Emotional sensitization highlights the attentional bias in blood–injection–injury phobics: An ERP study

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Abstract

The presence of an attentional bias towards disorder-related stimuli has not been consistently demonstrated in blood phobics. The present study was aimed at investigating whether or not an attentional bias, as measured by event-related potentials (ERPs), could be highlighted in blood phobics by inducing cognitive–emotional sensitization through the repetitive presentation of different disorder-related pictures. The mean amplitudes of the N100, P200, P300 and late positive potentials to picture onset were assessed along with subjective ratings of valence and arousal in 13 blood phobics and 12 healthy controls. Blood phobics, but not controls, showed a linear increase of subjective arousal over time, suggesting that cognitive–emotional sensitization did occur. The analysis of cortical responses showed larger N100 and smaller late positive potentials in phobics than in controls in response to mutilations. These findings suggest that cognitive–emotional sensitization induced an attentional bias in blood phobics during picture viewing, involving early selective encoding and late cognitive avoidance of disorder-related stimuli depicting mutilations.

Keywords:
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ERPs
Emotional sensitization
Arousal
Emotional pictures

Attentional bias, as documented by a host of studies spanning more than two decades of research on anxiety disorders, consists of the continuous scanning of the environment for sources of potential threat and the assignment of processing priority to threat-related information [2]. Although an impressive body of behavioral and electrophysiological investigations has demonstrated that the attentional bias is fairly ubiquitous across anxiety disorders and pathological fears, and that it may be a cognitive marker for anxiety vulnerability [17], blood phobia stands as an exception within this context. Indeed, an attentional bias towards phobia-related stimuli, reflected in larger amplitudes of event-related P300 and late positive potentials, can be effectively highlighted during picture viewing in other specific phobics [15,18,19], but not in blood phobics [7,8]. A reliable attentional bias seems to emerge in blood phobics only when the cognitive system is forced to distribute spatial attention between discrete stimuli in the visual field [9]. It is possible that stimuli depicting injuries and mutilation saturate the available attentional resources in healthy individuals [8,10] so that fear of blood does not (or perhaps cannot) further increase attentional allocation during picture processing.

From a different perspective, recent theories within the field of experimental psychopathology propose that sensitization processes play a central role in the etiology of anxiety disorders and subjective health complaints [5,12]. Sensitization is one of the basic forms of plasticity within the central nervous system, whereby repeated stimulation leads to increased neuronal responsivity due to enhanced synapse efficiency [21,24]. The underlying functional meaning of such a mechanism would be to enable the organism to respond more efficiently to situations with increased probability of harm [5]. It is worth noting that sensitization is more often obtained when the inducing stimulus is strong or harmful, and when repetition of the stimulus is relatively irregular or unpredictable [21]. Moreover, the organism’s level of arousal plays a central role in that stimulus repetition induces sensitization at high levels of arousal, whereas repetition of the same stimulus under conditions of low arousal would lead to habituation [21].

It has recently been proposed that basic sensitization processes at the neural level might have an analog in higher-order cognitive and emotional processes and, more specifically, in the phenomenon of attentional bias [5]. Attentional bias would theoretically be related to sensitization based on the feed-forward principle. The perception and/or experience of potential danger is thought to activate an associative network of interconnected threat-related representations such that subsequent selective attention to incoming threat stimuli is facilitated due to the long-lasting activation and re-activation of threat-related information. In this view, “cognitive–emotional” sensitization would result from a feed-forward process in that attending to threat leads to more and more attendance to threat [5]. Indeed, extensive and converging evidence suggests that anxiety can be viewed as a sensitization loop that promotes perseverative activity at a number of functional levels and, eventually, perpetuates anxiety itself [23]. Whereas flexible adap-
tation to environmental demands is related to orienting to novel stimulation followed by response habituation, anxiety is associated with a failure to habituate to repeated stimulation, leading to perseveration of defensive responses (i.e., sensitization), including selectively attending to threat [23].

