentraut, 2002) and the Dental Fear Survey (Kleinknecht, Klepac, & Alexander, 1973; Tönnies et al., 2002). The Dental Anxiety Scale is a four-item questionnaire capturing anxiety prior to actual dental treatment. Usually a score below 13 is considered as normal. The Dental Fear Survey consists of 20 items covering certain behavioural patterns, physiological reactions, and emotional aspects caused by dental fear. Posttraumatic symptoms and general psychopathology were assessed using the German version of the Brief Symptom Inventory (Derogatis, 1993; Franke, 2000), the Hospital Anxiety and the Depression Scale (HADS; Herrmann, Buss, & Snaith, 1995; Zigmond & Snaith, 1983), the Impact of Events Scale-Revised (Maercker & Schützwohl, 1998; Weiss, 2007), and the German version of the Dissociative Experience Scale, the "Fragebogen zu dissoziativen Symptomen" (Bernstein & Putnam, 1986; Freyberger, Spitzer, & Stieglitz, 2005), to cover dissociative symptoms. The Brief Symptom Inventory is a brief version of the Symptom Checklist 90 (Leonard R. Derogatis & Unger, 2010), covering a wide range of psychiatric symptoms. The global severity index of the Brief Symptom Inventory provides a measure of overall psychological distress level. Symptoms of anxiety and depression were captured using the HADS and for assessing symptoms of PTSD the Impact of Events Scale was applied. Both groups consisted of 14 females and 2 males between the age of 24 and 66 (controls: $M = 40.6$, $SD = 13.5$ years; patients: $M = 42.2$, $SD = 11.4$ years) and with a maximum of 13 years of education (controls: $M = 12.6$, $SD = 1.0$ years; patients:

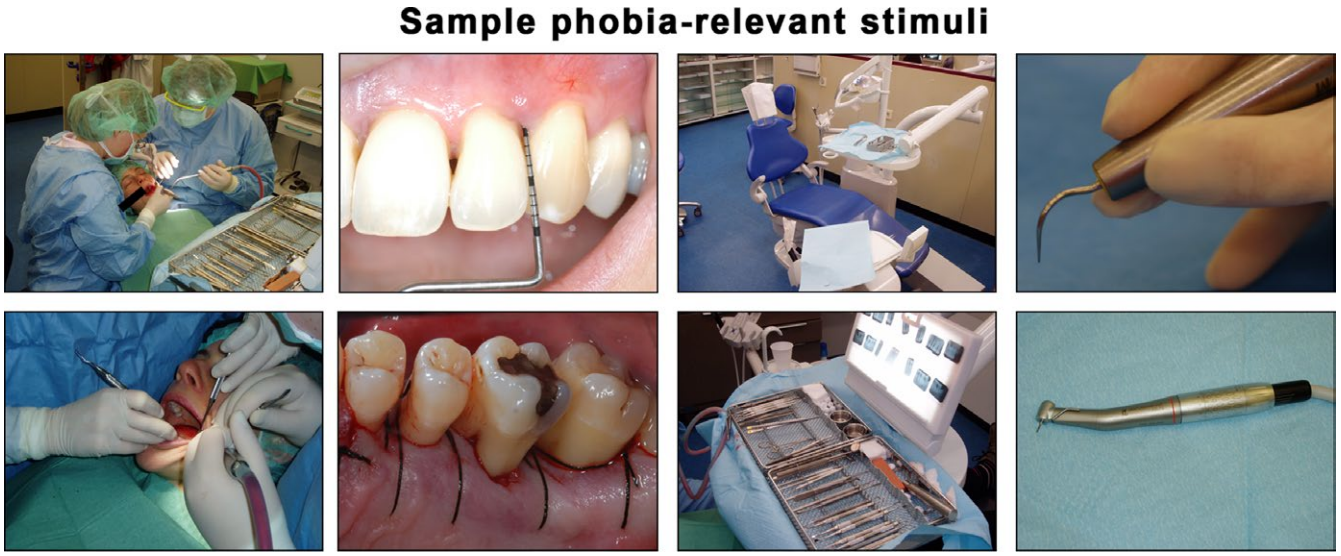

FIGURE 1 Sample stimuli of phobia-relevant images showing scenes of dental treatment and pictures of dental equipment. [Colour figure can be viewed at wileyonlinelibrary.com]

$M = 11.0$, $SD = 1.6$ years). According to the questionnaires, the two groups differed significantly (with $p \leq 0.001$ for all comparisons) with regard to depressive and anxiety symptoms, as well as dissociative and posttraumatic symptoms (for details, refer to Table 1). Written informed consent from each participant was obtained prior to the experiment. The study was conducted in accordance with the *Declaration of Helsinki* (1973, revised in 1983) and was approved by the ethical committee of the Medical Faculty of the University of Münster (ID: 2007-137-f-S).

