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<i>Author contact at KU Leuven</i>	andreas.vonleupoldt@ppw.kuleuven.be

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EMOTION PROCESSING DURING BREATHLESSNESS

RUNNING HEAD: EMOTION PROCESSING DURING BREATHLESSNESS

**Investigating the effect of respiratory bodily threat
on the processing of emotional pictures**

Georgiana Juravle¹, Maria Cornelia Stoeckel¹, Michael Rose¹, Matthias Gamer¹,
Christian Büchel¹, Matthias Johannes Wieser², & Andreas von Leupoldt^{1,3}

¹Department of Systems Neuroscience
University Medical Center Hamburg-Eppendorf
Hamburg, Germany

²Department of Psychology
University of Würzburg
Würzburg, Germany

³Research Group Health Psychology
University of Leuven
Leuven, Belgium

ADDRESS FOR CORRESPONDENCE:

Georgiana Juravle,
Department of Systems Neuroscience,
University Medical Center Hamburg-Eppendorf,
W34, Martinistr. 52, 20251 Hamburg,
Germany

E-mail: g.juravle@uke.de

TEL: +49-40-7410-54260; FAX: +49-40-7410-59955.

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Abstract

It has been demonstrated that emotions can substantially impact the perception and neural processing of breathlessness, but little is known about the reverse interaction. Here, we examined the impact of breathlessness on emotional picture processing. The continuous EEG was recorded while volunteers viewed positive/neutral/negative emotional pictures under conditions of resistive-load-induced breathlessness, auditory noise, and an unloaded baseline. Breathlessness attenuated *PI* and early posterior negativity (*EPN*) ERP amplitudes, irrespective of picture valence. Moreover, as expected, larger amplitudes for positive and negative pictures relative to neutral pictures were found for *EPN* and the late positive potential (*LPP*) ERPs, which were not affected by breathlessness. The results suggest that breathlessness impacts on the early attention-related neural processing of picture stimuli without influencing the later cognitive processing of emotional contents.

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Introduction

The perception of threatening bodily sensations plays an important role in somatic diseases, as well as in psychological disorders (Barlow, 2002; Domschke et al., 2010). Breathlessness is a key example for these bodily threat sensations: It is an aversive cardinal symptom in respiratory disorders such as asthma and chronic obstructive pulmonary disease (COPD), but also a feared sensation in anxiety or psychosomatic disorders (APA, 2000; ATS, 1999).

Studies on healthy volunteers and on patients with asthma or COPD have demonstrated that emotions can substantially influence the perception of breathlessness. Positive emotion attenuates the level of perceived breathlessness, whereas negative emotion usually increases the perceived level of breathlessness, irrespective of baseline respiratory status or ventilatory changes during experiments (Janssens et al., 2009; Livermore et al., 2008). For instance, at a behavioural level, when asked to passively watch emotional picture series, healthy participants rated the unpleasantness of resistive-load-induced breathlessness as being lowest during positive picture viewing and highest during negative picture viewing (von Leupoldt et al., 2008). More recent studies using functional magnetic resonance imaging (fMRI) and respiratory-related evoked potentials (RREP) in the EEG demonstrated that emotions also impact on the neural processing of respiratory sensations (von Leupoldt et al., 2013). For example, later RREP components (e.g., *P3*) have been shown to be reduced during arousing emotional contexts relative to a non-arousing neutral context (von Leupoldt et al., 2010). In addition, enhanced mean amplitudes of the RREP components *P2* and *P3* were observed during negative relative to neutral emotional contexts in high, as compared to low anxious individuals, suggesting that anxiety interferes with the higher-order neural processing of respiratory sensations (von Leupoldt et al., 2011).

Surprisingly, nothing is known about the reverse effect, i.e., the influence of breathlessness on the processing of emotions. Because of its threatening and thus, attention-demanding character, it seems reasonable to speculate that breathlessness is capable of interfering with the processing of emotional stimuli. This is supported by previous findings demonstrating high levels of negative emotionality (e.g., depression and anxiety) in patients suffering from breathlessness, including patients with asthma and COPD (Maurer et al., 2008; Ritz et al., 2012; von Leupoldt et al., 2012). Further support comes from recent research on pain, which is a similar aversive bodily threat sensation sharing important characteristics, as well as emotion-related brain processing areas with breathlessness (Banzett and Moosavi, 2001; von Leupoldt et al., 2009). In this regard, a recent study has utilized the ERP methodology to investigate the effect of painful pressure stimulation on the

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neural processing of different facial emotional expressions (e.g., happy, neutral, or fearful; Wieser et al., 2012). The results indicated that painful compared to non-painful pressure stimulation reduced the neural processing of concomitantly presented emotional faces, during both the early and later attention-related processing periods. Interestingly with regard to the aims of the current study, the authors found no emotion-specific ERP modulation as a result of the concomitant pain stimulation (Wieser et al., 2012).

