Neural responses to affective pictures while anticipating and perceiving respiratory threat

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Abstract

Emotional processes have an impact on the anticipation and perception of bodily threat sensations, such as breathlessness. However, little is known about the reverse influence of breathlessness on emotional processes, as well as its modulation by anxiety sensitivity (AS). Here, we investigated by means of visually evoked potentials how the perception versus anticipation of resistive-load-induced breathlessness (RLIB) influences emotional processing. High (HA) and low anxious (LA) participants viewed pictures of positive, neutral, or negative content under conditions of perceived RLIB, anticipated RLIB, or an unloaded baseline. The P2 (230–290 ms) was significantly less positive under perceived RLIB. Furthermore, the early late positive potential (LPP; 300–500 ms) was significantly less positive during both RLIB conditions, as compared to baseline. Overall, the P1 was significantly more positive in HA as compared to LA individuals. Additionally, across conditions, the late LPP (600–1,000 ms) was enhanced for positive and negative pictures as opposed to neutral ones for the LA group. In contrast, for the HA group only, the positive pictures elicited the typical enhanced LPP. Notably, for the HA participants, negative pictures elicited significantly blunted late LPPs during perceived RLIB as compared to anticipated RLIB and baseline. A reversed effect (i.e., more positivity) was observed for LA participants, suggesting motivational priming. Taken together, these results highlight the impact of perceived and anticipated respiratory threat on the neural processing of emotional picture stimuli, as well as its modulation by anxiety sensitivity levels.

Descriptors: Affective processing, Respiratory threat, Resistive load, Breathlessness, Anxiety sensitivity

The understanding of a severe bodily threat sensation, such as breathlessness, is crucial for somatic and psychological disorders (Barlow, 2002; Domschke, Stevens, Pfleiderer, & Gerlach, 2010; Hamm, Richter, & Pané-Farré, 2014). Moreover, the perception of bodily threat sensations is closely linked to emotional experience (James, 1894; Schachter & Singer, 1962). Researchers have thus far approached breathlessness by investigating how affective states influence its perception. For example, it has been convincingly demonstrated that affective states significantly alter the perception of breathlessness, a prominent effect evident both at a behavioral as well as at a neural level (Janssens, Verleden, De Peuter, Van Diest, & Van den Bergh, 2009; von Leupoldt, Chan, Esser, & Davenport, 2013; von Leupoldt, Mertz, Kegat, Burmester, & Dahme,

2006). However, the reverse path of how breathlessness itself affects the processing of emotional stimuli has not received as much attention.

Recently, we utilized ERPs in order to investigate the effect that breathlessness exerts on emotional processing (Juravle et al., 2014). Our participants viewed either positive, neutral, or negative pictures under conditions of resistive-load-induced breathlessness (RLIB). Results indicated that the ERPs locked to picture onset were significantly affected by the bodily threat stimulus. Specifically, breathlessness reduced the early deflections of the ERP within up to 300 ms poststimulus onset, thus suggesting that it is the early neural processing of visual picture stimuli that is affected during breathlessness, and thereby indicating a strong attentional capture of breathlessness. Similarly, a reduced P1, and also late positive potential (LPP), for emotional pictures were demonstrated during perceived pain (Wieser, Gerdes, Greiner, Reicherts, & Pauli, 2012).

Moreover, it has been suggested that the anticipation of breathlessness might be more important than its perception in respiratory and psychological disorders as it motivates (often maladaptive) avoidance behavior (Hayen, Herigstad, & Pattinson, 2013; Paulus,

Table 1. *Demographic Data (M ± SD)*

	High anxious (N = 17)	Low anxious (N = 17)	p
Age	27.8 ± 3.6	25.7 ± 3.1	.086
FVC	5.2 ± .1	5.4 ± 1.1	.693
FEV_1	4.1 ± .7	4.2 ± .8	.614
FVC%	100.7 ± 6	103.5 ± 11.8	.386
FEV_1%	96 ± 9	98.8 ± 14.8	.506
Load strength (kPA/L/s)	1.1 ± .1	1.2 ± .1	.377
Anxiety sensitivity (ASI3)	11.3 ± 4	26.9 ± 7	<.001

Note. FVC = forced vital capacity; FEV_1 = forced expiratory volume in 1 s.

2013). For example, the repeated aversive experience of breathlessness in patients with chronic obstructive pulmonary disease (COPD) can lead to fear of breathlessness. The subsequent fearful anticipation of breathlessness is believed to lead to avoidance of contexts that are associated with breathlessness (e.g., physical activity), thus fuelling a downward spiral of physical deconditioning, increased breathlessness, increased anticipatory fear, and progressive reductions in health status and quality of life (Troosters et al., 2013; von Leupoldt & Janssens, 2016). In this regard, several studies concerned with the anticipation of breathlessness have highlighted significant physiological fear responses, including activations of fear-related brain areas such as insula, anterior cingulate cortex, and amygdala (Holtz, Pané-Farré, Wendt, Lotze, & Hamm, 2012; Melzig, Michalowski, Holtz, & Hamm, 2008; Pappens, Smets, Vansteenwegen, Van Den Bergh, & Van Diest, 2012; Paulus et al., 2012; Stoeckel, Esser, Gamer, Büchel, & von Leupoldt, 2015; Stoeckel, Esser, Gamer, Kalisch et al., 2015).

In light of these results, we were interested to investigate whether not only the perception of breathlessness but also the mere anticipation of such a severe bodily threat would result in a similar modulation of the neural processing of affective picture stimuli. Recent research has highlighted altered startle responses (Nelson, Hajcak, & Shankman, 2015), modulations of the early electrophysiological responses during the anticipation of aversive events such as threat of shock (Nelson, Hajcak, & Shankman, 2015; Seidel et al., 2015) or public speaking (Wieser, Pauli, Reicherts, & Mühlberger, 2010), as well as during the experience of a smell-based threat context (Kastner, Flohr, Pauli, & Wieser, 2015). For example, it has been demonstrated that the later ERPs (e.g., P3 or the LPP) are reduced during the anticipation of threat (Nelson, Hajcak, & Shankman, 2015), as well as during perception of pain (Wieser et al., 2012).

In addition, breathlessness seems to be affected by trait anxiety levels, in that high anxious individuals demonstrate an increased perception of breathlessness, whereas low anxious individuals exhibit a decrease in the perception of breathlessness (Livermore et al., 2012; Stoeckel, Esser, Gamer, Büchel, & von Leupoldt., 2015). Especially high levels of anxiety sensitivity—a dimensional trait measure of the belief that physiological symptoms might signal severe bodily circumstances—seem to be related to specific bodily threat such as breathlessness (Alius, Pané-Farré, von Leupoldt, & Hamm, 2013; Melzig et al., 2008). Moreover, the modulation of neural responses during the anticipation of threat has been shown to correlate with increased trait levels of (anxious) cognitive, as well as physical, concerns (Nelson, Hodges, Hajcak, & Shankman, 2015).