2.2 | Stimulus material, paradigm, and procedure

In total, 100 visual stimuli representing three different emotional categories (neutral, negative, and phobia-relevant) were used. Twenty-five neutral and 50 negative pictures were obtained from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 1999). The selection of IAPS pictures was based on the normative valence and arousal ratings. Additional 25 phobia-relevant pictures were collected in the dental clinic of the University of Münster depicting either real scenes of a dental treatment or dental equipment and instruments (see examples in Figure 1). All images had a resolution of 512×384 pixels. Contrast and brightness of the pictures did not differ significantly across experimental conditions.

The whole experiment comprised of two consecutive sessions in which neural and behavioural data were measured. In the first session, 25 neutral and 25 fearful IAPS pictures were presented four times each in randomised order while magnetoencephalographic data were recorded. All pictures were presented centrally on a black background for 600 ms with a randomised inter-stimulus interval of $2{,}000 \pm 500$ ms. The experimental parameters of the second session were identical to the first session, except that the stimulus material consisted of another 25 negative IAPS pictures and 25 phobia-relevant pictures. After both MEG sessions, participants rated all pictures regarding its hedonic valence and emotional arousal with scores ranging from 1 (negative/low arousing) to 9 (positive/high arousing) using a computerised version of the Self-Assessment Manikin scale (Bradley & Lang, 1994). To avoid possible effects of induced phobia-related stress on a following measure, the first session with (phobia-unrelated) negative and neutral pictures always preceded the second session with phobia-relevant and negative pictures.

2.3 | MEG data acquisition, processing, and analysis

During stimulus presentation visual evoked magnetic fields were acquired using a 275-channel MEG whole-head sensor system (Omega 275, CTF, VSM Medtech Ltd.) with first-order axial SQUID (Super-conducting Quantum Interference Device) gradiometers. The Participant′s potion in the MEG scanner was monitored via landmark coils attached to the two auditory canals and the nasion. Individual head shapes were determined using Polhemus 3Space® Fasttrack system. Signals were digitised with a 600 Hz sampling rate and recorded within a frequency range from 0 to 150 Hz.

Data preprocessing and analysis were conducted with the Matlab-based EMEGS software (Peyk, De Cesarei, & Junghofer, 2011; www.emegs.org). Epochs of 600 ms following the presentation onset of the pictures were extracted and baseline-adjusted by subtracting a 150 ms interval before presentation onset. Artefacts were eliminated using the

method for statistical control of artefacts in high density EEG/MEG data (Junghöfer, Elbert, Tucker, & Rockstroh, 2000). The remaining trials were sorted by experimental condition (first session: negative, neutral; second session: negative, phobia-relevant) and averaged within each category. On average, 90.8 of overall 100 trials per experimental condition remained after artefact handling. The number of averaged trials did not differ significantly across conditions and groups. Based on the averaged response for each picture category the cortical generators of the magnetic fields were estimated using the L2-Minimum-Norm-Estimates approach (L2-MNE) (Hämäläinen & Ilmoniemi, 1994). This inverse modelling technique allows for estimating distributed neural network activity without prior assumptions regarding the location and/or number of current sources (Hauk, 2004). A sphere fitted to the scalp above a plane spanned by the nasion and both ear canals was used as conductivity model. A spherical shell with evenly distributed 2 (azimuthal and polar direction, radial dipoles do not generate magnetic fields outside of a sphere) × 350 dipoles was used as source model. A source shell radius of 87% of the individually fitted conductivity model was chosen, roughly corresponding to the grey matter depth. Across all participants and conditions a Tikhonov regularisation parameter k of 0.1 was applied. Topographies of source direction independent neural activities were calculated for each participant, picture category, and time-point.

The resulting L2-MNE topographies of all individuals were used to identify differences in the visual emotional processing of neutral, negative, and phobia-relevant stimuli. Time-intervals of interest were selected according to the waveform of mean neural activity, which was averaged across all participants and estimated sources. For the M100–which usually peaks around 100 ms after picture onset–an interval