Therefore, the present ERP study investigated the impact of respiratory bodily threat on the neural processing of emotions during resistive-load-induced breathlessness. For this, we recorded ERP responses under conditions of breathlessness and we compared them to the responses evoked during another sensory, but less bodily threatening auditory noise condition, as well as to the responses evoked during an unloaded-breathing control condition. Specifically, we examined the impact of these conditions on the ERPs evoked by positive, neutral, and negative emotional pictures, known to reflect early, rather automatic attentional processes (*PI* and the *EPN*) as well as later, more sustained and motivated attentional processes, such as the *LPP* (Hajcak et al., 2010; Olofsson et al., 2009). In accordance with previous findings from pain research (Bingel et al., 2007; Eccleston and Crombez, 1999; Wieser et al., 2012), we hypothesized a general amplitude reduction in these ERPs of interest during the breathlessness condition. In addition, we were interested to investigate whether these attenuated neural responses would be specifically pronounced for positive or negative emotional stimuli.

Method

Participants

Twenty participants (10 male) with a mean age of 27 years (age range: 21-39 years) were examined; see Table 1 for the demographic data. All participants reported normal hearing and respiratory status, as well as normal or corrected to normal vision. Normal baseline lung function was confirmed by spirometry according to the standards published by the European Respiratory Society (Miller et al., 2005). The transient (state) and dispositional (trait) level of anxiety in all participants was measured with the State-Trait Anxiety Inventory (STAI), a validated commonly used measure of anxiety symptoms (Spielberger et al., 1970). The level of depression was assessed with the Becks Depression Inventory (BDI-II, Beck et al., 1996). Participants received monetary remuneration for their participation. The study protocol was approved by the Hamburg Chamber of Physicians ethics committee and written informed consent was obtained from all participants.

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Resistive load breathing

Breathlessness was induced by inspiration through an inspiratory resistive load which superimposes increased work to the respiratory muscles (Harver and Mahler, 1998). Participants wore a nose clip and breathed via a mouthpiece attached to a breathing circuit consisting of 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 designed for the easy introduction and removal of the inspiratory resistive loads, while the expiratory port was left free. The magnitude of the load was estimated in a pre-test before the experiment consisting of the repeated presentation of various loads through the breathing circuit. As in our previous study, the selected load had to induce a sensation of “strong” breathlessness, corresponding to a Borg scale score for breathlessness intensity of ≥ 5 (von Leupoldt et al., 2008). The resulting average resistance of the load for the current sample of participants was 1.32 kPa/l/s. Throughout all experimental conditions, tidal volume, breathing frequency, inspiratory time, and inspiratory airflow were continuously monitored with a Biopac MP100 (Biopac Systems, Inc., Goleta, CA, USA).

Auditory noise

In order to compare breathlessness with another sensory, but less bodily threatening stimulus, auditory noise of matched intensity was chosen. Once the breathlessness stimulus intensity with a Borg-score value of 5 was achieved, the experimenter asked the participant to indicate the comparable intensity of auditory noise stimulation. For this, the experimenter turned the volume of the loudspeakers from a lower predefined noise level to a higher level until the participant would declare that the intensity of the auditory sensation was „strong“ and corresponded to a rating of „5“ on the same Borg scale previously used to rate the resistive load intensity. The resulting average auditory stimulus intensity for the current sample of participants was 87.7 dB.

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 et al., 2008). The emotional pictures were grouped into positive, neutral, and negative categories, each comprising 60 pictures. For each emotional category, 3 picture 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

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well as across blocks. That is, no significant statistical difference was found between the average normative scores of arousal and valence¹ for each of the three series within each category (all $F_s < 1$, $p = \text{n.s.}$).

Emotion and Perceptual ratings

Evaluative ratings of hedonic valence (unpleasant vs. pleasant) and arousal (calm vs. aroused) were collected after each of the experimental blocks by using a computer-based version of the 9-point scale Self-Assessment Manikin (SAM, Bradley and Lang, 1994). Moreover, participants also rated the experienced intensity, as well as the unpleasantness of the breathlessness and auditory noise stimulation after each experimental block. These perceptual ratings were collected on a computer-based horizontal visual analogue scale (100 mm), ranging from 0 (not noticeable/unpleasant) to 100 (maximally imaginable intensity/unpleasantness). A visual analogue scale was used instead of a Borg in order to prevent potential carry over effects from ratings given during the pre-tests to the ratings given during the actual experiment.

EEG-Measurement and Data Reduction

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 on-line to the FCz electrode and re-referenced offline to an average of the entire electrodes set; the recording reference was re-utilized for further analyses. The electrode impedances were kept below 20 k Ω . Vertical eye movements were measured with two additional electrodes placed beneath 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 and 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 on-line 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 pre-processing was conducted with VisionAnalyzer 2 (Brain Products GmbH). The EEG signal was initially segmented into bins of 200

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ms pre-, and 1000 ms post-stimulus delivery. The vertical electrooculogram segmented data were submitted to a blink artefact rejection (segments with an absolute voltage difference between maximum and minimum sample points higher than 60 μV were removed). Furthermore, a second artefact rejection was conducted on the remaining 60 scalp electrodes to inspect for movement and other amplifier artefacts (segments with an absolute voltage difference between maximum and minimum sample points higher than 100 μV , as well as segments with low activity for a period of more than 100 ms were removed). There was no significant difference between the investigated conditions with respect to the number of trials excluded from the data analysis as a result of the various enumerated artefacts ($F < 1$, $p = \text{n.s.}$). The remaining data (on average more than two thirds of the total number of trials per condition) were then averaged by condition and baseline corrected (200 ms pre-stimulus baseline). The averages for each block for each participant were exported to Matlab (Matlab 2009b, MathWorks, Natick, MA, USA) for the remaining analysis.

