The effect of dyspnea on recognition memory

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Abstract

Dyspnea is a debilitating symptom in various prevalent diseases. Previous research demonstrated several cognitive impairments in dyspneic patients including an impairment in recognition memory. Even though some factors contributing to these impairments have already been identified (e.g., smoking, medication), the relevance of dyspnea as one of those contributing factors is still unclear. Thus, the goal of the current study was to investigate whether acute dyspnea impairs recognition memory in a picture recognition task as indexed by reduced accuracy and a reduced old-new effect in event-related potentials (ERPs) in the electroencephalogram (EEG). Fifty healthy participants underwent a passive encoding phase without dyspnea induction, followed by the picture recognition task performed during an unloaded baseline and a resistive load induced dyspnea condition while EEG was continuously measured. Results indicated comparable accuracy during the baseline and dyspnea condition. A reduced fronto-central old-new effect during dyspnea compared to baseline was found for ERPs in the latency ranges 350-500, 500-800, 800-1100, and 1110-1400 ms. These findings suggest that dyspnea influences the process of familiarity (350-500 ms) and recollection (500-800 ms) as well as post-retrieval processes (800-1100 and 1100-1400 ms), highlighting a potential impairing effect of acute dyspnea on recognition memory.

Keywords: Recognition memory, Dyspnea, Breathlessness, EEG

1 Introduction

2 Dyspnea (= breathlessness) is a common and aversive bodily sensation in various
3 cardiopulmonary, neuromuscular, and other diseases and has widespread impairing effects on
4 functioning in daily life (American Thoracic Society, 1999; Kessler et al., 2011; Parshall et al.,
5 2012). Research demonstrated impairments for a wide range of cognitive functions in diseases
6 where dyspnea is highly prevalent such as in chronic obstructive pulmonary disease (COPD)
7 (Cleutjens, Janssen, Ponds, Dijkstra, & Wouters, 2014; Cleutjens et al., 2016; Dodd, Getov, &
8 Jones, 2010; van Beers, Janssen, Gosker, & Schols, 2018) or asthma (Irani, Barbone, Beausoleil,
9 & Gerald, 2017). Several factors contributing to cognitive impairments in these patients such as
10 age, education level, medication, comorbidities, or hypoxia (= deprived oxygen supply in tissue)
11 have been already identified (Celsis, 2000; Dodd et al., 2010; McIntyre et al., 2013). For example,
12 COPD patients might show cognitive impairments due to their typically older age (Celsis, 2000),
13 comorbid depression (McIntyre et al., 2013), medication usage such as opiates (Raghavan, Webb,
14 Amornputtisathaporn, & O'Donnell, 2011), or hypoxia (Huppert, 1982; Moss, Franks, Briggs,
15 Kennedy, & Scholey, 2005), with the latter leading to cognitive impairment in 77 percent of COPD
16 patients (Grant, Heaton, McSweeney, Adams, & Timms, 1982 as cited in Dodd et al., 2010).
17 However, the effect of acute dyspnea itself on cognitive functioning is less well explored. So far,
18 a first set of studies demonstrated that dyspnea has an impairing effect on cognitive functioning in
19 healthy subjects including picture processing (Juravle, Reicherts, Riechmann-Weinstein, Wieser,
20 & von Leupoldt, 2017; Juravle et al., 2014), inhibition (Sucec, Herzog, Van Diest, Van den Bergh,
21 & von Leupoldt, 2018b), face recognition (Vinckier, Morélot-Panzini, & Similowski, 2018), and
22 locomotor performance (Nierat et al., 2016). Furthermore, already the fearful anticipation of
23 dyspnea can lead to impairments in error-processing (Sucec, Herzog, Van Diest, Van den Bergh,
24 & von Leupoldt, 2018a). Since these studies reflect only a small fraction of cognitive functions
25 (Eysenck & Keane, 2000), future studies exploring other cognitive domains are warranted.