In the present study, our participants viewed pictures of emotional content under conditions of perceived RLIB, anticipated RLIB, as well as an unloaded baseline, while the continuous EEG was recorded. We were particularly interested in the early modulations of the picture-locked ERPs that we have previously observed, as well as the more common, later affect-related ERPs. The hypothesis predicted reduced ERPs for both RLIB conditions relative to the baseline, together with significantly enhanced ERPs to emotional relative to neutral picture viewing. In addition, we predicted modulations of the ERPs of interest as a function of anxiety sensitivity, during both perceived and anticipated breathlessness.

Method

Participants

Forty individuals participated in the experiment. They were recruited from an overall student database. Out of these, the data from four participants were removed because of amplifier failure severely affecting the EEG. Furthermore, during data analysis, another two participants were excluded from the final sample (see below for particulars). The remaining sample consisted of 34 participants (18 males) with an average age of 27 years (age range: 21–39 years). All participants reported normal respiratory status, as well as normal or corrected-to-normal vision. Baseline lung function was assessed by spirometry in accordance with the European Respiratory Society standards (Miller et al., 2005). The dispositional (trait) level of anxiety sensitivity in all participants was measured with the validated German version of the Anxiety Sensitivity Index-3 (the ASI-3 questionnaire, Kemper, Ziegler, & Taylor, 2009; Taylor & Cox, 1998; Taylor et al., 2007). The questionnaire was computer administrated, and the mean ASI score was 19.12 (SD = 9.74, general scores range: 5–41). No significant difference was observed when comparing the ASI scores between male and female participants in both the low anxious group, $t(15) = 1.39$, $p = .184$, $r = .34$, as well as the high anxious group of our sample, $t(15) = .098$, $p = .923$, $r = .03$. See Table 1 for a summary of the demographic data. Participants received monetary remuneration for their participation. The study protocol was approved by the ethics committee of the Medical Association Hamburg, and written informed consent was obtained from all participants before the beginning of the experiment.

Resistive Load Breathing

RLIB was induced by breathing through inspiratory resistive loads, a procedure known to increase the work of the respiratory muscles (Harver & Mahler, 1998). Participants wore a nose clip and breathed via a mouthpiece attached to a breathing circuit including an antibacterial filter, a pneumotachograph, and a non-rebreathing valve, all connected in series. The inspiratory port of the valve was connected to a tube facilitating the easy introduction and removal of the inspiratory resistive loads, while the expiratory port was left free.

The magnitude of the load was estimated during a pretest phase. The aim of the pretest was to derive, for each participant, a breathlessness threshold corresponding to a sensation of strong breathlessness, matched to a score for breathlessness intensity of ≥ 5 on a 0–10 Borg scale (Borg, 1982). Additionally, a load inducing a very strong sensation of breathlessness (Borg score of 9 or 10) was also determined. A breathlessness thresholding procedure consisting of maximum 20 trials was developed and administered. Participants were seated comfortably and instructed to fixate on a screen and breathe normally through the breathing system. One pretest trial consisted of 24 s of loaded breathing, followed by the presentation

of the Borg scale and the requirement to rate the breathlessness intensity. We utilized a set of 10 loads with their intensity derived based on previous experiments in our lab. Note that, since these load values were based on subjective ratings of intensity or unpleasantness of breathlessness, the physical difference from one load to another was not constant.[1] The staircase always started with the same value of the load for all the participants (test value = .76 kPa/l/s).

If the current rating for the trial was ≤ 5 and the current strength of the load was smaller or equal to the test value, the staircase always increased the strength of the load with a step. The staircase instead kept the previous load for those cases when either the current rating was ≤ 5 and the load was stronger than the test value, or for those cases when the rating was larger than 5 but the given load was smaller or equal to the test value. If the ratings were higher than 5, the staircase always decreased the load strength by one step when the intensity of the load was stronger than the test value. See Figure 1 for a depiction of the staircase procedure. The first four trials of the pretest were not considered for the calculation of the final threshold. The staircase procedure stopped as soon as three trials with ratings higher than 6 were recorded. The threshold was recorded as the last value of the staircase. The resulting average resistance of the load for the current sample of participants was 1.18 kPa/l/s.

Emotional Picture Series

A set of 180 pictures was chosen from the International Affective Picture System (IAPS), based on normative mean arousal and valence ratings (Lang, Bradley, & Cuthbert, 2008).[2,3] The

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1. The following loads (in kPa/l/s) were utilized in the study, in ascending order, with the bold value as the starting test load for all of the participants: 0.15, 0.31, **0.76**, 1.14, 1.43, 1.65, 2.07, 2.72, 2.87, 2.99.

2. Averages ($M \pm SD$) of the normative ratings of arousal and valence utilized in the present study. Note that there was no significant difference with respect to either arousal, $F(2,38) = .217$, $p = .806$, $\eta_p^2 = .011$, or valence, $F(2,38) = 1.01$, $p = .374$, $\eta_p^2 = .050$, between the three sets of pictures. Valence increased from negative to neutral to positive pictures, $F(2,38) = 1314.11$, $p < .001$, $\eta_p^2 = .986$, whereas arousal was comparable between negative and positive pictures, $F(1,19) = .002$, $p = .969$, $\eta_p^2 = .000$.

	Arousal			Valence		
	Positive	Neutral	Negative	Positive	Neutral	Negative
Set 1	5.9 ± .7	3.4 ± .4	6.0 ± .6	7.1 ± .5	5.2 ± .6	2.2 ± .4
Set 2	6.1 ± .5	3.1 ± .4	6.2 ± .6	7.0 ± .6	5.1 ± .6	2.1 ± .3
Set 3	6.0 ± .6	3.1 ± .4	6.0 ± .6	6.9 ± .5	5.0 ± .6	2.2 ± .4

3. The following IAPS pictures were utilized in the present study: Set 1—Negative: 2683, 2900, 3030, 3120, 3170, 3191, 3230, 3350, 6212, 6213, 6510, 9300, 9419, 9428, 9500, 9560, 9600, 9800, 9900, 9922; neutral: 2191, 2214, 2272, 2280, 2302, 2385, 2396, 2480, 2495, 2512, 2880, 2890, 5390, 5410, 5875, 7100, 7130, 7290, 7493, 7550; positive: 2208, 2216, 2352, 4606, 4611, 4612, 4641, 4643, 4668, 4670, 4680, 4693, 7330, 8041, 8163, 8179, 8186, 8370, 8380, 8420. Set 2—Negative: 2800, 3060, 3101, 3181, 3220, 3266, 3530, 6350, 6360, 7380, 9250, 9252, 9253, 9321, 9571, 9810, 9901, 9910, 9921, 9925; neutral: 2102, 2200, 2221, 2381, 2383, 2393, 2397, 2499, 2514, 2516, 2840, 4000, 5510, 5726, 5731, 5870, 7002, 7004, 7700, 9070; positive: 2209, 2345, 4599, 4607, 4623, 4645, 4651, 4652, 4660, 4664, 4669, 4694, 5621, 7289, 8161, 8190, 8191, 8200, 8210, 8490. Set 3—Negative: 2095, 2688, 2730, 3100, 3180, 3261, 3500, 6260, 6560, 9040, 9050, 9340, 9400, 9410, 9420, 9435, 9520, 9530, 9570, 9903; neutral: 2037, 2038, 2190, 2210, 2215, 2271, 2440, 2441, 2493, 2570, 2595, 2749, 2850, 2870, 5471, 5740, 5800, 7025, 7234, 7590; positive: 4597, 4608, 4610, 4625, 4626, 4649, 4658, 4659, 4676, 4690, 4697, 5629, 7460, 7660, 8034, 8170, 8185, 8206, 8350, 8496.