After visual inspection of our data, and in accordance with previous ERP literature on emotional picture processing (Hajcak et al., 2010; Olofsson et al., 2009), we focused our analysis on three deflections commonly related to emotional picture processing. The first analyzed positive deflection was the *PI* at posterior occipital electrodes (POz, Oz, and PO7/8) in the early latency range of 120 – 160 ms post-stimulus onset. *PI* is associated with early sensory stimulus processing and selective attention (Olofsson et al., 2009). The next considered ERP deflection was the *EPN* at temporo-occipital sites (POz, Oz, PO3/PO4, PO7/8, and O1/2) in the middle latency range of 200 – 280 ms post-stimulus onset. The *EPN* is a relative negativity occurring for arousing emotional compared to neutral stimuli, and has been linked to selective attention (Bublitzky et al., 2010; Schupp et al., 2003a). Finally, the later slow positive deflection (the *LPP*) usually found 300 ms post-stimulus onset over centro-parietal sites was analyzed in the 300 – 550 ms latency range (P3/4 and PO3/4). The *LPP* has been described as an index of sustained emotional processing and motivated attention (Cuthbert et al., 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, questionnaires and spirometric lung function measurements, participants underwent the pre-tests for selecting the individual resistive load and auditory noise of matched intensity. Thereafter, the EEG cap and nose clip were positioned and participants were

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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 Presentation software (Presentation 14.9, Neurobehavioral Systems Inc., Albany, NY, USA). Loudspeakers (Harman/Kardon HK206) were positioned to the left and right of the monitor at a distance of 110 cm from the participant.

Participants performed on 9 blocks of 40 trials each. Each trial the participants viewed one single emotional picture for 4 s; see Figure 1b for a depiction of the trial timeline. The inter-trial interval was set to 2 s. Each block consisted of 20 pictures presented twice, amounting to a total block duration of 240 s. For each participant, the order of the picture presentation within each block was randomized. The manipulated independent variables were Condition (breathlessness, baseline, and noise) and Emotion (positive, neutral, and negative); see Figure 1a for a depiction of the experimental design.

Participants were instructed to passively watch the pictures within each block, while keeping the amount of eye-movements to a minimum. For the breathlessness and noise conditions, the participants viewed the emotional pictures while breathing through resistive loads, or while listening to the auditory noise, respectively. During the unloaded baseline trials, participants breathed through the breathing circuit, but without any resistive loads being presented. The order of the experimental blocks was counterbalanced across participants.

Statistical data analysis

For each of the dependent measures (emotional and perceptual ratings, respiratory parameters, and ERPs), separate repeated measures analyses of variance (ANOVAs) were carried out with the factors Condition (breathlessness vs. baseline vs. noise) and Emotion (positive vs. neutral vs. negative). 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

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Perceptual and emotion ratings

All mean ratings split by the experimental factors of Condition and Emotion are presented in Table 2.

For the breathlessness intensity ratings, a significant Condition main effect was observed on the breathlessness data ($F(2, 38) = 82.07, p < .001, \varepsilon = .526, \eta^2_p = .812$). Post-hoc tests demonstrated that participants rated the intensity of breathlessness as being stronger in the breathlessness condition as compared to the auditory noise ($t(19) = 8.92, p < .001$), and the baseline conditions ($t(19) = 9.12, p < .001$). Similarly, a main effect of Condition was found on the auditory noise data ($F(2, 38) = 192.46, p < .001, \varepsilon = .500, \eta^2_p = .910$), with participants rating the intensity of the auditory noise as being stronger in the noise condition as compared to the baseline ($t(19) = 13.91, p < .001$), and the breathlessness conditions ($t(19) = 13.84, p < .001$). Importantly, no difference in intensity ratings between conditions of breathlessness and noise was observed, suggesting comparable sensory stimulation levels ($F < 1, p = \text{n.s.}$).

A main effect of Condition was also observed for the breathlessness unpleasantness ratings data ($F(2, 38) = 49.73, p < .001, \varepsilon = .517, \eta^2_p = .724$), with participants reporting higher breathlessness unpleasantness during the breathlessness condition as compared to both the auditory noise ($t(19) = 7.02, p < .001$), and the baseline conditions ($t(19) = 7.15, p < .001$). Similarly to the intensity ratings, a main effect of Condition was also present for the noise unpleasantness ratings data ($F(2, 38) = 47.30, p < .001, \varepsilon = .501, \eta^2_p = .713$), with participants reporting higher noise unpleasantness during the noise condition as compared to both the breathlessness ($t(19) = 6.81, p < .001$), and baseline conditions ($t(19) = 6.95, p < .001$).