26
27 Overall, cognitive impairment in dyspneic patients is paralleled by a decline in active recall and
28 passive recognition memory (Incalzi et al., 1997). Recognition memory is essential for the ability
29 to assess whether an item is new or has been encountered before (Clark, 2013), which might be
30 important in disease management. For example, patients usually receive detailed information from
31 medical staff about their illness and the subsequently required treatment procedures such as

1 medication usage, which are essential to be accurately remembered in daily life for treatment
2 success (Kessels, 2003). Patients suffering from COPD show worse task performance in
3 recognition memory compared to healthy controls (Incalzi et al., 1997). This is problematic
4 because the amount of immediately forgotten medical information can already be higher than 40
5 percent in non-dyspneic patients (Kessels, 2003; McGuire, 1996) and it might be assumed that
6 dyspnea leads to a further worsening of this percentage due to a dyspnea-cognition interference
7 (Nierat et al., 2016; Sucec et al., 2018b). However, the direct effect of acute dyspnea on recognition
8 memory has never been explored.

9
10 Recognition memory is commonly subdivided into the slower process of recollection, where
11 detailed recall of previously studied information is absolutely essential, and the faster process of
12 familiarity, which varies according to the closeness between presented cues and previously studied
13 information (Rugg & Curran, 2007; Shiffrin & Steyvers, 1997). Many researchers consider these
14 two processes as independent from each other during retrieval and only minimally overlapping
15 during the encoding phase (Yonelinas, 2002). The advances in cognitive neuroscience and the
16 usage of the event-related potential (ERP) technique in the electroencephalogram (EEG) allow
17 distinguishing between these two processes (Rugg & Curran, 2007). So far, the effects of dyspnea
18 on the ERPs related to recognition memory and its two underlying processes, familiarity, and
19 recollection, have not yet been examined.

20
21 Recognition memory is typically investigated by old-new paradigms, where participants have to
22 indicate whether they have encountered a presented item (e.g., words, pictures) before (= old) or
23 not (= new) (Curran, 1999; Finnigan, 2002; Friedman & Johnson, 2000; Johansson, Mecklinger,
24 & Treese, 2004; Maratos, Allan, & Rugg, 2000; Rugg & Curran, 2007; Van Strien, Langeslag,
25 Strekalova, Gootjes, & Franken, 2009; Weymar, Löw, & Hamm, 2011; Xu, Zhang, Li, & Guo,
26 2015). Recognition memory is typically operationalized as behavioral performance indexed as
27 accuracy according to signal-detection theory (Abdi, 2007; Malmberg, 2008), and as an old-new
28 effect in the EEG that can be expressed as an old-new difference score of ERPs elicited by these
29 items (e.g., Weymar, Bradley, Hamm, & Lang, 2013). Importantly, overall accuracy is reduced
30 when an aversive bodily symptom such as acute pain is introduced. Specifically, more false alarms
31 during acute pain compared to a baseline condition have been demonstrated (Kuhajda, Thorn,

Klinger, & Rubin, 2002). Since pain shares many characteristics with dyspnea including the threatening and aversive nature, as well as similar underlying emotion-related brain networks (Banzett & Moosavi, 2001; Gracely, Udem, & Banzett, 2007; von Leupoldt & Dahme, 2007; von Leupoldt et al., 2009) similar effects of dyspnea on recognition memory performance might be expected. In the EEG, participants typically show an old-new effect during the recognition memory task such that correctly identified old items elicit a more positive going ERP deflection compared to correctly identified new items (e.g., Curran, 1999; Rugg & Curran, 2007; Xu et al., 2015). The latency window for this effect varies widely across studies with a typical latency range between 300-1400ms (Maratos et al., 2000; Schloerscheidt & Rugg, 1997; Xu et al., 2015). It is assumed that the old-new effect relates to the correct recognition of the presented items with early latency windows ($\approx$ 300-500 ms) reflecting familiarity and later latency windows ($\approx$ 500-800 ms) reflecting subsequent recollection followed by post-retrieval processes (Johansson et al., 2004; Maratos et al., 2000; Mecklinger, 2000; Rugg & Curran, 2007).