The main aim of the present study was to assess whether or not an attentional bias, as measured by event-related potentials (ERPs), could be highlighted in blood phobics by inducing cognitive–emotional sensitization through the repetitive processing of different disorder-related pictures. Different picture exemplars of two phobia-related contents were randomly presented interspersed with neutral pictures in order to make the threatening stimulus highly probable but relatively unpredictable. Unlike previous studies [cf. 7.8], no other emotional contents were employed.

A secondary aim of this study was to investigate possible differences in the processing of blood-related contents by distinguishing between the typical contents employed in the literature (i.e., injured or mutilated bodies) and the blood depicted in isolation (i.e., blood stains on different surfaces) without any reference to human bodies. In this way, it would be possible to disentangle the aversive impact of pictures depicting blood per se from that produced by pictures representing harm to the body. To the best of our knowledge, no studies have yet addressed this issue, which might contribute to the characterization of information processing and emotional responses in blood phobics.

Because blood phobia has a higher prevalence among females [3], only women were recruited for the present study. The Italian version of the Mutilation Questionnaire (MQ) [14] was administered to 150 undergraduates, and subjects who scored above the 80th percentile of the obtained scoring distribution (MQ > 17) were included in the preliminary phobic group. They were further screened with the Anxiety Disorders Interview Schedule for DSM-IV (ADIS-IV) [6] to assess whether they fulfilled the DSM-IV criteria for specific phobia, blood–injection–injury type [1]. The final sample included 13 females (age range 20–33 years; M = 23.92, S.D. = 3.55). Their mean MQ score was 21.92 (range 19–28; S.D. = 2.60).

Control subjects (N = 12; age range, 20–28 years; M = 23.08, S.D. = 1.93) were randomly selected from the initial pool of subjects with an MQ score under the 50th percentile (MQ < 10) and no specific fears. Their mean MQ score was 6.67 (range, 2–9; S.D. = 1.92). Sixty digitized color pictures (1024 × 768 pixel resolution) were presented, divided into three emotional categories: mutilation (injuries and mutilated bodies), blood (blood stains on different surfaces, without human bodies) and neutral (people, urban landscapes and household objects). Neutral and mutilation pictures were selected from the International Affective Picture System (IAPS) [16]. Blood pictures were downloaded from websites and standardized for valence (pleasant–unpleasant) and emotional arousal (activated–calm) ratings on the Self-Assessment Manikin (SAM) [16]. The pictures were presented in a randomized order via a 19-in. monitor on an IBM-compatible computer, positioned at a distance of about 1 m from the subject.

Upon arrival at the laboratory, the participants read and signed an informed consent form. After the electrodes were attached, they were informed that a series of pictures would be shown and that each picture should be viewed for its entire duration. The pictures were presented for 2 s. Immediately after picture offset, the participants rated the picture using a computerized version of the SAM 1–9 point scale of Valence and Arousal. Then, an inter-trial interval of 1–3 s elapsed before the next stimulus was presented.

The electroencephalogram (EEG) was recorded from nine positions (F3, Fz, F4, C3, Cz, C4, P3, Pz, P4) referenced to linked mastoids, according to the International 10–20 system. For artifact scoring, vertical and horizontal electro-oculograms (EOGs) were recorded from electrode pairs (bipolar) placed at the supra- and suborbit of the right eye and the external canthi of both eyes. All electrode impedances were less than 10 kΩ. The EEG and the EOGs were amplified using Neuroscan Synamps (El Paso, TX, USA), bandpass filtered (0.1–40 Hz), digitized at 250 Hz (16 bit A/D converter, accuracy 0.084 μV/LSB) and stored on to a Pentium IV computer. Picture presentation was accomplished using E-prime software (Psychology Software Tools, Pittsburgh, PA, USA).