For arousal ratings, an expected main effect of Emotion was observed ($F(2, 38) = 9.36, p = .003, \varepsilon = .642, \eta^2_p = .330$), with higher ratings for the negative as compared to both the neutral ($t(19) = 3.18, p = .003$), and the positive picture viewing ($t(19) = 3.27, p = .002$). An additional quadratic trend was found which demonstrated higher ratings for positive and negative pictures, as compared to neutral pictures ($F(1, 19) = 7.98, p = .011$). Moreover, a main effect of Condition was observed on the arousal data ($F(2, 38) = 3.72, p = .033, \eta^2_p = .164$), with lower arousal ratings during the baseline condition as compared to the breathlessness ($t(19) = 2.43, p = .012$) and noise conditions ($t(19) = 2.37, p = .014$), with the latter conditions not differing from each other ($t(19) = .88, p = \text{n.s.}$).

With respect to the hedonic valence ratings, a main effect of Emotion was observed ($F(2, 38) = 25.8, p < .001, \varepsilon = .655, \eta^2_p = .900$). As expected, valence ratings increased linearly from

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negative to neutral to positive pictures ($F(1, 19) = 28.87, p < .001$), with significant differences between all pairings: negative vs. neutral ($t(19) = 5.42, p < .001$), negative vs. positive ($t(19) = 5.37, p < .001$), and neutral vs. positive ($t(19) = 3.08, p < .001$). We did not observe a significant influence of Condition on the valence ratings ($F(2,38) = 1.15, p = \text{n.s.}$).

Respiratory parameters

Main effects of Condition were observed for breathing frequency ($F(2, 38) = 17.35, p < .001, \eta^2_p = .477$), mean airflow ($F(2, 38) = 20.13, p < .001, \varepsilon = .643, \eta^2_p = .514$), and inspiratory time data ($F(2, 38) = 29.5, p < .001, \varepsilon = .553, \eta^2_p = .608$); see Table 2 for averages of the respiratory parameters. As expected due to the experimental manipulation, participants showed lower breathing frequency during the breathlessness condition as compared to both baseline ($t(19) = 4.55, p < .001$), and noise conditions ($t(19) = 4.67, p < .001$). Similarly, the measured mean airflow was lower for the breathlessness condition as compared to the baseline ($t(19) = 3.95, p < .001$), and noise conditions ($t(19) = 5.83, p < .001$). Conversely, inspiratory time was significantly longer in the breathlessness condition as compared to the baseline ($t(19) = 5.47, p < .001$), and auditory noise conditions ($t(19) = 5.58, p < .001$). No differences in respiratory parameters were observed between the noise and baseline conditions (all $ps = \text{n.s.}$).

ERPs

Averages of the ERP data split according to the manipulated experimental variables are presented in Table 3.

As depicted in Figure 2B, a main effect of Condition was observed on the *PI* mean amplitudes ($F(2, 38) = 4.06, p = .025, \eta^2_p = .176$). Post hoc tests indicated that the *PI* mean amplitudes were significantly smaller during the breathlessness condition as compared to the baseline condition ($t(19) = 2.53, p = .010$). When comparing the *PI* mean amplitudes under conditions of breathlessness and noise only a non-significant trend for smaller *PI* mean amplitudes during breathlessness was found ($t(19) = 1.37, p = .093$). No main effect of Emotion, as well as no interaction between Emotion and Condition were identified for the *PI* deflection (all $F_s < 1, p = \text{n.s.}$).

For the *EPN*, a significant effect of Emotion was observed ($F(2, 38) = 3.85, p = .030, \eta^2_p = .168$; see Figure 3A). As expected, post hoc tests indicated larger relative negativity for the *EPN* mean amplitudes for the positive ($t(19) = 3.45, p = .001$) and negative pictures ($t(19) = 1.84, p =$

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.040) as compared to the neutral pictures; see Figure 4b. Importantly, the *EPN* data also indicated a main effect of Condition ($F(2, 38) = 4.94, p = .012, \eta^2_p = .207$; see Figure 4a for a depiction of this effect). Post hoc tests showed that the mean amplitudes in the *EPN* time window were significantly smaller during the breathlessness condition, as compared to both baseline ($t(19) = 2.32, p = .016$) and noise conditions ($t(19) = 3.04, p = .003$). The control conditions did not differ from each other ($t(19) = .50, p = \text{n.s.}$). Lastly, no interaction was observed between Emotion and Condition for the *EPN* ($F < 1, p = \text{n.s.}$).

With regard to the *LPP* mean amplitudes, a significant main effect of Emotion was observed ($F(2, 38) = 5.62, p = .007, \eta^2_p = .228$). Post hoc tests highlighted that the *LPP* was significantly more positive during the emotional negative picture presentation, as compared to both the positive ($t(19) = 2.58, p = .009$) and neutral picture viewing conditions ($t(19) = 3.45, p = .001$; see Figure 5A). An additional quadratic trend nevertheless demonstrated higher mean *LPP* amplitudes for positive and negative pictures, as compared to neutral pictures ($F(1, 19) = 4.90, p = .039$). In addition, we detected a trend towards a main effect of Condition on the *LPP* data, however, this failed to reach statistical significance ($F(2, 38) = 2.89, p = .092, \varepsilon = .655, \eta^2_p = .132$). An exploratory analysis suggested that this trend was caused by smaller *LPP* amplitudes during the breathlessness condition as compared to the baseline and noise conditions and that this effect was primarily driven by smaller mean *LPP* amplitudes for positive pictures during the breathlessness condition. No significant interaction effect between Emotion and Condition was identified for the *LPP* ($F(4, 76) = 1.67, p = .167, \eta^2_p = .081$).