The present study investigated whether experimentally induced dyspnea would impair recognition memory in healthy participants. Dyspnea was induced by inspiratory resistive loaded breathing and compared to an unloaded baseline condition while participants were performing a picture recognition task. Based on the findings from pain research (Kuhajda et al., 2002) and a potential dyspnea-cognition interference (Nierat et al., 2016; Sucec et al., 2018b; Sucec, Herzog, Van den Bergh, Van Diest, & von Leupoldt, 2019) we expected reduced accuracy during dyspnea, which would be paralleled by a reduced old-new effect in the ERPs. In an additional exploratory analysis reaction times were investigated.

Methods

Participants

50 healthy participants (41 females) with normal or corrected to normal vision took part in the current study in return for either course credits or 16 € as compensation. Exclusion criteria included a history of self-reported acute or chronic disorders. Additional exclusion criteria were nicotine consumption, medication usage, pregnancy, and alcohol consumption 24 hours prior to testing. Normal lung function was confirmed prior to testing via standard spirometry (Miller et al., 2005).

Ethical approval for this study was obtained from the Social and Societal Ethics Committee of the University of Leuven (G-2016-02-484).

Passive encoding phase

During the passive encoding phase, 160 color pictures of humans originating from the International Affective Picture System (IAPS, Lang, Bradley, & Cuthbert, 2008) and a recently developed visual stimuli database¹ (Herzog, Sucec, Van Diest, Van den Bergh, Chenivesse, et al., 2018) were presented in four blocks of 40 pictures each in a resolution of 2560×1440 pixels. The picture order was semi-randomized within each block. Pictures were presented for 4000 ms and followed by a fixation cross with jittered presentation time (mean: 2000 ms; range: 1800-2200 ms). The total duration of each block was 4 min. While passively viewing the pictures, participants were unaware of the subsequent picture recognition task.

Picture recognition phase

During the picture recognition phase, 160 pictures from the passive encoding phase (= “old”) and 160 matched new pictures (= “new”) were presented. The “new” pictures were matched to the “old” pictures based on affective valence, arousal, picture content, and picture composition. The total of 320 pictures was divided into four blocks each containing 80 pictures. The pictures in each block were presented in semi-random order consisting of 40 “old” and 40 “new” pictures. Two of the blocks of the picture recognition task were performed during an unloaded baseline condition and two during a dyspnea condition. In all four blocks, participants were breathing through a breathing circuit. Baseline and dyspnea blocks were alternated (either “A-B-A-B” or “B-A-B-A”) to reduce respiratory muscle fatigue with a counterbalanced order across participants. Similar to previous research (Alexander-Miller & Davenport, 2010; Brack, Jubran, & Tobin, 1998; Herzog, Sucec, Van Diest, Van den Bergh, Chan, et al., 2018) dyspnea was induced during the dyspnea condition via breathing through an inspiratory resistive load (Hans Rudolph, Inc., Shawnee, USA) of 20 cmH₂O/l/s that was applied to the breathing circuit. During each block, participants had to indicate via button press on a response box whether pictures had already been presented (= “old”) or not (= “new”) during the passive encoding phase. Again, each picture was presented in a 2560×1440-pixel resolution until a response was given or for maximally 2000 ms. Subsequently,

¹ The technical report for this database is currently in preparation.

each block of the picture recognition task lasted maximally 2 min and 40 s. Responses for each picture were allowed from picture onset until 2000 ms after picture onset.

Ratings

Dyspnea was explained to participants as “difficult and uncomfortable breathing”. Dyspnea was rated via a modified Borg scale (Borg, 1982) ranging from 0 (= “not noticeable”) to 10 (= “unbearable (impossible to tolerate)”. Additionally, participants rated their affective state by indicating their affective valence (1 = “unpleasant” to 9 = “pleasant”) and arousal (1 = “calm” to 9 = “aroused”) via the 9-point Self-Assessment Manikin (Bradley & Lang, 1994). Furthermore, participants rated the difficulty of the recognition memory task (1 = “not difficult at all” to 7 = “extremely difficult”) and how motivated they were to perform the task on a 7-point Likert scale (1 = “not motivated at all” to 7 = “extremely motivated”). All ratings referred to the preceding block.