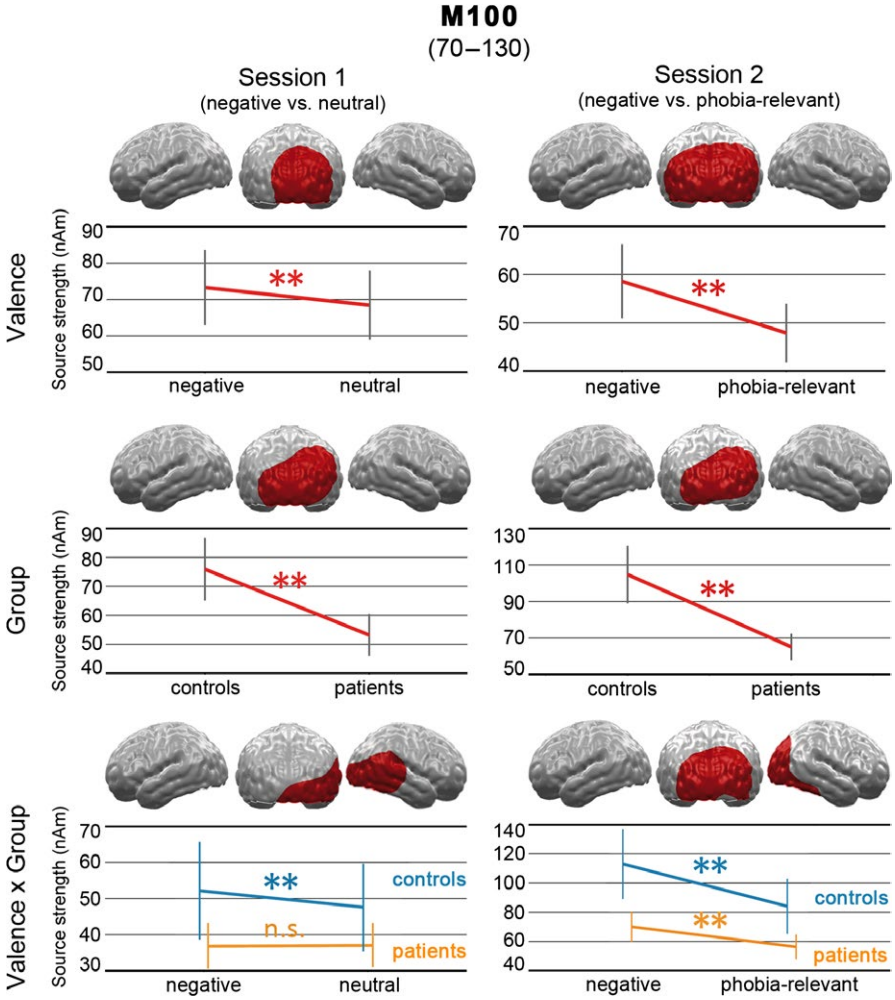

FIGURE 2 MEG effects of negative vs. neutral (Session 1) and negative vs. phobia-relevant (Session 2) emotional scenes in the predefined M100 time-interval for the main effect of Valence (upper row) and Group (middle row) and the interaction of both factors (lower row). Every single element (e.g. upper left corner) consists of three different views (left view, back view, right view) of a 3-D brain model (top) together with a corresponding line graph (bottom) depicting the mean neural activity within each spatio-temporal cluster. Spherical projections of the significant clusters are shown in red. Asterisks indicate the level of significance (*$p < 0.05$; **$p < 0.01$). [Colour figure can be viewed at wileyonlinelibrary.com]