Discussion

The present study investigated the impact of resistive-load-induced breathlessness on the neural processing of emotions. To this end, we compared ERPs elicited by positive, neutral, and negative emotional pictures during conditions of breathlessness, auditory noise, as well as an unloaded baseline condition.

At a behavioural level, the perceptual ratings demonstrated the expected results: That is, higher intensity ratings were given for both breathlessness and noise compared to the baseline condition. Similar intensity ratings across conditions of breathlessness and noise indicated comparable sensory stimulation levels. Furthermore, the emotion ratings highlighted an overall successful emotional manipulation with decreases in valence from positive to neutral and further to negative emotional pictures, as well as higher arousal for positive and negative, compared to neutral

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emotional pictures. These results replicate previous findings in that this pattern of modulation is associated with emotional engagement (Bradley and Lang, 2007; Cuthbert et al., 2000; Lang et al., 1993). However, no distinct effect of breathlessness on emotion ratings was observed, but only a higher arousal level during both breathlessness and noise conditions, as compared to the control baseline condition. This effect might be related to higher demands on the cognitive system when two stimuli have to be processed in parallel (Lavie, 2010).

At a neural level, enhanced mean amplitudes for the *EPN* and *LPP* were observed for arousing emotional compared to neutral pictures across all investigated conditions. This result is in line with previous findings and reflects greater early selective and later sustained motivated attention for salient emotional picture stimuli (Codispoti et al., 2006; Hajcak et al., 2013; Schupp et al., 2013, 2003). Most importantly, breathlessness had no impact on the emotional modulation observed on the *EPN* and *LPP* mean amplitudes, suggesting that at the present level of stimulation, breathlessness does not impact the neural processing of emotions. In contrast, breathlessness led to overall reductions in the mean amplitudes of the *PI*, as well as those registered in the *EPN* time window, irrespective of the emotional valence of the presented pictures. As such, our findings highlight that breathlessness has a strong attention-demanding effect, mostly pronounced during the early stages of emotional stimulus processing. These early neural processing stages have typically been associated with sensory (Olofsson et al., 2009) and selective attentional processing (Schupp et al., 2003a; Wieser et al., 2012), respectively. However, during the later processing stages commonly related to sustained and motivated attention (Schupp et al., 2003), the observed impact of breathlessness seems to wane, as indicated by the weak and non-significant effects of breathlessness manipulations on the mean *LPP* amplitudes. Taken together, these electrophysiological findings suggest that respiratory bodily threat, as evoked in the current study, captures attention at an early time in the processing stream of emotional stimulation and reduces the neural processing capacity of concurrent visual stimulation irrespective of its emotional characteristics.

The present findings are in line with previous studies in the field of pain, where the impact of pain on attentional processes has long been established (Bingel et al., 2007; Eccleston and Crombez, 1999; Moore et al., 2009). For example, Wieser and colleagues (2012) demonstrated that painful pressure stimulation reduced the *PI* mean amplitudes elicited by concomitantly presented emotional faces. However, their results also described a more sustained effect of pain, as indicated by the additional reduction of the later *LPP* mean amplitudes for painful stimulation. Note that such an effect failed to reach significance in the present study. This discrepancy might be related to

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differences in the stimulus physical quality, stimulus intensities and/or the study design (i.e., within-participants design in the current study, as opposed to the between-participants study design of Wieser and his colleagues' study, 2012). Notably, in a similar manner to the current findings, the authors did not observe any influence of pain on the processing of the different emotional facial expressions (Wieser et al., 2012). Therefore, these observations suggest that moderate levels of experimentally induced bodily threat seem to leave emotional processing intact. It might be speculated that such an effect could be related to cortical automatization (see e.g., Wu, Chan, & Hallett, 2008; Wu, Kansaku, & Hallett, 2004), a process by which a certain task is performed without focusing attention on a specific motor sequence. Recently, cortical automatization has been linked to the compensation of inspiratory threshold loading (Raux et al., 2013). However, future studies are needed to examine the effects of graded and/or stronger stimulation levels, as well as to directly compare the occurrence of cortical automatization during the time course of resistive load-induced breathlessness.

Interestingly, whereas previous studies using RREPs demonstrated a significant influence of emotional contexts on the later processing of respiratory sensations (e.g., *P3* component, von Leupoldt et al., 2010), the present study indicates that the reverse effect of respiratory bodily threat on emotional picture processing occurs rather early (e.g., in the time window of the *P1* and *EPN*). In order to explain this difference, in future studies it would be interesting to investigate both directions of this effect between respiratory sensations and emotion processing in the same volunteers. Moreover, this study used inspiratory resistive-load-induced breathlessness, which causes a sensation of increased work and effort of breathing. In this respect, our results cannot account for other qualities of breathlessness such as air hunger and chest tightness. Furthermore, when interpreting the present results it should be kept in mind that we only examined healthy young individuals without respiratory diseases and with low levels of negative emotionality. Therefore, it remains unclear to which degree the findings can be generalized to populations affected by breathlessness, such as patients with asthma and COPD, or to individuals with clinically relevant levels of anxiety and depression.