Breathing circuit

During the picture recognition phase, participants were breathing via a mouthpiece through the breathing circuit with a nose clip preventing nasal respiration. The breathing circuit consisted of a two-way T-shaped non-rebreathing valve (Hans Rudolph Inc., Shawnee, USA). The expiratory port of the non-rebreathing valve was connected via a sampling line to a capnograph (VacuMed, CO₂ Analyzer, Gold Edition, Ventura, USA) measuring end-tidal CO₂ (ETCO₂). Furthermore, at the center of the non-rebreathing valve, mouth pressure was measured. The inspiratory port of the non-rebreathing valve was connected via tubing to a pneumotachograph (Hans Rudolph Inc., Shawnee, USA) measuring airflow and subsequently to a loading manifold used to apply the inspiratory resistive load (Hans Rudolph Inc., Shawnee, USA). During all blocks of the recognition memory phase airflow, mouth pressure, and ETCO₂ were measured continuously. To calculate the respiratory variables including breathing frequency (f), inspiratory time (T_I), tidal volume (V_T), mean airflow (V'), peak inspiratory mouth pressure ($P_{I_{max}}$), and ETCO₂, AcqKnowledge 4.2 (Biopac, Goleta, USA) was used.

Psychophysiological recordings and data reduction

During the picture recognition phase, the 129-channel EEG (Philips Electrical Geodesics Inc.,

Eugene, USA) was continuously recorded with a sampling rate set at 250 Hz and Cz as reference. Impedance was kept below 50 k Ω . Subsequently, Brain Electrical Source Analysis Research 6.0 (BESA GmbH, Gräfelting, Germany) was used to process the EEG data offline. Raw data were filtered using a half amplitude cut-off with a high-pass filter of 0.01 Hz (forward-phase Butterworth filter, 6 dB/octave roll-off), a low-pass filter of 40 Hz (zero-phase Butterworth filter, 24 dB/octave roll-off), and an additional notch filter of 50 Hz (2 Hz width). Artifacts were corrected using spatial filters implemented in BESA designed to separate artifacts and brain activity (Ille, Berg, & Scherg, 2002). Brain activity was estimated by scanning the data in intervals of 16 ms. Data were considered brain activity when the criteria of correlation (correlation between data and artifact < .50) and amplitude ($\pm 100 \mu\text{V}$) were fulfilled. Spatial topographies describing the artifacts were manually selected. Next, an adaptive algorithm based on principal component analysis described in Ille, Berg, & Scherg (2002) was applied. All principal component analyses explaining more than 10% of the variance were retained. Then, the recorded EEG data was deconstructed into topographies separating artifact and brain activity via a linear combination resulting in the subtraction of artifact activity and subsequently artifact removal. A comparable number of artifacts, specifically blink artifacts ($t(38) = 0.78$, $p = .52$, $r = .13$), was removed in the baseline ($M = 65.18$, $SD = 48.66$) and dyspnea condition ($M = 60.97$, $SD = 38.23$). Based on established recommendations for high-density EEG (Dien, 1998; Luck, 2014), data were re-referenced to the average reference. Stimulus-locked epochs ranging from -200 to 2000 ms were extracted and averaged for correctly categorized pictures. Epochs that did not fulfill the criteria for amplitude ($< 200 \mu\text{V/ms}$), gradient ($> 75 \mu\text{V/ms}$), and low signal ($< 0.01 \mu\text{V/ms}$) were automatically excluded from averaging. For the ERPs of the baseline condition on the average 24 trials (range: 11-44) were rejected for the hits and 15 trials (range: 6-35) for the correct rejection while for the dyspnea condition 24 trials (range: 9-56) were rejected for the hits and 16 trials (range: 3-41) for the correct rejection. The average number of trials of the ERPs was for the baseline condition 56 trials (range: 36-69) for the hits and 65 trials (range: 45-74) for the correct rejection and in the dyspnea condition 56 trials (range: 24-71) for the hits and 64 trials (range: 39-77) for the correct rejection. The pre-stimulus interval ranging from -100 to 0 ms was used as baseline. Similar to previous research (Rugg et al., 1998; Weymar et al., 2011) and visual inspection of the signal, fronto-central electrodes (electrodes left hemisphere: 7, 13, 20, 28, 29, 30, 35; electrodes right hemisphere: 105, 106, 110, 111, 112, 117, 118) and centro-parietal electrodes