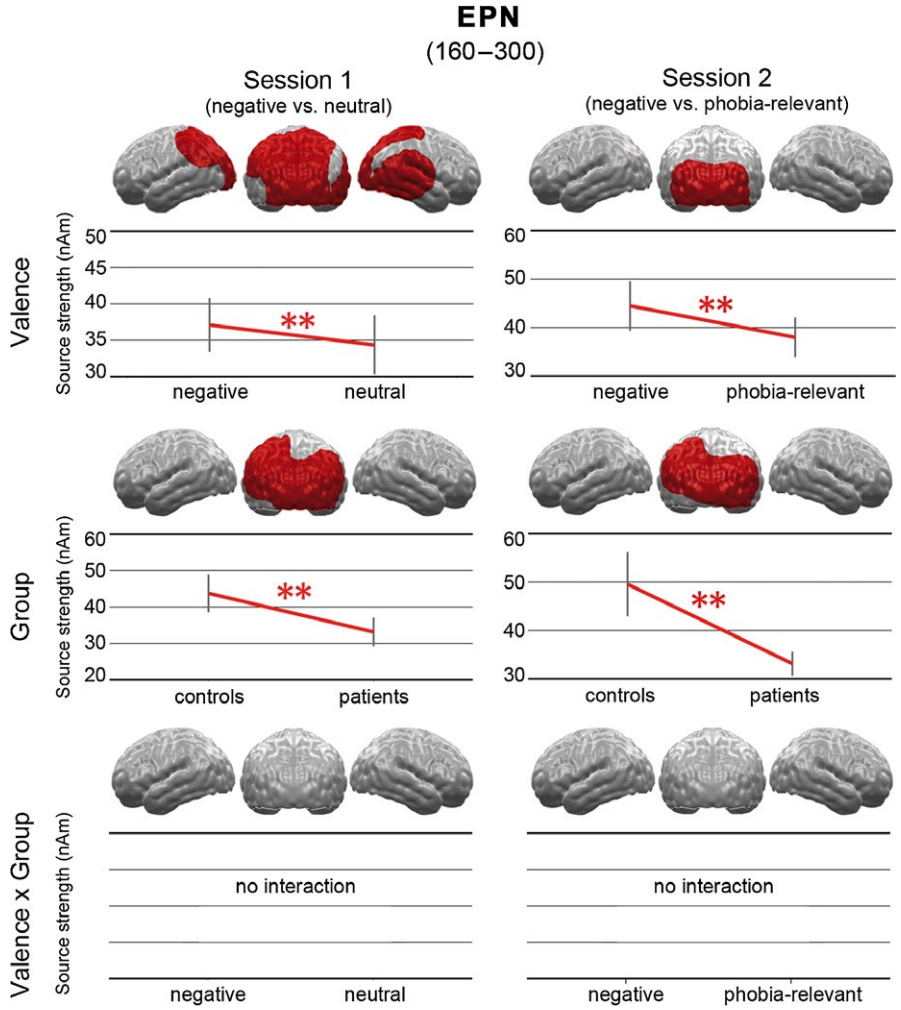

FIGURE 3 Same as Figure 2 for the predefined EPN time-interval. Asterisks indicate the level of significance (*$p < 0.05$; **$p < 0.01$). [Colour figure can be viewed at wileyonlinelibrary.com]

ranging from 70 to 130 ms was defined. The EPN was quantified as the average neural activity in the 170–300 ms time-interval. Finally, the LPP time-interval started at 330 ms and lasted up to the end of the averaged epoch (600 ms).

Neural data from the M100, EPN and LPP time-intervals were submitted to repeated-measures ANOVAs including the within factor Condition (session one: neutral vs. negative; session two: negative vs. phobia-relevant) and the between factor Group (controls vs. patients). As a result, a spatiotemporal distribution of statistical values for each test source over time and across subjects was obtained that served to optimise the identification of source regions within the specified time-intervals. Neural difference activity of estimated sources was further analysed statistically by applying non-parametric cluster-based permutation tests as suggested by Maris and Oostenveld (2007). As part of this procedure, *F*-values of test-sources were summed to so-called spatio-temporal cluster masses (cluster integrals) when the main effect of Condition or the Condition x Group interaction exceeded a critical alpha-level of $p = 0.05$ (sensor-level criterion). Cluster masses were compared against a random permutation cluster-based alpha-level of $p = 0.05$, which was established via Monte Carlo simulations of identical analyses based on 1,000 permuted drawings of experimental conditions. Only spatio-temporal cluster masses exceeding an alpha-level of $p = 0.05$ in the respective time-intervals were considered (cluster-level criterion). Thus, all reported main effects and Condition x Group interactions were significant on sensor- and cluster-levels of $p < 0.05$.

3 | RESULTS

3.1 | MEG results

3.1.1 | Negative vs. neutral pictures

Early M100 time-interval (70–130 ms; Figure 2 left column)

For both patients and controls major differences between neutral and negative picture processing (main effect of valence) were observed in a cluster over the occipital cortex