Conclusion

In summary, our results suggest that resistive-load-induced breathlessness impacts on the early neural processing of emotional pictures, indicating a clear automatic attention capture effect. However, breathlessness as utilized in the present study does not interact with later and more

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cognitive processing of emotional picture stimuli. Our results thus imply an early sensory-related influence of respiratory bodily threat on emotional processing. Future studies using stronger levels and/or different qualities of breathlessness as well as patient groups suffering from respiratory diseases are necessary in order to examine the clinical relevance of these findings.

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References

- American Psychiatric Association (APA), 2000. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition: DSM-IV-TR.
- American Thoracic Society (ATS), 1999. Dyspnea. Mechanisms, assessment, and management: a consensus statement. *Am. J. Respir. Crit. Care Med.* 159, 321–340.
- Banzett, R., Moosavi, S., 2001. Dyspnea and pain: similarities and contrasts between two very unpleasant sensations. *APS Bull* 11, 1–8.
- Barlow, D., 2002. *Anxiety and its disorders: The nature and treatment of anxiety and panic.* Guilford Press.
- Beck, A., Steer, R., Ball, R., Ranieri, W., 1996. Comparison of Beck Depression Inventories -IA and -II in psychiatric outpatients. *J. Pers. Assess.* 67, 588–597.
- Bingel, U., Rose, M., Gläscher, J., Büchel, C., 2007. fMRI reveals how pain modulates visual object processing in the ventral visual stream. *Neuron* 55, 157–167.
- Bradley, M., Lang, P., 2007. The International Affective Picture System (IAPS) in the study of emotion and attention.
- Bradley, M.M., Lang, P.J., 1994. Measuring emotion: the self-assessment manikin and the semantic differential. *J. Behav. Ther. Exp. Psychiatry* 25, 49–59.
- Bublitzky, F., Fleisch, T., Stockburger, J., Schmälzle, R., Schupp, H.T., 2010. The interaction of anticipatory anxiety and emotional picture processing: an event-related brain potential study. *Psychophysiology* 47, 687–696. doi:10.1111/j.1469-8986.2010.00966.x
- Codispoti, M., Ferrari, V., Bradley, M.M., 2006. Repetitive picture processing: autonomic and cortical correlates. *Brain Res.* 1068, 213–220. doi:10.1016/j.brainres.2005.11.009
- Cuthbert, B., Schupp, H., Bradley, M., Birbaumer, N., Lang, P., 2000. Brain potentials in affective picture processing: covariation with autonomic arousal and affective report. *Biol. Psychol.* 52, 95–111.
- Domschke, K., Stevens, S., Pfleiderer, B., Gerlach, A., 2010. Interoceptive sensitivity in anxiety and anxiety disorders: an overview and integration of neurobiological findings. *Clin. Psychol. Rev.* 30, 1–11.
- Eccleston, C., Crombez, G., 1999. Pain demands attention: A cognitive–affective model of the interruptive function of pain. *Psychol. Bull.* 125, 356.

Formatted: English (U.S.)

EMOTION PROCESSING DURING BREATHLESSNESS

- Hajcak, G., MacNamara, A., Foti, D., Ferri, J., Keil, A., 2013. The dynamic allocation of attention to emotion: simultaneous and independent evidence from the late positive potential and steady state visual evoked potentials. *Biol. Psychol.* 92, 447–455.
doi:10.1016/j.biopsycho.2011.11.012
- Hajcak, G., MacNamara, A., Olvet, D.M., 2010. Event-related potentials, emotion, and emotion regulation: an integrative review. *Dev. Neuropsychol.* 35, 129–155.
doi:10.1080/87565640903526504
- Harver, A., Mahler, D., 1998. Perception of increased resistance to breathing. *Lung Biol. Heal. Dis.* 113, 147–193.
- Janssens, T., Verleden, G., De Peuter, S., Van Diest, I., Van den Bergh, O., 2009. Inaccurate perception of asthma symptoms: a cognitive-affective framework and implications for asthma treatment. *Clin. Psychol. Rev.* 29, 317–327. doi:10.1016/j.cpr.2009.02.006
- Lang, P., Greenwald, M., Bradley, M.M., Hamm, A.O., 1993. Looking at pictures: Affective, facial, visceral, and behavioral reactions. *Psychophysiology* 30, 261–273.
- Lang, P.J., Bradley, M.M., Cuthbert, B.M., 2008. International affective picture system (IAPS): Affective ratings of pictures and instruction manual. Tech. Rep. A-8.
- Lavie, N., 2010. Attention, distraction, and cognitive control under load. *Curr. Dir. Psychol. Sci.* 19, 143–148.
- Livermore, N., Butler, J.E., Sharpe, L., McBain, R.A., Gandevia, S.C., McKenzie, D.K., 2012. Panic attacks and perception of inspiratory resistiveloads in chronic obstructive pulmonary disease. *Am. J. Respir. Crit. Care Med.* 178, 7–12.
- Maurer, J., Rebbapragada, V., Borson, S., Goldstein, R., Kunik, M., Yohannes, A., Hanania, N., 2008. Anxiety and Depression in COPD Current understanding, unanswered questions, and research needs. *Chest J.* 134, 43S–56S.
- Miller, M., Crapo, R., Hankinson, J., Brusasco, V., Burgos, F., Casaburi, R., Wanger, J., 2005. General considerations for lung function testing. *Eur. Respir. J.* 26, 153–161.
- Moore, D., Keogh, E., Eccleston, C., 2009. Identifying experimental methods to determine the effect of pain on attention: a review of pain, caffeine, alcohol and nicotine studies. *Hum. Psychopharmacol. Clin. Exp.* 24, 601–618.
- Olofsson, J.K., Nordin, S., Sequeira, H., Polich, J., 2009. Affective picture processing: An integrative review of ERP findings. *Biol. Psychol.* 77, 247–265.
- Oostenveld, R., Praamstra, P., 2001. The five percent electrode system for high-resolution EEG and ERP measurements. *Clin. Neurophysiol.* 112, 713–9.