	Load weaker than test value	Load stronger than test value
Rating </= 5	Previous load + 1	Previous load
Rating > 5	Previous load	Previous load - 1

Figure 1. Visual depiction of the staircase decision rule, as utilized in this study.

emotional pictures were grouped into positive (e.g., erotica, individuals laughing), neutral (e.g., objects, neutral sceneries), and negative (e.g., mutilations, threatening scenes) categories, each comprising 60 pictures. For each emotional category, three series of 20 pictures each were created, carefully matched with regard to their normative ratings of valence/arousal and their physical content, both within each block, as well as across blocks.

Subjective Ratings

Participants rated the experienced intensity and unpleasantness of breathlessness as well as fear after each experimental block. These subjective ratings were collected on a computer-based horizontal visual analogue scale ranging from 0 (*not noticeable/unpleasant/ fearful*) to 100 (*maximally imaginable intensity/unpleasantness/ fearful*), which is an established and commonly used measure of breathlessness in experimental studies (Dyspnea, 1999; Meek, Lareau, & Hu, 2003; von Leupoldt et al., 2008).

EEG Recording and Preprocessing

The EEG was recorded continuously from 60 Ag/AgCl scalp electrodes mounted on a custom elastic cap with 64 electrode positions (active electrodes; ActiCAP, Brain Products GmbH, Gilching, Germany). The signal was referenced online to the FCz electrode and rereferenced offline to an average of the entire electrodes set; the recording reference was reutilized for further analyses. The electrode impedances were kept below 20 kΩ. Vertical eye movements were measured with two additional electrodes placed below and above the left eye, using the same reference as for the other electrodes. Horizontal eye movements were calculated offline by subtracting the signal recorded at two additional electrodes positioned outside the cap near the outer canthi of the eyes (i.e., electrodes F9 and F10 in the 10-10 electrode system; Oostenveld& Praamstra, 2001).

The electrode signals were amplified using two BrainAmp amplifiers with 32 channels each (Brain Products GmbH) and digitally stored using the BrainVision Recorder software (Brain Products GmbH). The analogue EEG signal was sampled at 500 Hz and filtered online with a high cutoff at 1000 Hz. The signal was then filtered offline with a high cutoff at 30 Hz, 24 dB/Oct.

As a first step in the ERP analysis, the EEG data preprocessing was conducted with VisionAnalyzer 2 (Brain Products GmbH). The EEG signal was initially segmented into bins of 200 ms pre-, and 1,000 ms postvisual-stimulus delivery. The vertical electrooculogram segmented data were submitted to a blink artifact rejection (segments with an absolute voltage difference between maximum and minimum sample points higher than 60 μV were removed). For the remaining 60 scalp electrodes, segments with an absolute voltage difference between maximum and minimum sample points higher than 100 μV, as well as segments with low activity (<.5

μV) for a period of more than 100 ms were removed, to reject other movement and amplifier artifacts. The remaining artifact-free data were then averaged by condition and baseline corrected (200 ms prestimulus baseline). The averages for each block for each participant were exported to MATLAB (MATLAB 2009b, MathWorks, Natick, MA) for the remaining analysis. Topographic maps were derived in EEGLAB (Delorme & Makeig, 2004).

After visual inspection of our data, and in accordance with previous ERP literature on emotional picture processing (Hajcak, MacNamara, & Olvet, 2010; Olofsson, Nordin, Sequeira, & Polich, 2009), we focused the analysis on three deflections commonly related to emotional picture processing. The first positive deflection we considered was the P1 analyzed at the posterior occipital electrode POz in the early latency range of 120–140 ms poststimulus onset. P1 is associated with early sensory stimulus processing and selective attention (see Olofsson et al., 2009, for a review). The next ERP deflection taken into account was the P2 analyzed at Pz in the middle latency range of 230–290 ms poststimulus onset, an ERP commonly related to modality-specific selective attention (e.g., Crowley & Colrain, 2004). Finally, the slow positive deflection (the LPP), usually found 300 ms poststimulus onset over centroparietal sites, was analyzed in an early time window between 300–500 ms latency range (at CPz and Pz), as well as in a later time window between 600–1,000 ms, at central posterior sites (Cz, CPz, Pz). The LPP has been described as an index of sustained emotional processing and motivated attention (Cuthbert, Schupp, Bradley, Birbaumer, & Lang, 2000). All investigated ERPs in the current study were calculated as averaged activity over the particular time window of interest, at the specified groups of electrodes.

Procedure

After standardized instructions and spirometric lung function measurements, the participants underwent the pretest for the selection of the individual resistive loads. Thereafter, the EEG cap and nose clip were attached. The participants were seated in a comfortable chair at 110-cm viewing distance from the monitor (Samsung SyncMaster P2370, refresh rate of 60 Hz). The experiment was conducted on a Windows XP computer with a GeForce 6600 graphics card (PCIe/S8E 2 2.1.2), using MATLAB and Psychophysics toolbox v3 (Brainard, 1997; Pelli, 1997).

Participants performed nine blocks of 40 trials each while breathing through the custom breathing circuit, with each picture thus being presented twice within a block. Each trial, the participants viewed one single emotional picture for 4 s, with a jittered intertrial interval of 2–2.5 s. For each participant, the order of the picture presentation within each block was randomized. The manipulated independent variables were condition (perceived RLIB, anticipated RLIB, baseline) and emotion (positive, neutral, negative); see Juravle et al., 2014, for a similar methodology. So as to reinforce the current experimental condition, each of the pictures presented within the block was enclosed in a colored rectangle (i.e., blue for perceived RLIB, red for anticipated RLIB, and green for the baseline condition, see Bublatzky, Guerra, Pastor, Schupp, & Vila, 2013; Bublatzky & Schupp, 2012, for a comparable paradigm).