The EEG was corrected for blink artifacts using a regression-based weighting coefficients technique (SCAN 4.3 software; Neurosoft, Inc.). All EEG recordings were further visually scored for artifacts, and each portion of data containing residual artifacts greater than ±70 μV in any recording channel was excluded from the averaging. The mean number of trials retained for the ERP analysis after artifact rejection was 18.76, 18.76, and 18.12 for neutral, blood and mutilations, respectively. EEG epochs of −200 to 1000 ms poststimulus, baseline-corrected by subtraction of the mean prestimulus voltage, were averaged separately for each subject and experimental condition. On the basis of visual inspection of the grand-average ERP waveforms, the mean amplitudes of the following ERP components were computed: N100, as the most negative peak between 60 and 130 ms from stimulus onset; P200, as the most positive peak between 140 and 240 ms from stimulus onset; P300, as the most positive peak between 280 and 420 ms from stimulus onset. Moreover, the mean amplitude of the late positive potential (LPP) was calculated in three time windows after picture onset (400–600 ms, 600–800 ms, and 800–1000 ms). The mean amplitudes of the ERP components were analyzed using a 2 × 3 × 3 ANOVA, with Blood Phobics, Controls) as the between-subjects factor and Category (Mutilations, Neutral, Blood), Region (Frontal, Central, Parietal) and Laterality (Left, Midline, Right) as within-subjects variables.

Affective ratings were analyzed using a 2 × 3 analysis of variance (ANOVA), with Group as the between-subjects factor and Category as the within-subjects variable. Moreover, Valence and Arousal ratings, averaged across Blood and Mutilation pictures (40 pictures in total), were split into four blocks of ten pictures each, according to their order of presentation, and analyzed using a 2 × 4 ANOVA. This analysis aimed to assess the changes in self-reported emotional ratings (especially in arousal) over time as a possible index of sensitization effects. Splitting the Valence and Arousal ratings into four blocks allowed the temporal development of sensitization (if any) to be explored in sufficient detail, while including a reasonable number of data points.

The Greenhouse–Geisser corrected p-values for effects within variables with more than two levels are reported together with the uncorrected degrees of freedom. Significant main effects and interactions (p < 0.05) were followed by Tukey’s HSD post hoc tests.

For the Valence ratings, the significant Group × Category interaction (F(2,46) = 7.16; p = 0.006, n_p2 = 0.24) showed that Phobics rated Blood (p < 0.001) and Mutilations (p < 0.09), but not Neutral pictures, as more unpleasant than the Controls. Both groups rated Mutilations as the most unpleasant content, followed by Blood and Neutral (ps < 0.04).

For Arousal ratings, the significant Group × Category interaction (F(2,46) = 7.56; p = 0.002, n_p2 = 0.25) indicated that Phobics rated Blood (ps < 0.0002), but not Neutral, as more arousing than the Controls. Both groups judged Mutilations to be the most arousing content, followed by Blood and Neutral (ps < 0.0002).

The means and standard deviations for Valence and Arousal ratings by the Blood Phobics and Controls are presented in Table 1. The analysis by block on Valence ratings only yielded an overall Group main effect, showing that Phobics rated these pictures as more unpleasant than the Controls (F(1,23) = 10.32; p = 0.004, n_p2 = 0.31). Interestingly, the analysis by block on Arousal ratings yielded a significant Group × Block interaction (F(3,69) = 2.69; p = 0.05, n_p2 =
Fig. 1. Grand-averaged event-related potentials for the different emotional categories recorded at the midline electrodes in Blood Phobics and Controls.

0.11), showing that arousal increased progressively from the first to the last block for the Phobics \( (p < 0.007) \), whereas for the Controls an increase was only found from the first to the second block \( (p < 0.02) \). In addition, a significant linear trend of block was only found for the Phobics \( (F(1,11) = 11.93, p = 0.005, \eta_p^2 = 0.52) \).

Grand-averaged ERPs elicited by the different emotional categories at midline sites in Blood Phobics and Controls are shown in Fig. 1.

The significant Group × Category × Laterality interaction \( (F(4,92) = 2.96; p = 0.04, \eta_p^2 = 0.11) \) demonstrated that at midline and on the left hemisphere, the N100 amplitude to Mutilations was larger in Phobics than in the Controls \( (ps < 0.005) \), whereas the N100 amplitude to Blood was larger in the Controls than in the Phobics \( (ps < 0.004) \). No significant differences were found between groups in the N100 amplitude to Neutral pictures at any laterality site. Furthermore, the Phobics responded with larger N100 amplitudes to Mutilations than to Blood at every laterality site \( (ps < 0.0001) \), whereas the Controls did not show any differences in amplitudes between the conditions (Fig. 2).