Formatted: Dutch (Belgium)

Formatted: English (U.S.)

Formatted: French (France)

Formatted: English (U.S.)

EMOTION PROCESSING DURING BREATHLESSNESS

Picton, T.W., Bentin, S., Berg, P., Donchin, E., Hillyard, S., Johnson, R., Miller, G., Ritter, W., Ruchkin, D., Rugg, M., Taylor, M., 2000. Guidelines for using human event-related potentials to study cognition: recording standards and publication criteria. *Psychophysiology* 37, 127–152.

Raux, M., Tyvaert, L., Ferreira, M., Kindler, F., Bardinet, E., Karachi, C., Morelot-Panzini, C., Gotman, J., Pike, G.B., Koski, L., Similowski, T., 2013. Functional magnetic resonance imaging suggests automatization of the cortical response to inspiratory threshold loading in humans. *Respir. Physiol. Neurobiol.* 189, 571–580. doi:10.1016/j.resp.2013.08.005

Formatted: Dutch (Belgium)

Rietveld, S., Everaerd, W., van Beest, I., 2000. Excessive breathlessness through emotional imagery in asthma. *Behav. Res. Ther.* 38, 1005–1014. doi:10.1016/S0005-7967(99)00134-5

Formatted: English (U.S.)

Ritz, T., Meuret, A., Trueba, A., Fritzsche, A., von Leupoldt, A., 2012. Psychosocial factors and behavioral medicine interventions in asthma.

Schupp, H., Junghöfer, M., Weike, A., Hamm, A., 2003a. Emotional Facilitation of Sensory Processing in the Visual Cortex. *Psychol. Sci.* 14, 7–13. doi:10.1111/1467-9280.01411

Formatted: English (U.S.)

Schupp, H., Junghöfer, M., Weike, A., Hamm, A., 2003b. Attention and emotion: an ERP analysis of facilitated emotional stimulus processing. *Neuroreport* 14, 1107–1110. doi:10.1097/01.wnr.0000075416.59944.49

Formatted: English (U.S.)

Schupp, H., Schmäzle, R., Flaisch, T., Weike, A., Hamm, A., 2013. Reprint of “Affective picture processing as a function of preceding picture valence: an ERP analysis”. *Biol. Psychol.* 92, 520–525. doi:10.1016/j.biopsycho.2013.02.002

Formatted: English (U.S.)

Spielberger, C., Gorsuch, R., Lushene, R., 1970. State-trait anxiety inventory: STAI.

Formatted: English (U.S.)

Von Leupoldt, A., Chan, P., Esser, R., Davenport, P., 2013. Emotions and neural processing of respiratory sensations investigated with respiratory-related evoked potentials. *Psychosom. Med.* 75, 244–252.

Von Leupoldt, A., Fritzsche, A., Trueba, A., Meuret, A., Ritz, T., 2012. Behavioral medicine approaches to chronic obstructive pulmonary disease. *Ann. Behav. Med.* 44, 52–65.

Formatted: English (U.S.)

Von Leupoldt, A., Mertz, C., Kegat, S., Burmester, S., Dahme, B., 2006a. The impact of emotions on the sensory and affective dimension of perceived dyspnea. *Psychophysiology* 43, 382–386. doi:10.1111/j.1469-8986.2006.00415.x

Formatted: English (U.S.)

Von Leupoldt, A., Riedel, F., Dahme, B., 2006b. The impact of emotions on the perception of dyspnea in pediatric asthma. *Psychophysiology* 43, 641–644. doi:10.1111/j.1469-8986.2006.00453.x

Formatted: English (U.S.)

Von Leupoldt, A., Sommer, T., Kegat, S., Baumann, H., Klose, H., Dahme, B., Büchel, C., 2009. Dyspnea and pain share emotion-related brain network. *Neuroimage* 48, 200–206. doi:10.1016/j.neuroimage.2009.06.015

Formatted: English (U.S.)