Participants were instructed to watch the pictures within each block, while keeping the amount of eye movements to a minimum. For the RLIB condition, the participants viewed the emotional pictures while breathing through resistive loads. The baseline condition was kept unloaded. In the anticipated RLIB condition, the participants also breathed through the unloaded system. However,

they were told to expect up to three occurrences of a very severe load, which they rated in the pretest phase as inducing a breathlessness intensity of 9 or higher on the Borg scale. For each block, we only delivered one severe load (8-s duration); this load was delivered at the beginning of a randomly chosen trial from the last third of the trials in the anticipated RLIB block. These severely loaded trials from the anticipated RLIB condition were excluded from final data analysis, such that the baseline and the anticipated RLIB had the same physical characteristics with respect to the respiratory processes, but only the expectations with regard to the experimental manipulation differed. The order of the experimental blocks was counterbalanced across participants. The total duration of the experiment was approximately 1 h.

Statistical Data Analysis

For each of the dependent measures (perceptual and threat ratings, ERPs), separate repeated measures analyses of variance (ANOVAs) were carried out with the factors condition (perceived RLIB vs. anticipated RLIB vs. baseline) and emotion (positive vs. neutral vs. negative), and the between factor of group (low vs. high anxious). We performed a median split on our sample based on the ASI-3 questionnaire summary scores. Two of our participants' scores coincided with the sample median (ASI-3 summary score equal to 19); these two participants were removed from all analyses. The final sample thus consisted of 34 participants with 17 participants in each of the low and high anxious participant groups. Each experimental group was composed of 8 female participants and 9 male participants.

Mauchly's test of sphericity was used to ensure that the data did not violate the sphericity assumption. If the assumption was violated, then the Greenhouse-Geisser correction was applied to correct the degrees of freedom; corrected *p* values are reported throughout (Picton et al., 2000). Significant main effects found in the data were followed up with one-tailed paired-samples *t* tests. Partial η^2 is reported as an effect size estimate for the ANOVA results.

Results

Subjective Ratings

All mean ratings split by the experimental factors of condition, emotion, and group are presented in Table 2. Subjective ratings main effects are depicted in Figure 2. Note that for one of the participants in the high anxious group the ratings data were overwritten at the time of data collection, therefore, the sample sizes for the reported ratings analyses are $N = 17$ for the low anxious group, and $N = 16$ for the high anxious group.

Intensity ratings. A significant effect of condition was observed for the breathlessness intensity ratings, $F(2,62) = 95.67$, $p < .001$, $\eta_p^2 = .755$, indicating that breathlessness intensity was rated as significantly lower during the baseline unloaded condition, as compared to both the perceived RLIB, $F(1,31) = 205.17$, $p < .001$, $\eta_p^2 = .869$, and the anticipated RLIB, $F(1,31) = 118.77$, $p < .001$, $\eta_p^2 = .793$, with the anticipated RLIB rated as significantly less intense relative to the perceived RLIB, $F(1,31) = 6.16$, $p = .019$, $\eta_p^2 = .166$. Furthermore, a main effect of emotion was also evident in the intensity ratings, $F(2,62) = 3.46$, $p = .038$, $\eta_p^2 = .100$, with breathlessness being rated significantly more intense when participants viewed negative pictures as compared to neutral pictures, $F(1,31) = 5.53$, $p = .025$, $\eta_p^2 = .151$. All other main effects and

Table 2. *Mean Values Together with Standard Errors for Subjective and Fear Ratings and ERPs*

| | Low anxious | | | | | | | | | High anxious | | | | | | | | |
| | Perceived RLIB | | | Anticipated RLIB | | | Baseline | | | Perceived RLIB | | | Anticipated RLIB | | | Baseline | | |
	Positive	Neutral	Negative	Positive	Neutral	Negative	Positive	Neutral	Negative	Positive	Neutral	Negative	Positive	Neutral	Negative	Positive	Neutral	Negative
Intensity	44.9±5	54.9±5	52.4±5	45.7±6	46.8±5	52.7±6	9.4±4	4.9±2	14.1±5	55.4±5	54.8±5	61.7±5	42.4±6	38.9±5	43.8±6	15.6±2	9.6±2	14.8±5
Unpleasantness	34.7±5	45.1±6	49.6±4	33.0±6	37.9±5	49.8±6	12.1±4	9.2±3	20.3±6	36.7±6	37.6±6	55.3±4	31.1±5	35.1±5	48.7±6	11.1±4	10.5±3	28.8±6
Fear	8.4±3	11.7±5	15.9±5	13.0±3	11.8±5	21.0±5	4.2±3	2.7±1	9.8±4	16.1±3	20.9±5	30.8±5	11.2±3	29.1±5	28.3±6	6.3±3	4.9±2	14.8±4
P1 (µV)	2±.6	2.2±.7	3.0±.7	2.7±.7	2.7±.7	1.8±.6	3.1±.6	2.6±.6	2.1±.7	5.3±.6	4.1±.7	5.1±.6	4.8±.7	4.1±.7	4.8±.6	5.3±.6	4.6±.6	5.4±.7
P2 (µV)	1.6±.8	1.5±.8	2.0±.9	2.1±.9	1.6±.8	1.5±.9	2.2±.8	2.1±.8	2.2±.9	3.8±.8	2.8±.8	3.3±.9	3.1±.9	2.9±.8	3.5±.8	3.6±.9	3.0±.8	3.9±.9
Early LPP (µV)	0.2±.7	−1.2±.7	0.6±.7	1.2±.7	−1.4±.6	−0.2±.7	1.4±.7	−0.9±.6	0.2±.7	1.9±.7	−0.6±.7	0.8±.7	1.4±.7	−0.7±.6	1.3±.7	1.8±.7	−0.3±.6	1.6±.7
Late LPP (µV)	0.3±.4	−0.9±.4	0.7±.4	0.5±.4	−0.6±.3	−0.1±.4	1.0±.4	−0.6±.4	0.5±.5	0.7±.4	−1.2±.4	−0.5±.4	0.3±.4	−1.7±.3	0.4±.4	0.4±.5	−1.1±.4	0.3±.5

interactions did not reach significance on the intensity ratings data (all $ps > .113$).

Unpleasantness ratings. The unpleasantness ratings revealed a main effect of condition, $F(2,62) = 47.99$, $p < .001$, $\eta_p^2 = .608$, with participants rating the perceived RLIB, $F(1,31) = 84.01$, $p < .001$, $\eta_p^2 = .730$, and the anticipated RLIB, $F(1,31) = 64.17$, $p < .001$, $\eta_p^2 = .674$, as significantly more unpleasant as compared to baseline; no difference was found between the two RLIB conditions, $F(1,31) = 1.48$, $p = .234$, $\eta_p^2 = .045$. Further, a main effect of emotion was found, $F(2,62) = 14.30$, $p < .001$, $\varepsilon = .644$, $\eta_p^2 = .316$, indicating that breathlessness was perceived significantly more unpleasant when participants were viewing negative pictures, as compared to both positive, $F(1,31) = 20.10$, $p < .001$, $\eta_p^2 = .393$, and neutral pictures, $F(1,31) = 11.46$, $p = .002$, $\eta_p^2 = .270$, with no significant difference in reported unpleasantness ratings between viewing neutral and positive pictures, $F(1,31) = 2.95$, $p = .096$, $\eta_p^2 = .087$. No other main effects or interactions were significant for the unpleasantness rating data (all $ps > .490$).