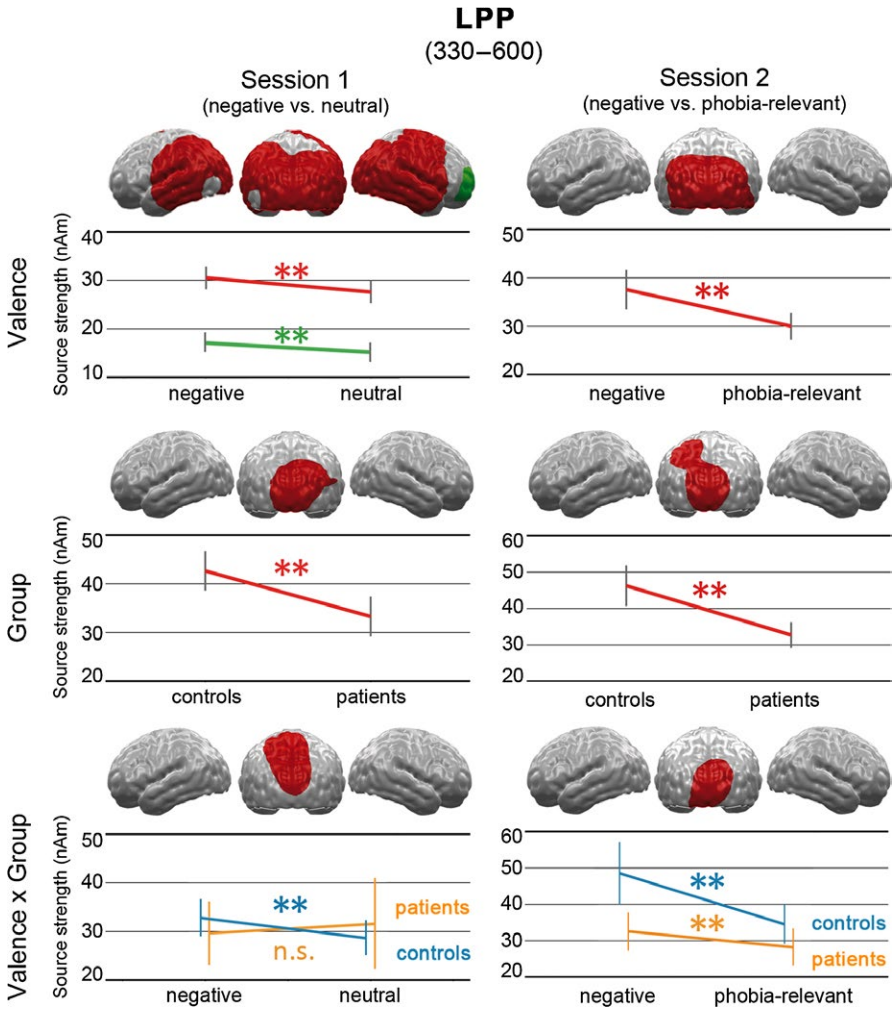

FIGURE 4 Same as Figure 2 for the predefined LPP time-interval. One additional significant cluster (upper left corner) and its corresponding line graph are shown in green. Asterisks indicate the level of significance (*$p < 0.05$; **$p < 0.01$). [Colour figure can be viewed at wileyonlinelibrary.com]

($F(1, 30) = 25.87$; $p = 0.001$; $\eta^2 = 0.48$), with greater neural activity for pictures with negative content. In a similar and overlapping occipital cluster, patients showed generally less cortical activity compared to controls as reflected by the main effect of group ($F(1, 30) = 13.95$; $p = 0.001$; $\eta^2 = 0.33$). Consequently, both main effects were modulated by a Valence × Group interaction visible at a right occipito-temporal cluster ($F(1, 30) = 20.26$; $p < 0.001$; $\eta^2 = 0.42$). Post-hoc paired t tests calculated for the two groups separately revealed enhanced responses for negative compared to neutral pictures in the control group (negative: $M = 53.15$, $SD = 25.15$; neutral: $M = 47.86$, $SD = 22.47$; $t(1, 15) = 6.17$, $p < 0.001$; $d = 1.12$) but not in the patient group (negative: $M = 36.49$, $SD = 11.62$; neutral: $M = 36.36$, $SD = 10.21$; $t(1, 15) = 0.174$, $p = 0.864$; $d = 0.03$).

EPN time-interval (160–300 ms; Figure 3 left column)

Within a widely distributed parieto-occipital and right posterior temporal cluster, data obtained in the EPN time interval revealed a significant main effect for the factor Valence ($F(1, 30) = 61.78$; $p < 0.001$; $\eta^2 = 0.69$). Again, pictures with negative valence were followed by enhanced neural activity compared to neutral pictures. The factor Group also reached significance ($F(1, 30) = 12.68$; $p = 0.001$; $\eta^2 = 0.98$) in a cluster covering parieto-occipital regions. Again, neural activity in the control group was generally enhanced compared to the neural activity found in the group of patients. However, for the interaction between Valence and Group no significant clusters could be identified.

LPP time interval (330–600 ms; Figure 4 left column)

As expected, in the LPP time-interval, cortical activity was even more distributed. For the main effect of valence, two significant clusters were found. The first cluster covered large portions of the occipital, parietal, and temporal lobe. Negative pictures elicited more neural activity compared to neutral pictures ($F(1, 30) = 93.00$; $p < 0.001$; $\eta^2 = 0.77$). The second cluster was located in the right inferior frontal cortex and showed the same direction of effect as the first cluster ($F(1, 30) = 19.89$; $p < 0.001$; $\eta^2 = 0.41$).

Strongest group differences were found in a central occipital region and again, this cluster of neural sources was associated with stronger activity in the group of controls than in the group of patients ($F(1, 30) = 20.34$; $p < 0.001$; $\eta^2 = 0.42$).

Finally, one cluster located in a central occipital region was associated with a significant Valence x Group interaction ($F(1, 30) = 21.28$; $p < 0.001$; $\eta^2 = 0.43$). Post-hoc paired t tests calculated for the two groups separately in the very same cluster revealed significantly enhanced activity in response to negative compared to neutral pictures in the control group (negative: $M = 36.82$, $SD = 15.00$; neutral: $M = 31.06$, $SD = 11.15$; $t(1, 15) = 4.37$, $p = 0.001$; $d = 0.80$) with but not in the patient group (negative: $M = 27.15$, $SD = 7.56$; neutral: $M = 27.00$, $SD = 8.73$; $t(1, 15) = -1.51$, $p = 0.151$; $d = 0.27$).