(electrodes left hemisphere: 31, 37, 42, 52, 53, 54, 60, 61, 67; electrodes right hemisphere: 77, 78, 79, 80, 85, 86, 87, 92, 93) were selected for each hemisphere (Figure 1). The hemisphere was considered based on previous literature which found hemispheric differences for recollection and post-retrieval processes (Johansson et al., 2004; Maratos et al., 2000; Rugg & Curran, 2007; Schloerscheidt & Rugg, 1997). The electrodes were then clustered for the latency windows 350-500, 500-800, 800-1100, and 1100-1400 ms as mean amplitudes based on previous literature (e.g., Maratos et al., 2000; Rugg & Curran, 2007).

####Figure 1####

Procedure

Before any data was collected, all participants signed the informed consent and exclusion criteria form and normal pulmonary function was confirmed via standard spirometry. Then, the EEG net was mounted, and participants were seated, with their upper body and feet being supported, approximately 148 cm in front of a 32-inch standard screen. Subsequently, participants underwent the four blocks of the passive encoding phase followed by a short break. Afterwards, detailed instructions regarding the picture recognition phase followed and participants were familiarized with the inspiratory resistive load. Then, the four blocks of the picture recognition phase followed. Two of these blocks were performed during unloaded baseline breathing while two other blocks were performed during dyspnea. Each block was followed by a short resting period during which the ratings of dyspnea, affective state, task difficulty, and task motivation were obtained. Finally, participants were thanked and debriefed.

Statistical analysis

Due to technical malfunction leading to failure to store sufficient data, ten participants had to be excluded from data analysis. Moreover, one participant was excluded from data analysis due to a procedural mistake committed by the experimenter. Thirty-nine participants (31 females) with a mean age of 23.51 years ($SD = 7.53$) were included in the final analysis which was performed using IBM SPSS Statistics 25. All ratings, respiratory variables as well as behavioral measures and ERPs of the picture recognition phase were averaged across the two baseline and the two dyspnea blocks, respectively. To confirm successful dyspnea induction, ratings of dyspnea,

valence, and arousal, as well as respiratory variables, were compared between the baseline and dyspnea condition using dependent t-tests. Additionally, the ratings of task difficulty and task motivation were compared between conditions using dependent t-tests. In case not all assumptions for dependent t-tests were met, non-parametric Wilcoxon signed-rank tests were applied. To investigate recognition memory, accuracy and ERPs were explored. Accuracy rates were analyzed based on signal detection theory (Abdi, 2007; Malmberg, 2008) including the indices hit rate (H), false alarm rate (FA), recognition accuracy ($Pr = H - FA$), and response bias ($Br = p(FA)/p(1 - Pr)$). To investigate a potential dyspnea effect on the accuracy indices, dependent t-tests were calculated. For the ERPs, an old-new mean amplitude difference score (= old minus new) for correctly categorized items was calculated. For each brain region (fronto-central, centro-parietal) and latency range (350-500, 500-800, 800-1100, 1100-1400 ms) separate 2 x 2 repeated measures ANOVAs were computed for the old-new difference scores with the within factors dyspnea (baseline, dyspnea) and hemisphere (left, right). For the exploratory analysis of reaction times, a 2 x 2 repeated measures ANOVA with the within factors dyspnea (baseline, dyspnea) and familiarity (old, new) was calculated. Only correctly categorized items were analyzed for the reaction times. The effect size used for the ANOVAs and dependent t-tests/Wilcoxon signed-rank tests were η^2_p and r , respectively. The level of significance was set at $\alpha = .05$.