EMOTION PROCESSING DURING BREATHLESSNESS

Von Leupoldt, A., Sommer, T., Kegat, S., Klose, H., Dahme, B., Büchel, C., 2008. The unpleasantness of perceived dyspnea is processed in the anterior insula and amygdala. *Am. J. Respir. Crit. Care Med.* 177, 1026–1032.

Formatted: English (U.S.)

Von Leupoldt, A., Taube, K., Henkhus, M., Dahme, B., Magnussen, H., 2010a. The impact of affective states on the perception of dyspnea in patients with chronic obstructive pulmonary disease. *Biol. Psychol.* 84, 129–134. doi:10.1016/j.biopsycho.2009.07.010

Von Leupoldt, A., Vovk, A., Bradley, M., Keil, A., Lang, P., Davenport, P., 2010b. The impact of emotion on respiratory-related evoked potentials. *Psychophysiology* 47, 579–586. doi:10.1111/j.1469-8986.2009.00956.x

Wieser, M.J., Gerdes, A.B.M., Greiner, R., Reicherts, P., Pauli, P., 2012. Tonic pain grabs attention, but leaves the processing of facial expressions intact-evidence from event-related brain potentials. *Biol. Psychol.* 90, 242–8. doi:10.1016/j.biopsycho.2012.03.019

Formatted: English (U.S.)

Wu, T., Chan, P., Hallett, M., 2008. Modifications of the interactions in the motor networks when a movement becomes automatic. *J. Physiol.* 586, 4295–4304. doi:10.1113/jphysiol.2008.153445

Wu, T., Kansaku, K., Hallett, M., 2004. How self-initiated memorized movements become automatic: a functional MRI study. *J. Neurophysiol.* 91, 1690–1698. doi:10.1152/jn.01052.2003

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Footnotes

1

	Positive pictures			Neutral pictures			Negative pictures		
	Series 1	Series 2	Series 3	Series 1	Series 2	Series 3	Series 1	Series 2	Series 3
Arousal	5.7(0.2)	5.8(0.2)	5.8(0.2)	3.4(0.1)	3.4(0.2)	3.5(0.1)	5.7(0.2)	5.9(0.2)	6(0.1)
Valence	7.5(0.1)	7.6(0.1)	7.5(0.1)	4.9(0.1)	4.8(0.1)	4.8(0.1)	2.2(0.1)	2.1(0.1)	2.1(0.1)

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Figure captions

Figure 1. Depictions of the experimental design (*a*) and trial timeline (*b*).

Figure 2. (*A*) Head topographies for the *PI* in the 120 – 160 ms post-stimulus onset time window. The data are collapsed over the three Emotions (positive, neutral, negative), for each of the three Conditions (breathlessness, baseline, and noise). (*B*) The analysed mean *PI* amplitudes are depicted at an exemplary electrode (PO8) for the three different Conditions and are marked with a grey rectangle. Traces represent the grand averages of all respective trials. *PI* mean amplitudes were significantly smaller during the breathlessness condition as compared to the baseline condition ($p = .010$)

Figure 3. (*A*) Mean *EPN* amplitudes (grey rectangle) depicted at an exemplary electrode (PO8) for the three different Emotions, for each of the three Conditions (breathlessness in the upper left corner, baseline in the middle, and noise in the upper right corner). Traces represent the grand averages of all respective trials. Significantly larger relative negativity for the mean *EPN* amplitudes were observed for the positive ($p = .001$) and negative ($p = .040$), as compared to the neutral pictures. (*B*) Head topographies for the *EPN* in the 200 – 280 ms post-stimulus onset window for each of the three Conditions (breathlessness in the left column, baseline in the middle, and noise in the right column). The upper row depicts head topography data derived by subtracting the neutral picture series from the positive picture series, whereas the lower row presents difference waves between negative and neutral picture series.

Figure 4. Main effects of Condition (*a*) and Emotion (*b*) on the *EPN* mean amplitudes collapsed over Emotions at the electrodes Oz, PO3/PO4, PO7/8, and O1/2. Vertical error bars represent the standard error of the mean. Mean amplitudes in the *EPN* time window were significantly smaller during breathlessness as compared to the baseline ($p = .016$) and noise conditions ($p = .003$) (*a*). Significantly larger relative negativity for the mean *EPN* amplitudes were found for positive ($p = .001$) and negative ($p = .040$), as compared to neutral pictures (*b*).

Figure 5. (*A*) The mean *LPP* amplitudes (grey rectangle) at an exemplary electrode (PO4) for the

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three different Emotions, for each of the three Conditions (breathlessness in the upper left corner, baseline in the middle, and noise in the upper right corner). Traces represent the grand averages of all respective trials. Higher mean *LPP* amplitudes were observed for positive and negative as compared to neutral pictures ($p = .039$). **(B)** Head topographies for the *LPP* in the 300 – 550 ms post-stimulus onset window for each of the three Conditions (breathlessness in the left column, baseline in the middle, and noise in the right column). The upper row depicts head topography data derived by subtracting the neutral picture series from the positive picture series, whereas the lower row presents difference waves between negative and neutral picture series.