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Blood Phobics</th>
<th>Controls</th>
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<tbody>
<tr>
<td>Valence ratings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mutilations</td>
<td>1.41 (0.57)</td>
<td>2.21 (0.98)</td>
</tr>
<tr>
<td>Neutral</td>
<td>4.75 (1.19)</td>
<td>4.48 (1.26)</td>
</tr>
<tr>
<td>Blood</td>
<td>2.30 (0.92)</td>
<td>3.52 (1.29)</td>
</tr>
<tr>
<td>Arousal ratings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mutilations</td>
<td>6.65 (1.55)</td>
<td>4.37 (1.05)</td>
</tr>
<tr>
<td>Neutral</td>
<td>1.56 (0.73)</td>
<td>1.17 (0.19)</td>
</tr>
<tr>
<td>Blood</td>
<td>4.36 (1.84)</td>
<td>2.15 (0.86)</td>
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</tbody>
</table>

Fig. 2. Mean N100 amplitudes to the different emotional categories as a function of laterality in Blood Phobics and Controls. Standard errors are marked.
disorder-related stimuli in a picture viewing paradigm.

phobia-related stimuli when cognitive–emotional sensitization
involving the Group factor were obtained.

As highlighted by the significant Category × Region interaction (F(4,492) = 11.53; p = 0.0001; n^2 = 0.33), a larger positivity was found in the 400–600 ms window for Blood relative to Neutral pictures in the central and parietal regions (p < 0.0002) and for Mutilations relative to Blood and Neutral contents in all regions (p < 0.0002).

No significant effects involving the Group factor were obtained.

Importantly, a significant Group × Category interaction was found in the 600–800 ms window (F(2,46) = 3.86; p = 0.03; n^2 = 0.14), showing that cortical positivity during the viewing of Mutilations was significantly lower in the Phobics than in the Controls (p < 0.03) (see Fig. 1). No significant differences were found between the groups for the other emotional categories. Furthermore, the Controls showed a larger positivity to Mutilations than to the Neutral contents (p < 0.002), with no significant differences between the two unpleasant categories, whereas the Phobics did not show amplitude differences among categories.

Lastly, in the 800–1000 ms window, the significant Category × Region interaction (F(4,492) = 6.20; p = 0.002; n^2 = 0.21) reflected a lower positivity for Mutilations than Neutral pictures in the central and parietal regions (p < 0.04). No significant effects involving the Group factor were obtained.

The present study aimed to investigate whether or not blood phobic participants would show an attentional bias towards phobia-related stimuli when cognitive–emotional sensitization was induced through the repetitive processing of different disorder-related stimuli in a picture viewing paradigm.

In previous studies, the presentation of mutilation pictures in a picture-viewing context did not highlight any attentional bias in blood phobics in that the amplitudes of P300 and LPP ERP components [8] and the electromagnetic activity pattern [7] did not differ relative to the controls. By contrast, in the present study, an attentional bias affecting both early and late processing stages was found by manipulating the context of phobic picture presentation.

The presentation of different picture exemplars of two disorder-related categories (i.e., blood and mutilations), randomly interspersed with neutral pictures and no other emotional contents, induced cognitive–emotional sensitization in Phobic individuals. This was supported by the finding of a linear increase in subjective arousal over time, specifically in fearful participants. Previous research on healthy individuals reported that exposure to blocks of unpleasant pictures led to significant increases in corrugator muscle activity over time, suggesting an increasing aversive impact of unpleasant stimulation [4]. Also, the cumulative increase in affective responses during sustained exposure to unpleasant pictures has been shown to be greater for individuals with higher state anxiety, suggesting increased defensive activation [11]. Our finding complements such results and extends research on information processing in blood phobia by showing that sensitization occurs in phobic individuals, but not in controls, even without presenting the pictures in blocked fashion. More specifically, the presentation of phobic cues interspersed with neutral contents might have rendered the repetition of phobic stimulation relatively irregular and unpredictable, thus increasing sensitization [21].