Fear ratings. The fear rating data revealed a main effect of condition, $F(2,62) = 20.69$, $p < .001$, $\eta_p^2 = .400$, with participants indicating significantly elevated fear under conditions of both perceived RLIB, $F(1,31) = 21.83$, $p < .001$, $\eta_p^2 = .413$, and anticipated RLIB, $F(1,31) = 34.34$, $p < .001$, $\eta_p^2 = .526$, relative to baseline, with no difference in fear ratings between the two breathlessness conditions, $F(1,31) = 1.02$, $p = .321$, $\eta_p^2 = .032$. Furthermore, a main effect of emotion was also found, $F(2,62) = 19.04$, $p < .001$, $\varepsilon = .788$, $\eta_p^2 = .381$, indicating a significantly lowered fear for positive picture viewing as compared to both neutral, $F(1,31) = 9.69$, $p = .004$, $\eta_p^2 = .238$, and negative pictures, $F(1,31) = 27.92$, $p < .001$, $\eta_p^2 = .474$. The fear ratings were also significantly higher for negative relative to the neutral picture viewing, $F(1,31) = 12.94$, $p = .001$, $\eta_p^2 = .295$. A significant interaction of Condition × Emotion × Group was also found, $F(4,124) = 2.73$, $p = .031$, $\eta_p^2 = .082$. Separate ANOVAs were conducted for each of the low and high anxious group with the factors condition and emotion. The interaction between the two factors was not significant in the case of the low anxious group, $F(4,60) = .59$, $p = .673$, $\eta_p^2 = .035$. However, it reached significance for the high anxious group, $F(4,60) = 3.46$, $p = .013$, $\eta_p^2 = .187$. Post hoc tests indicated that fear ratings were significantly elevated for positive picture viewing during perceived RLIB as compared to baseline, $t(15) = 3.38$, $p = .005$, $r = .39$, for neutral picture viewing during both perceived RLIB, $t(15) = 5.21$, $p = .004$, $r = .50$, and anticipated RLIB, $t(15) = 6.23$, $p < .001$, $r = .04$, relative to baseline, as well as for negative pictures viewing during perceived RLIB as compared to baseline, $t(15) = 5.19$, $p = .004$, $r = .48$.

ERPs

Averages of the ERP data split according to the manipulated experimental variables are presented in Table 2. We report the ERP results split into affective processing results (i.e., any emotion main effects encountered for all analyzed ERP deflections), perceived RLIB and anticipated RLIB results (i.e., any condition main effects encountered for all analyzed ERP deflections), and group effects (i.e., any group main effect as well as interaction effects encountered for all analyzed ERP deflections).
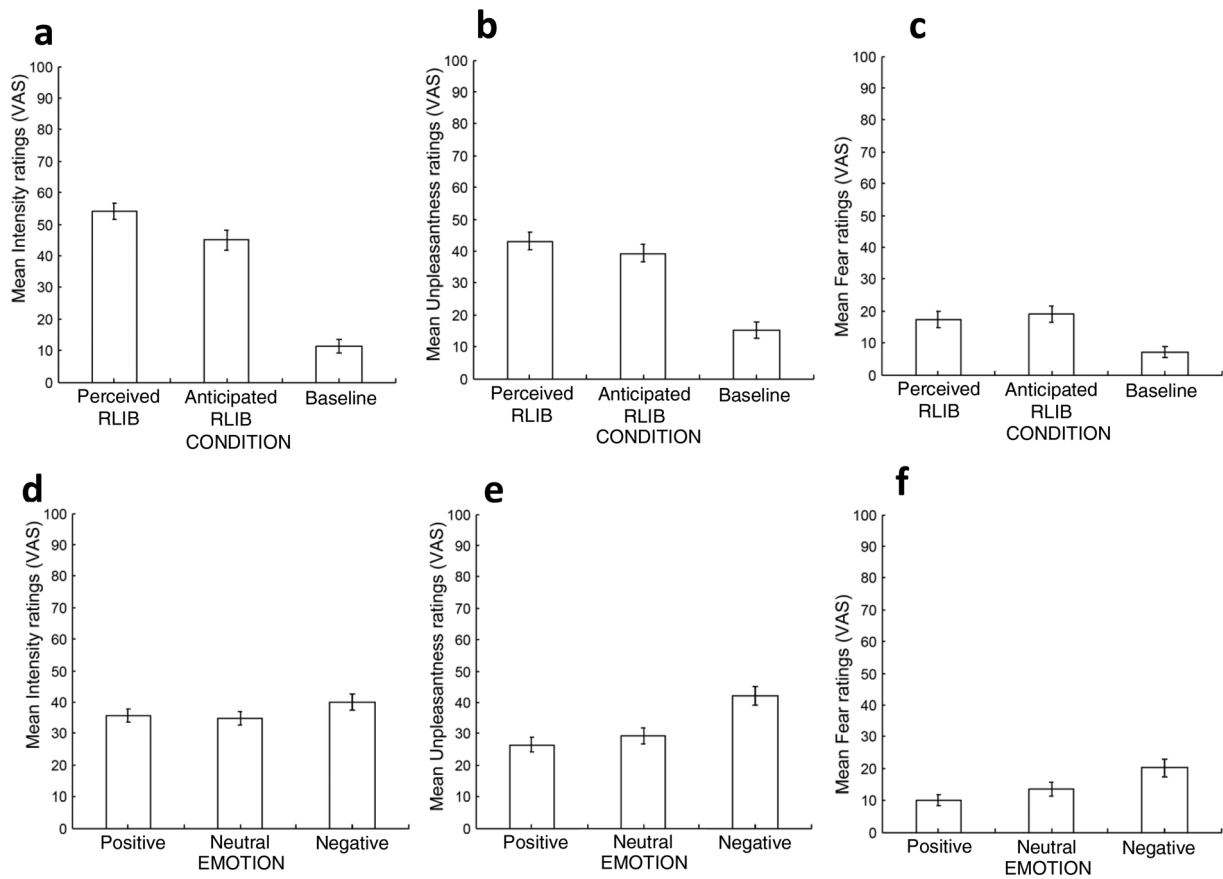
Figure 2. Main effects of condition (upper row) and emotion (lower row) on mean intensity ratings (a, d), mean unpleasantness ratings (b, e), and mean fear ratings (c, f). Error bars represent the standard error of the mean. Participants were subjected to a perceived resistive-load-induced breathlessness (RLIB) condition, an unloaded baseline, and to another anticipated RLIB condition.