Results

Ratings

Higher dyspnea ratings were found for the dyspnea compared to the baseline condition ($z = -4.69$, $p < .001$, $r = .53$). Moreover, lower valence ratings, indicating more unpleasantness, ($t(38) = 4.93$, $p < .001$, $r = .62$) and higher arousal ratings ($t(38) = -2.23$, $p = .032$, $r = .34$) were found for the dyspnea compared to the baseline condition. While for the dyspnea condition higher task difficulty was reported ($t(38) = -2.42$, $p = .021$, $r = .37$), the motivation to perform the task was comparable between both conditions ($t(38) = 0.30$, $p = .77$, $r = .05$; Table 1).

####Table 1####

Respiratory variables

The analysis of the respiratory variables demonstrated lower f ($z = -4.49, p < .001, r = .50$) and V' ($z = -5.32, p < .001, r = .60$) as well as higher T_I ($t(38) = -6.40, p < .001, r = .72$), $P_{I_{max}}$ ($z = -5.44, p < .001, r = .62$), and $ETCO_2$ ($z = -4.08, p < .001, r = .46$) for the dyspnea compared to the baseline condition. Values for V_T were comparable between both conditions ($t(38) = 1.15, p = .26, r = .18$; Table 2).

####Table 2####

Behavioral performance

The accuracy indices H ($t(38) = -1.11, p = .28, r = .18$), FA ($t(38) = -0.18, p = .86, r = .03$), Pr ($t(38) = -0.86, p = .40, r = .14$), and Br ($t(38) = -0.47, p = .64, r = .08$) were comparable between the baseline and dyspnea condition (Table 3). The exploratory analysis of the reaction times showed a main effect for familiarity ($F(1,38) = 24.54, p < .001, \eta^2_p = .39$) with faster reaction times for old compared to new pictures (Table 4). No significant main effect for the factor dyspnea ($p = .39$) or an interaction effect was observed ($p = .92$).

####Table 3####

####Table 4####

ERPs

Figure 2 illustrates ERPs for old and new pictures during both experimental conditions at fronto-central and centro-parietal sites showing the typical enhanced positivity for old compared to new pictures.

####Figure 2####

Fronto-central

A main effect of the factor dyspnea was found for the latency ranges 350-500 ms ($F(1,38) = 4.87, p = .033, \eta^2_p = .11$), 500-800 ms ($F(1,38) = 6.89, p = .012, \eta^2_p = .15$), 800-1100 ms ($F(1,38) = 4.34, p = .044, \eta^2_p = .10$), and 1100-1400 ms ($F(1,38) = 6.55, p = .015, \eta^2_p = .15$; Figure 3, 4).

Furthermore, for the latency ranges 500-800 ($F(1,38) = 6.24, p = .017, \eta^2_p = .14$) and 1100-1400 ($F(1,38) = 6.34, p = .016, \eta^2_p = .14$) a main effect for the factor hemisphere was found. For the latency 500-800 ms larger old-new differences were observed for the left hemisphere while for 1100-1400 ms larger old-new differences were found for the right hemisphere (Table 5). No significant interaction effects were observed ($p > .05$).

####Figure 3####

####Figure 4####

####Table 5####

Centro-parietal

Neither a significant main effect nor a significant interaction effect was observed for any latency range ($p > .05$; Table 6).

####Table 6####

Discussion

The aim of the present study was to investigate whether experimentally induced dyspnea impairs recognition memory in a picture recognition task. Based on previous findings from other aversive bodily sensations (Kuhajda et al., 2002) and a potential dyspnea-cognition interference (Nierat et al., 2016; Sucec et al., 2018b), reduced accuracy and a reduced old-new effect in the ERPs were hypothesized during acute dyspnea compared to an unloaded baseline condition.

In line with previous research (Curran, 1999; Rugg & Curran, 2007; Xu et al., 2015) a more positive going deflection for correctly identified old items compared to correctly identified new items was found in the baseline and dyspnea condition. This supports a successful execution of the old-new picture paradigm in the present study. Moreover, a successful dyspnea induction was confirmed by higher ratings of dyspnea and arousal, as well as lower affective valence indicating more unpleasantness during the dyspnea compared to the baseline condition (Herzog, Sucec, Van