3.1.2 | Negative vs. phobia-relevant pictures

Early M100 time interval (70–130 ms; Figure 2 right column)

Across groups, major differences in the processing of negative and phobia-relevant pictures were found over the occipital lobe spreading into parietal regions. Similar to session one, main effects of Valence ($F(1, 30) = 147.43$; $p < 0.001$, $d = 4.589$; $\eta^2 = 0.84$) and the Group ($F(1, 30) = 12.06$; $p = 0.002$; $\eta^2 = 0.30$) were revealed. That is, negative compared to phobia-relevant pictures elicited stronger brain responses and the general level of neural activity was lower in patients compared to controls. The interaction of valence and group also reached significance ($F(1, 30) = 14.83$; $p = 0.001$; $\eta^2 = 0.73$). Pictures with negative content were followed by enhanced neural activity compared to pictures with phobia-relevant content in both groups (controls: $t(1, 15) = 8.05$; $p < 0.001$; $d = 1.47$; patients: $t(1, 15) = 8.48$; $p < 0.001$; $d = 1.55$). However, the differentiation between negative and phobia-relevant pictures was stronger in controls relative to patients when the differences (negative – phobia-relevant) are compared between groups (controls: $M = 28.77$; $SD = 14.30$; patients: $M = 13.67$; $SD = 6.44$; $t(30) = -3.85$; $p = 0.014$; $d = 0.70$).

EPN time-interval (160–300 ms; Figure 3 right column)

In the EPN time-interval we found main effects for the factors Valence ($F(1, 30) = 54.96$; $p < 0.001$; $\eta^2 = 0.66$) and Group ($F(1, 30) = 11.26$; $p = 0.002$; $\eta^2 = 0.29$). Negative compared to phobia-relevant pictures were associated with higher neural activity in left and right occipital regions while in patients the general level of cortical activity was lower than in controls. Although these two clusters share common regions no significant interaction effects could be observed.

LPP time-interval (330–600 ms; Figure 4 right column)

In the LPP time-interval, effects of Valence ($F(1, 30) = 57.23$; $p < 0.001$; $\eta^2 = 0.67$) were biggest over occipital and inferior posterior parietal regions, driven by stronger activation in response to negative compared to phobia-relevant pictures. Clusters showing a main effect of Group ($F(1, 30) = 9.91$; $p = 0.004$; $\eta^2 = 0.26$) were located more centrally in the occipital cortex and extending towards parietal regions on the left side. Again, general neural activity was increased in the group of controls relative to the group of patients.

Clusters associated with a significant interaction of Valence by Group ($F(1, 30) = 13.86$; $p = 0.001$; $\eta^2 = 0.33$) were located in the central occipital cortex, mainly driven by differences between groups in the processing of negative pictures. That is, negative (controls: $t(1, 15) = 8.05$; $p < 0.001$; $d = 1.47$; patients: $t(1, 15) = 8.48$; $p < 0.001$; $d = 1.55$) compared to phobia-relevant (controls: $t(1, 15) = 6.10$; $p < 0.001$; $d = 1.11$; patients: $t(1, 15) = 3.70$; $p = 0.002$; $d = 0.68$) material elicited more neural activity in both groups. However, groups did differ in the processing of negative pictures ($t(30) = -3.42$; $p = 0.002$; $d = 0.62$) which was stronger in controls ($M = 48.54$; $SD = 16.04$) compared to patients ($M = 32.58$; $SD = 9.59$). In the phobia-relevant condition, this difference was only marginally significant ($t(30) = -1.84$; $p = 0.076$; $d = 0.34$).

3.2 | Valence and arousal ratings

3.2.1 | Negative vs. neutral pictures

Ratings of the Self-Assessment Manikin scale were analysed by 2 by 2 ANOVAs including the between factor Group and the within factors Valence or Arousal. There was a main effect of Valence ($F(1, 30) = 262.52$; $p < 0.001$; $\eta^2 = 0.90$) indicating lower (more negative) valence rating for negative ($M = 2.61$; $SD = 0.71$) compared to neutral ($M = 5.36$; $SD = 0.68$) pictures. No main effect of Group or interaction with this factor could be found in the analysis. Similarly, there was a main effect of Arousal ($F(1, 30) = 117.16$; $p < 0.001$; $\eta^2 = 0.80$) showing that negative pictures ($M = 6.23$; $SD = 1.47$) were perceived as more arousing than neutral ($M = 3.23$; $SD = 1.42$) pictures. As for valence, arousal evaluations did not differ across groups (see Figure 5 left column).

3.2.2 | Negative vs. phobia-relevant pictures

The analyses for valence and arousal ratings in the second session were identical to session one. For the valence ratings, there were significant main effects of Valence ($F(1, 30) = 44.25$, $p < 0.001$; $\eta^2 = 0.61$) and Group ($F(1, 30) = 26.63$, $p < 0.001$; $\eta^2 = 0.49$) which were modulated by a significant interaction of Valence and Group ($F(1, 30) = 51.89$, $p < 0.001$; $\eta^2 = 0.65$). That is, negative ($M = 2.61$; $SD = 0.89$) compared to phobia-relevant pictures