Affective processing. The emotion main effects found in the ERP data are presented in Figure 3a. No main effects of emotion were evident for the P1. Significant main effects of emotion were observed for the P2, $F(2,64) = 3.31$, $p = .043$, $\eta_p^2 = .094$, the early LPP, $F(2,64) = 62.93$, $p < .001$, $\eta_p^2 = .663$, and the late LPP, $F(2,64) = 43.80$, $p < .001$, $\eta_p^2 = .578$. Planned comparisons indicated that the P2 was significantly elevated for negative picture viewing, relative to the neutral ones, $F(1,32) = 5.62$, $p = .024$, $\eta_p^2 = .149$. The early LPP was also, as expected, significantly less positive in response to neutral picture viewing, as compared to both the positive pictures, $F(1,32) = 92.08$, $p < .001$, $\eta_p^2 = .742$, and the negative pictures, $F(1,32) = 87.24$, $p < .001$, $\eta_p^2 = .732$, with the positive pictures also eliciting a significantly more positive early LPP as compared to the negative ones, $F(1,32) = 8.34$, $p = .007$, $\eta_p^2 = .205$. A similar effect was also found for the late LPP time window, with a significantly less positive late LPP elicited for the neutral pictures viewing, as compared to both the positive, $F(1,32) = 73.19$, $p < .001$, $\eta_p^2 = .696$, and the negative late LPPs, $F(1,32) = 47.85$, $p < .001$, $\eta_p^2 = .599$; no significant difference was observed between the late LPPs for the positive and negative picture viewing, $F(1,32) = 3.60$, $p = .067$, $\eta_p^2 = .101$.

Perceived RLIB and anticipated RLIB manipulations. Results indicated no main effects of condition on the P1 and the late LPP, but on the P2, $F(2,64) = 3.56$, $p = .044$, $\varepsilon = .868$, $\eta_p^2 = .100$, and the early LPP, $F(2,64) = 3.98$, $p = .023$, $\eta_p^2 = .111$. Planned comparisons indicated that the P2 was significantly less

positive during the perceived RLIB as compared to the baseline condition, $F(1,32) = 7.85$, $p = .009$, $\eta_p^2 = .197$. Similarly, the early LPPs derived for the perceived RLIB, $F(1,32) = 7.16$, $p = .012$, $\eta_p^2 = .183$, and the anticipated RLIB, $F(1,32) = 5.68$, $p = .023$, $\eta_p^2 = .151$, were significantly less positive as compared to baseline, with no significant difference found between the RLIB conditions, $F(1,32) = .074$, $p = .787$, $\eta_p^2 = .002$. See Figure 3b for a depiction of the condition main effects encountered in the ERP data.

Group effects. *P1.* Group effects were evident for the P1 deflection, with high anxious participants eliciting a significantly more positive P1, as compared to the low anxious participants, $F(1,32) = 9.11$, $p = .005$, $\eta_p^2 = .222$. See Figure 4 for a depiction of the group effect on the P1 deflection. For the P1, we also found an interaction of Group $\times$ Emotion on the ERP data, $F(2,64) = 3.22$, $p = .046$, $\eta_p^2 = .092$, with the high anxious participants eliciting a significantly more positive P1 in response to viewing both positive pictures, $t(32) = 3.20$, $p = .001$, $r = .49$, as well as negative pictures, $t(32) = 3.41$, $p = .001$, $r = .52$, relative to viewing neutral pictures. No group effects or interactions were found for the P2 deflection.

Three-way interactions between the manipulated variables of condition and emotion and the between-variable group were found for both the early LPP, $F(4,128) = 3.64$, $p = .008$, $\eta_p^2 = .102$, as well as the late LPP deflections, $F(4,128) = 4.21$, $p = .003$, $\eta_p^2 = .116$. Since the overall main effects of condition and emotion were reported in the sections above, here we concentrate on the
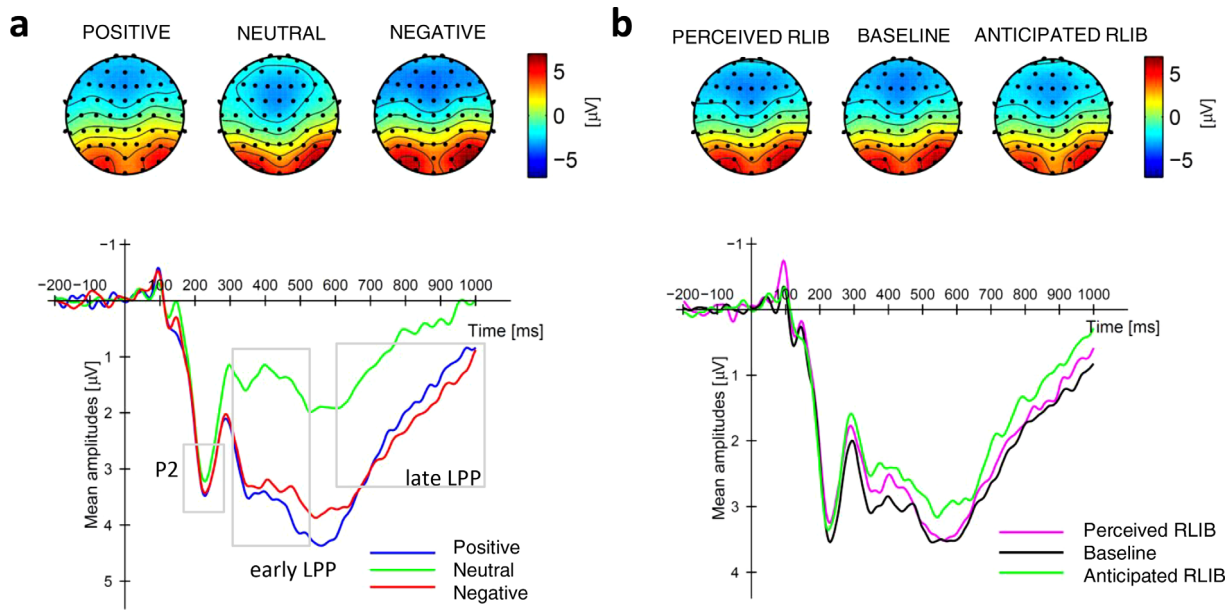
Figure 3. Main effects of condition (a) and emotion (b) plotted at the central electrode Pz. Topographies are calculated for the P2 time window of 230–290 ms. Participants were subjected to a perceived resistive-load-induced breathlessness (RLIB) condition, an unloaded baseline, and to another anticipated RLIB condition.

resulting interesting two-way interactions of Condition × Emotion found for the low/high anxious groups, as well as any significant interaction existing between our between-participants variable group and either condition or emotion. The LPP interaction is depicted in Figure 5.