Cognitive–emotional sensitization and increasing emotional arousal over time in Blood Phobics led to the emergence of a processing bias involving early selective encoding and late cognitive avoidance. The larger parietal N100 amplitude elicited by Mutilations in Phobics compared with the Controls indicates that visual attention is biased in favor of these contents in the early stages of processing. The N1 ERP component is known to reflect the exogenous, stimulus-driven orienting of attention, feature selection, and discrimination processes within the focus of attention [25]. Within this context, a larger N100 amplitude to disorder-related stimuli would index early implicit selective attention facilitating sensory encoding. Such an attentional bias did not involve later processing stages, as no differences between Phobics and Controls were found in the P200, P300 or LPP amplitudes up to 600 ms after picture onset. However, in the time range of these components, both Mutilations and Blood elicited a significantly larger positivity than the Neutral pictures, as previously reported for mutilations only [8,22], indicating facilitated access to attentional resources and greater attentional engagement [8,22]. Interestingly, the analysis on LPP in the 600–800 ms time window revealed lower cortical positivity to Mutilations in Phobics than in Controls, indicating that less attentional resources were allocated to this content. Taken together, these results are consistent with what the vigilance–avoidance model would predict. According to this model, anxiety-related attentional biases vary over time, i.e., after the initial orienting to threatening cues, attention is directed away from the threat in an attempt to reduce the anxious state elicited by aversive stimulation [20]. Our data suggest that cognitive avoidance began in Blood Phobics at about 600 ms after the onset of Mutilation pictures, whereas, in the same time window, increased attentional resources towards Mutilation relative to Neutral contents were still maintained in the Controls.

As a secondary aim, we investigated possible processing differences between contents depicting injured or mutilated bodies, which have been typically employed in the literature as phobia-related stimuli, and those depicting blood in isolation, with no presence of human bodies. In the present study, subjective and electrophysiological measures consistently demonstrated that Mutilations resulted in greater aversiveness and, consequently, a greater processing bias for the Blood Phobics. Despite evaluating both phobia-related contents as significantly more unpleasant and arousing than the Controls, Phobic participants assigned processing and emotional priority to Mutilation contents. This was supported by the findings of (a) greater unpleasantness and arousal relative to Blood contents and relative to the Controls; (b) larger N100 amplitudes relative to Blood contents and relative to the Controls; and (c) lower cortical positivity in the 600–800 ms time window relative to the Controls. On the other hand, the finding of reduced sensitivity to stimuli depicting blood in isolation in Blood Phobics was somehow unexpected and warrants further investigation. However, our data strongly suggest that for blood phobics the most effective phobic object is not the blood per se, but rather all circumstances where there is a high probability of associated injury, any violation of the integrity of the body (i.e., “body envelope violations”) [13], or even death. From an evolutionary perspective, such phobic responses might have evolved from an originally adaptive reaction to stimuli signaling life-threatening dangers, just like it occurs in snake or spider phobias. Such considerations might have significant implications for the definition of possible fear domains in blood phobia.

A different response pattern emerged in the control group. In the early processing stages, higher attentional priority was assigned to Blood contents by the Controls relative to Phobics, as reflected by a larger N100 amplitude. Furthermore, the Controls did not show any significant differences in N100 amplitudes between Blood and Mutilations, indicating that both contents were relevant for attentional selection. It is possible that in non-fearful individuals stimuli depicting blood without visible injuries become particularly salient because of their ambiguity in signaling danger. Indeed, such ambiguity seemed to be resolved in the successive processing stages,
with Blood stimuli requiring lower attentional demands relative to Mutilation contents. In fact, in both Phobics and the Controls, larger P200, P300 and cortical positivity in the 400–600 ms window were observed in response to Mutilations than Blood.

To summarize, an attentional bias can be highlighted in blood phobia under conditions that either force the cognitive system to distribute spatial attention between discrete stimuli in the visual field [9] or during picture viewing by inducing the development of increasing emotional arousal and cognitive–emotional sensitization via repeated exposure to the phobic object. Furthermore, stimuli depicting injuries and mutilations are more effective than those depicting isolated blood in eliciting subjective and electrophysiological indications of processing biases in blood phobics.

References