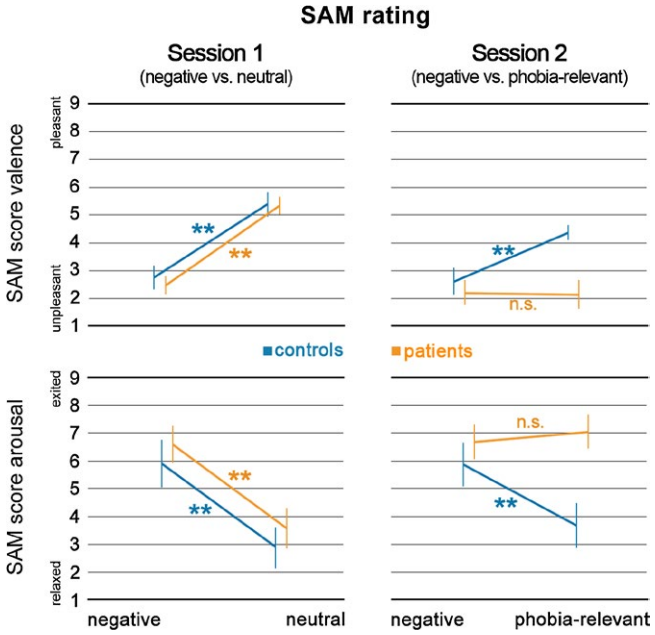

FIGURE 5 Results of the valence and arousal ratings. Self-Assessment Manikin ratings for valence (upper row) and arousal (lower row) for session one (left column) and session two (right column). Asterisks indicate the level of significance (*$p < 0.05$; **$p < 0.01$). [Colour figure can be viewed at wileyonlinelibrary.com]

($M = 4.37$; $SD = 0.48$) were rated significantly more negative in the control group ($t(1, 15) = -9.05$; $p < 0.001$; $d = 1.65$). In the patients group, negative ($M = 2.19$; $SD = 0.82$) and phobia-relevant pictures ($M = 2.13$; $SD = 0.96$) were rated as equally negative ($t(1, 15) = 0.43$; $p = 0.674$; $d = 0.07$).

Similar results were obtained for the arousal ratings. There were main effects of Arousal ($F(1, 30) = 24.48$; $p < 0.001$; $\eta^2 = 0.47$) and Group ($F(1, 30) = 23.23$; $p < 0.001$; $\eta^2 = 0.45$) which were again modulated by an interaction of both factors ($F(1, 30) = 47.8$; $p < 0.001$; $\eta^2 = 0.63$). In the control group, negative ($M = 5.88$; $SD = 1.48$) pictures were rated more arousing than phobia-relevant ($M = 3.68$; $SD = 1.53$) pictures ($t(1, 15) = 6.87$; $p < 0.001$; $d = 1.25$), whereas in the patients group there was no significant difference between negative ($M = 6.69$; $SD = 1.16$) and phobia-relevant ($M = 7.06$; $SD = 1.13$) pictures ($t(1, 15) = -1.95$; $p = 0.070$; $d = 0.36$; see Figure 5 right column).

4 | DISCUSSION

In the visual system, the allocation of motivated attention is indexed by two event-related potential components – the EPN and the LPP. Enhanced EPN and LPP amplitudes are reliably observed, for instance, in animal phobics viewing pictures of fear-related material or in individuals with social anxiety viewing pictures of angry, threatening, or ambiguous faces (Moser et al., 2008; Muhlberger et al., 2009; Wieser et al., 2010). The aim of this study was to reveal whether a similar bias in motivated attention can be found towards phobia-relevant material in individuals suffering from dental phobia.

Throughout all analysed time-intervals (early, mid-latency, and late) and irrespective of emotional content of the pictures, the group of patients with dental phobia, demonstrated less evoked neural activation at predominantly parietal and temporal regions compared to controls. In early and late time-intervals patients additionally showed less differentiation between picture categories compared to the group of controls. Individuals without dental anxiety, in turn, responded consistent with existing literature demonstrating higher activation during the mid-latency EPN and late LPP time interval for negative compared to neutral pictures.

Thus, results of this study indicate that, in contrast to other anxiety disorders, dental phobia cannot be associated with the typical effect of biased motivated attention seen for negative or phobia-relevant pictures. As outlined earlier, frequency of fainting and gender distribution already indicate that dental phobia could be considered as a distinct form of the B-I-I subtype. Further evidence is provided by neuroimaging studies. For instance, individuals suffering from snake, spider, or blood-injection-injury phobia exhibit increased neural activity in brain regions of the fear circuit, especially the insula, the anterior cingulate cortex, thalamus, and amygdala (Caseras, Giampietro, et al., 2010; Caseras, Mataix-Cols, et al., 2010) when viewing phobia-specific stimuli. These activations in limbic and paralimbic regions were further associated with increases in autonomic arousal. In contrast, dental phobia patients often show a general non-responsiveness or indifference in response to emotional and phobia-relevant material. Their autonomic reactivity is low and neural activity in brain regions of the fear circuit is reduced or even absent (Lueken et al., 2011). Neither during anticipation nor during immediate processing of feared stimuli, hypervigilance could be reported in these individuals (Lueken et al., 2013). Only one study using auditory stimuli (compared to video sequence or pictures) found higher activation in dental phobia patients compared to healthy controls. This heightened activation occurred in areas associated with phobia-related fear, but again, no increase in autonomic arousal has been observed (Hilbert, Evens, Maslowski, Wittchen, & Lueken, 2014).