Early LPP. For the early LPP, a significant interaction between condition and emotion was found for the low anxious group, $F(4,64) = 3.44$, $p = .013$, $\eta_p^2 = .177$. Post hoc tests indicated that the early LPP was significantly less positive when the low anxious participants viewed positive pictures during perceived RLIB as compared to both the anticipated RLIB, $t(16) = 2.29$, $p = .018$, $r = .88$, and the unloaded baseline conditions, $t(16) = 3.16$, $p = .003$, $r = .89$. Conversely, a significantly more positive early LPP was evident during negative pictures viewing under perceived RLIB, as compared to anticipated RLIB, $t(16) = 2.58$, $p = .010$, $r = .91$. The high anxious participants in turn elicited a less positive

early LPP during perceived RLIB negative picture viewing as compared to the unloaded baseline, $t(16) = 2.55$, $p = .010$, $r = .90$.

Late LPP. For the late LPP, on the anticipated RLIB data we found the direct group effect; that is, the late LPPs were significantly more positive in the high anxious group during neutral picture viewing, as compared to the low anxious group, $t(32) = 2.28$, $p = .014$, $r = .37$. Furthermore, we found a significant interaction of Condition × Emotion for the high anxious group, $F(4,64) = 3.00$, $p = .025$, $\eta_p^2 = .158$. Post hoc tests indicated that the late LPP was significantly less positive when participants viewed negative pictures during perceived RLIB as compared to both anticipated RLIB, $t(16) = 2.62$, $p = .009$, $r = .69$, and the unloaded baseline conditions, $t(16) = 2.60$, $p = .009$, $r = .79$. A significant interaction between condition and group was further found on the late LPPs during negative picture viewing only, $F(4,64) = 5.18$, $p = .008$, $\eta_p^2 = .139$. The low anxious participants elicited a significantly more positive late LPP during the perceived RLIB negative picture viewing, as compared to the anticipated RLIB, $t(16) = 2.23$, $p = .020$, $r = .70$.

## Discussion

The present study investigated the effect of anticipated and perceived breathlessness on the processing of emotional stimuli and the role of anxiety sensitivity. For this, we concentrated on ERPs elicited in response to positive, neutral, and negative affective pictures under conditions of anticipated and perceived breathlessness, as compared to an unloaded baseline.

In regard to the subjective ratings, our results highlight the expected effects, with participants rating breathlessness in both RLIB conditions as being significantly more intense and unpleasant, relative to the baseline conditions. Similarly, participants reported elevated fear during both anticipated and perceived breathlessness, as compared to baseline. These findings are in line with other studies that utilized RLIB (e.g., Alius et al., 2013; Pappens, Vandenbossche, Van den Bergh, & Van Diest, 2015;
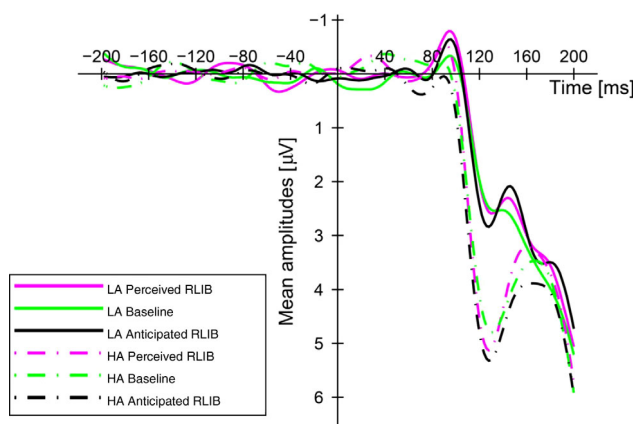
Figure 4. Group effect on P1 (120-140 ms) plotted at POz for low anxious (LA) versus high anxious (HA) participants. Participants were subjected to a perceived resistive-load-induced breathlessness (RLIB), an unloaded baseline condition, and to another anticipated RLIB condition.
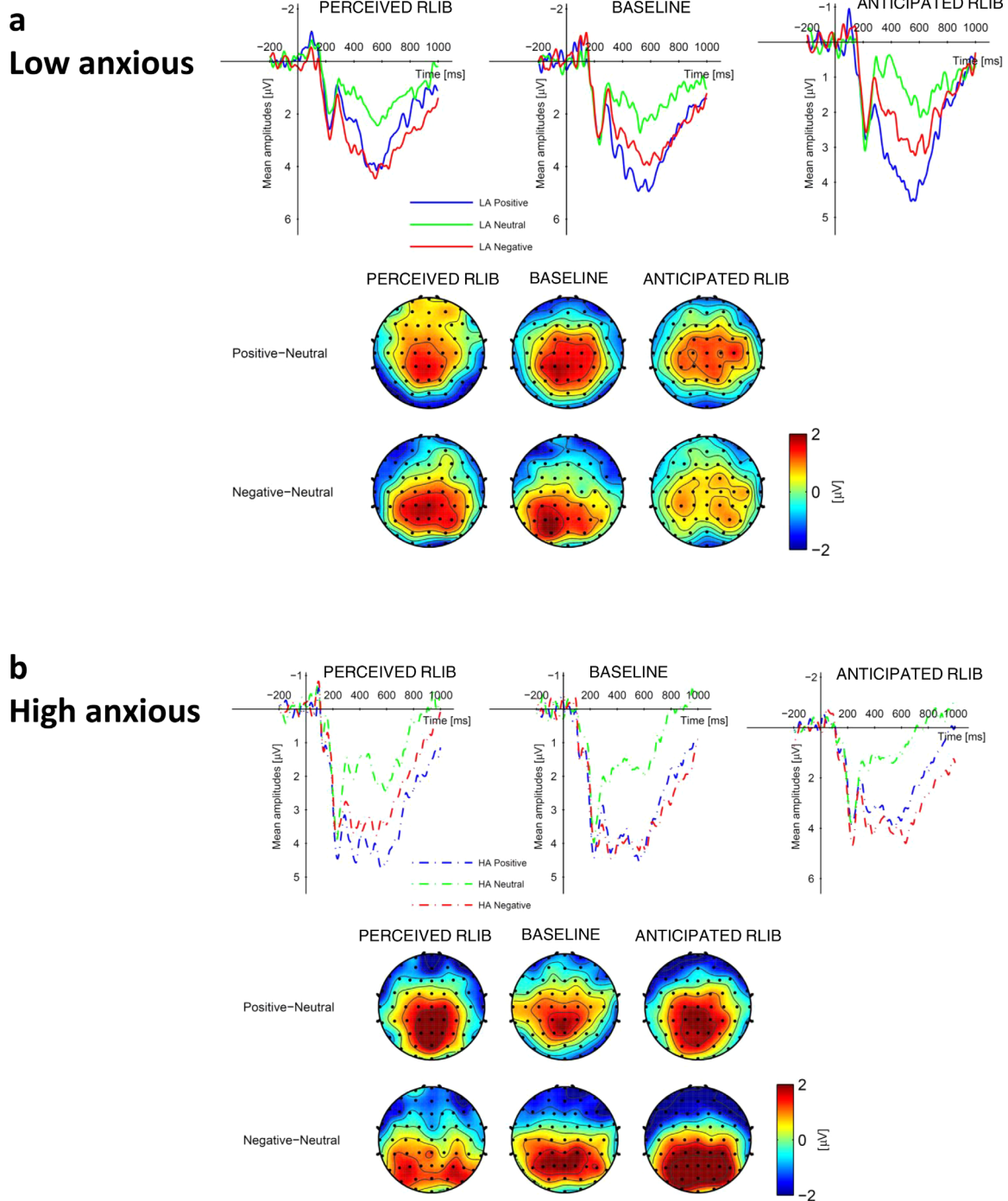
Figure 5. The late LPP interaction effect plotted at Pz for both the low anxious (LA) versus high anxious (HA) participants. Topographies are calculated for the late LPP time window of 600–1,000 ms. Participants were subjected to a perceived resistive-load-induced breathlessness (RLIB) condition, an unloaded baseline, and to another anticipated RLIB condition.