Diest, Van den Bergh, & von Leupoldt, 2019). The successful dyspnea induction was further supported by respiratory variables demonstrating lower f and V' as well as higher T_I and $P_{I_{max}}$ during the dyspnea compared to the baseline condition. These respiratory related findings are in line with previous research using similar dyspnea induction methods (Alexander-Miller & Davenport, 2010; Alius, Pané-Farré, Von Leupoldt, & Hamm, 2013; Herzog, Sucec, Vukovic, et al., 2019; Peiffer, Costes, Hervé, & Garcia-Larrea, 2008). A small, but statistically significant difference for $ETCO_2$ was found, which was within the normal range and, thus, presumably had no effect on the outcome measures (Bloch-Salisbury, Lansing, & Shea, 2000)

Confirming our hypothesis, dyspnea affected the ERPs related to recognition memory. A reduced old-new effect during dyspnea was found in fronto-central regions in all analyzed time windows (350-500, 500-800, 800-1100, 1100-1400 ms), but not in centro-parietal regions. This is in line with research showing more frontal activation for picture stimuli in old-new paradigms (Schloerscheidt & Rugg, 1997). Furthermore, this research (Schloerscheidt & Rugg, 1997) demonstrated stronger old-new differences left hemispheric in earlier latency windows and right hemispheric in later latency windows. A similar pattern was also observed in the current study with stronger old-new effects for the left hemisphere in the latency window 500-800 ms, which shifted towards the right hemisphere where it became pronounced in the latency window 1100-1400 ms. Overall, the occurring differences in all time windows between conditions suggest that dyspnea influences the process of familiarity (350-500 ms) and recollection (500-800 ms) as well as post-retrieval processes (800-1400 ms) (Johansson et al., 2004; Maratos et al., 2000; Mecklinger, 2000; Rugg & Curran, 2007), which is indicative of a potential impairing effect of acute dyspnea on recognition memory.

The reduced old-new effect in the ERPs caused by dyspnea can be most likely attributed to a dyspnea-cognition interference (Nierat et al., 2016; Sucec et al., 2018b). Based on the dyspnea-cognition interference it is assumed that dyspnea draws attentional resources which then cannot be allocated to a cognitive task performed in parallel. This attentional shift potentially causing dyspnea-cognition interference is further supported by our observation of increased ratings of task difficulty for the dyspnea compared to the baseline condition while the motivation to perform the task remained comparable. Moreover, it seems unlikely that the current old-new effect was affected

1 by emotions (McGaugh, 2004; Ochsner, 2000; Sterpenich et al., 2009) that were evoked by the
2 dyspnea induction. The reasons are twofold: Firstly, the ratings of negative valence and arousal
3 during the dyspnea condition are suggestive of a relatively mild negative emotional state.
4 Secondly, research usually shows a boosting effect of negative emotions on familiarity and
5 recollection (Ochsner, 2000), which is in contrast to the present finding that dyspnea reduces the
6 old-new effect in the EEG. Since blink artifacts and overall rejected trials were comparable
7 between the baseline and dyspnea condition, it seems highly unlikely that the current findings can
8 be attributed to differences in data quality between conditions.

9
10 Although we observed that dyspnea attenuates the old-new effect in the ERPs, we did not find the
11 expected effect of dyspnea on accuracy (Kuhajda et al., 2002; Sucec et al., 2018b) nor any effect
12 on reaction times. Interestingly, we found, even though not significant, slightly faster reaction
13 times during dyspnea together with higher arousal ratings which might point into the direction of
14 a facilitation effect of dyspnea. The non-significant behavioral findings are in contrast to previous
15 pain research (Kuhajda et al., 2002) which showed that acute pain reduces the accuracy in a
16 recognition memory task. More specifically, during the acute pain condition, the false-alarm rate
17 was increased compared to the baseline condition (Kuhajda et al., 2002). Furthermore, respiratory
18 research indicated behavioral impairments of dyspnea on other cognitive functions (e.g., Juravle
19 et al., 2014; Nierat et al., 2016; Sucec et al., 2018b). For example, experimental dyspnea reduced
20 the accuracy in a task measuring inhibition (Sucec et al., 2018b). The current contrasting findings
21 might be due to the induced level of dyspnea in the present study, which was still in a moderate
22 range during the dyspnea condition and might have been too low to result in any stronger
23 behavioral effect in healthy young individuals. For example, in the study by Sucec et al. (2018b),
24 the level of resistive load induced dyspnea was more than 45 % of the full scale, whereas in the
25 present study the level of resistive load induced dyspnea was only 32 % of the full scale.
26 Alternatively, already the “very weak” to “weak” levels of dyspnea reported by our participants in
27 the baseline condition, might have had a mild impact on neural processing resources and
28 behavioral performance, thereby creating a ceiling effect. In other words, the relative increase in
29 perceived dyspnea between baseline and dyspnea conditions might have been too limited to result
30 in significant further impairments in behavioral accuracy indices. This interpretation would be in
31 line with previous observations (Alius, Pané-Farré, Löw, & Hamm, 2015), showing that respiring