In a comprehensive Meta-Analysis Etkin and Wager (Etkin & Wager, 2007) contrasted neuroimaging findings on PTSD, Social Anxiety Disorder, and Specific Phobia. Hypoactivation, lower activation in patients than in controls, was found only in studies on PTSD. Most of these studies reported reduced activation in prefrontal, occipital, limbic, and paralimbic areas and an association between hypoactivation and symptom severity was observed (Adenauer et al., 2010; Burgmer et al., 2013; Catani et al., 2009; Elbert et al., 2011; Felmingham et al., 2003; Kounios et al., 1997). Interestingly, Catani et al. (2009), Adenauer et al. (2010), Elbert et al.

(2011), and Burgmer et al. (2013) found elevated activity over prefrontal areas preceding the reduced responses over the parieto-occipital and occipito-temporal cortex regions. The authors concluded that the rapid prefrontal hyperactivation to aversive stimuli might initiate a subsequent process of attentional avoidance reflected by reduced activity in parieto-occipital and occipito-temporal cortex regions. Thus, the attentional bias seen in traumatised individuals might be an adaptive strategy to limit perceptual input and to prevent the cortex from overstimulation (Adenauer et al., 2010; Bryant et al., 2005).

Although we found evidence for reduced motivated attention, as indexed by less or no differences between LPP and EPN amplitudes in response to emotional and neutral stimuli, such elevated early prefrontal activity was not found in the broad analysis of this study. However, when the cluster analysis is restricted by corresponding spatio-temporal priors (<120 ms and frontal regions only), in fact, prefrontal clusters show differential responses between conditions and groups (please see Supporting Information Figure S1) in the predicted direction.

On that note, our data seem to confirm the notion proposed by de Jongh et al. (2003) wherein dental phobia should be considered as a mild form of PTSD, or in other words, a specific phobia that shares characteristics with PTSD symptomatology. de Jongh and colleagues based their assumption on the fact that about 73% of individuals with high dental anxiety report at least one traumatic event. Half of them experienced a traumatic dental treatment; the second most mentioned experience was a traumatic medical treatment followed by violent crime or sexual assault. These findings are in line with several previous studies who found even higher rates of traumatic experiences (Berggren & Meynert, 1984). It is therefore not surprising, that trauma-focused treatment, originally developed to treat PTSD, shows beneficial effects in individuals suffering from dental phobia (de Jongh et al., 2003, 2006; Doering, Ohlmeier, de Jongh, Hofmann, & Bisping, 2013).

Nevertheless, our data contradict findings of the research group around Schienle and Leutgeb. They reported enlarged late positive potentials over centro-parietal regions in dental phobia patients following the presentation of phobia-relevant pictures. Likewise, no difference between patients and controls for other picture categories (disgust, fear, and neutral) could be observed (Leutgeb et al., 2011). However, in their study patients and controls did not differ with respect to trait and state anxiety. In contrast, in the study at hand, eight patients scored above the cut-off on the HADS anxiety subscale. Additionally, all patients reported a traumatic dental experience and to different degrees, symptoms of PTSD according to the Impact of Events Scale-Revised. Thus, differences in study outcome might be explained by differences between patient groups. As outlined previously, hypoactivation was only found in studies investigating traumatised compared to non-traumatised patients. Given that previous studies, with apparently "more healthy" subjects, found enhanced activity in response to phobia-relevant material, one might assume that either dental phobia can manifest itself with different levels of severity, or that at least there has to be made a distinction between subjects suffering from dental phobia with or without traumatic experience. Of course, this assumption needs to be proven in further studies. Since we explicitly focused on a highly homogenous group of subject, conclusions from our dataset are limited because it does not allow any in-depth subgroup analysis; neither do we have the possibility to study differences between traumatised and non-traumatised patients.

To conclude, our data suggest that dental phobia should be distinguished from other types of phobia, especially from the B-I-I subtype, since our results diverge from the general hypervigilance found in blood-fearful individuals and do not show the attentional bias found in other type of phobias, e.g. animal phobia. In contrast, patients in this study exhibit a general hypoactivation usually found in severely traumatised individuals with and without PTSD. Consequently, this could have some important implications for the clinical practice, as it may emphasise the relevance of trauma-focused therapies as an additional treatment for, at least, individuals suffering from severe forms ofdentalphobia.

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CONFLICT OF INTEREST

All authors declare that they have no conflict of interest.

DATA ACCESSIBILITY

Data used in this article are available upon request to the corresponding author.

AUTHORS' CONTRIBUTION

Authors JA, CS, SD, and MJ were involved in the concept and design of the study. NELK and BH had major contributions to data extraction and analysis. Authors JA, CS, and MJ conducted the statistical analysis. Authors JA, CS, and MJ wrote the first draft of the manuscript and all authors contributed to and have approved the final manuscript.

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