Stoeckel, Esser, Gamer, Büchel, & von Leupoldt, 2015) and suggest that our experimental manipulations of breathlessness were successful.

Across conditions, the intensity and especially the unpleasantness of breathlessness were rated as significantly elevated during negative relative to positive and neutral picture viewing, which corresponds with previous findings (von Leupoldt et al., 2008). Likewise, experienced fear significantly increased from positive to neutral to negative picture viewing. Notably, the high anxious participants exhibited elevated fear during neutral picture viewing under conditions of both perceived and anticipated breathlessness, as compared to the baseline condition. This enhanced fear aligns with previous reports in anxiety-sensitive individuals (Alius et al., 2013; Melzig et al., 2008; Paulus, 2013). Even more, our results indicate that, when exposed to a respiratory threat context, high anxious individuals demonstrate heightened fear as a sort of "baseline behavior," which is not encountered in low anxious individuals.

Affective processing highlighted the expected results: That is, positive and negative picture viewing resulted in significantly more positive ERPs (e.g., P2, early and late LPPs) as compared to the ERPs elicited to the neutral pictures. As such, our results underline the increased selective and sustained attentional processing of motivationally salient stimuli as demonstrated in previous studies (Codispoti, Ferrari, & Bradley, 2006; Hajcak, MacNamara, Foti, Ferri, & Keil, 2013; Schupp, Junghöfer, Weike, & Hamm, 2003; Schupp, Schmälzle, Flaisch, Weike, & Hamm, 2013).

With respect to the respiratory threat manipulations, replicating our previous results of altered ERPs under conditions of perceived breathlessness (Juravle et al., 2014), we find that perceived breathlessness leads to less positive P2 and early LPP, as compared to the unloaded baseline condition. Results such as these suggest that breathlessness reduces the neural processing capacity for affective picture viewing, as it was previously demonstrated for painful stimulation (Wieser et al., 2012). Our previous study also indicated a trend toward a reduced LPP during breathlessness specifically in relation to positive picture viewing. We now replicate this result in the low anxious group of participants, as well as report an additional LPP increase for negative picture viewing during RLIB. We argue in favor of this LPP response pattern related to breathlessness to likely reflect motivational priming. Motivational priming theory suggests that threatening stimuli activate the defensive system and activate negative affective processing, whereas appetitive stimuli that promote survival will activate the appetitive system and facilitate positive affective processing in turn (Bradley, Codispoti, Cuthbert, & Lang, 2001; Lang, 1995).

Importantly, the sustained early LPP is also significantly less positive during the anticipated RLIB. Such a result suggests that the mere anticipation of respiratory threat reduces sustained attention for parallel affective stimuli and captures neural processing capacities in a comparable manner to the real perception of breathlessness. These results are in line with previous studies demonstrating that anticipating breathlessness results in pronounced physiological fear-related responses (Holtz et al., 2012; Melzig et al., 2008; Stoeckel, Esser, Gamer, Kalisch et al., 2015). These findings thus support recent accounts that the anticipation of breathlessness might play a crucial role in respiratory and anxiety disorders (Hayen et al., 2013; Paulus, 2013).

We have previously demonstrated a significantly blunted P1 elicited under conditions of breathlessness, as opposed to an unloaded baseline (Juravle et al., 2014). Here, we bring further evidence that this effect is modulated by anxiety sensitivity levels in a particularly early time window. High anxious participants exhibit a significantly more positive P1 as compared to low anxious participants. Even more, behavioral ratings of fear are significantly elevated for the high anxious participants, as compared to the low anxious ones. These early ERP modulations as a function of anxiety sensitivity affecting the ERP are taken to reflect an early attention enhancement to affective pictures (e.g., hypervigilance), evident in a context of both perceived and anticipated respiratory threat for the high anxious individuals. This finding converges with previous studies demonstrating that anxiety sensitivity has a marked impact on the processing of emotional stimuli (Sussman, Szekely, Hajcak, & Mohanty, 2016) and is prominently related to respiratory threat signals such as breathlessness (Alius et al., 2013; Melzig et al., 2008).

Additionally, our results indicate a further dissociation between the two groups of participants, particularly with respect to negative picture viewing: In line with the motivational priming theory (Bradley et al., 2001; Lang, 1995), low anxious participants elicit significantly more positive early and late LPPs during perceived breathlessness as compared to baseline, whereas the same effect is reversed for the high anxious participants, who in turn show significantly blunted LPPs for the perceived breathlessness condition relative to both baseline and anticipated breathlessness conditions. Therefore, it seems that for high anxious individuals negative emotional material is distinctly processed in the later time window of the sustained LPP, presumably because they focus more on the bodily threatening stimulation, with the direct result of a reduced neural capacity for the picture processing. This interpretation is in line with previous observations in high-anxiety sensitive individuals who showed stronger and prolonged activation of fear-related brain areas in response to respiratory threat cues (Holtz et al., 2012).

Taken together, the present results demonstrate that both the perception as well as the anticipation of breathlessness result in significantly diminished neural processing of affective picture stimuli. Furthermore, our results highlight that anxiety sensitivity impacts on the neural affective processing during breathlessness both in an early, as well as later time window. That is, whereas in low anxiety perceived breathlessness affects picture processing according to the motivational priming hypothesis, high anxious participants exhibit a significantly hypervigilant state at the beginning of the picture presentations, which turns to reduced attention capture for negative affective picture stimuli in the later time windows during the perception of breathlessness. Future studies in individuals with clinical levels of breathlessness and/or anxiety are required in order to examine the clinical relevance of these findings. These studies would benefit from including further physiological measures such as measures of the startle reflex, which could provide additional insights into fearful responses during affective picture processing under anticipated and perceived breathlessness.

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