1 through a breathing circuit in the absence of an additional resistive load can already impair the
2 neural processing of sensory stimuli such as startle probes. Therefore, in order to increase the
3 difference between the conditions, future studies on recognition memory might benefit from
4 applying higher levels of dyspnea in the dyspnea condition.

5
6 Even though the implications of this study have yet to be tested in a dyspneic sample, our results
7 still hold potential clinical relevance. The current study shows impaired neural processing of
8 recognition memory during acute dyspnea in healthy participants. Since experimentally induced
9 dyspnea in healthy students cannot fully mimic the existential fear of a chronically dyspneic patient
10 (Currow & Johnson, 2015; Demoule & Similowski, 2018; Hayen, Herigstad, & Pattinson, 2013),
11 it might be argued that similar or even stronger effects of dyspnea on cognitive functioning could
12 be present in affected patients. This could result in several impairments in daily life, such as not
13 following prescriptions to treatment, mixing up or forgetting medications, etc., which might
14 interfere with the disease-management and further contribute to a more unfavorable course of the
15 disease. However, future studies in dyspneic patient groups are clearly needed to investigate these
16 assumptions.

17
18 Limitations of the present study include the testing of healthy, young, and predominantly female
19 participants, which limits the generalizability of the findings, as well as the induction of only one
20 quality of dyspnea (work and effort to breathe, ATS, 1999). Although similar findings might be
21 observed when using other dyspnea qualities such as air hunger or chest tightness, future studies
22 are warranted, especially in patients suffering from dyspnea, to determine possible effects of other
23 dyspnea qualities on recognition memory. Another limitation of the current study is the absence of
24 any behavioral measures (i.e., confidence ratings) for the underlying recognition memory
25 processes of familiarity and recollection which future studies should incorporate. Furthermore, so
26 far it is not clear whether the suggested dyspnea-cognition interference is specific to dyspnea itself
27 or whether other stressors (i.e., aversive auditory stimulation) might cause a similar effect.
28 Therefore, future studies should include a non-dyspneic stress condition to investigate this.
29 Furthermore, future studies should also explore the effects of dyspnea on the encoding stage of
30 memory processes by applying, for example, a two by two design that compares baseline vs.
31 dyspnea in the encoding vs. retrieval phase.

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1 **Conflict of Interest Statement**

2 The authors declare that there is no conflict of interest related to the present paper.

3
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Tables

Table 1. Means (SD) for ratings of dyspnea, affective valence and arousal, task difficulty, and task motivation for the baseline and dyspnea condition.

	Baseline	Dyspnea
Dyspnea (Borg)	1.44 (1.42)	3.21 (1.80)**
Valence (SAM) [#]	5.46 (1.57)	4.38 (1.87)**
Arousal (SAM)	3.90 (1.59)	4.27 (1.78)*
Task difficulty (Likert)	3.26 (1.22)	3.59 (1.45)*
Task motivation (Likert)	5.87 (1.08)	5.83 (1.07)

Note: Borg = modified Borg scale ranging from 0-10. SAM = Self-Assessment Manikin ranging from 1-9. Likert scale ranging from 1-7. # Lower valence ratings indicate more unpleasantness. Asterisks indicate a significant difference between the baseline and dyspnea condition with * $p < .05$, ** $p < .001$.

1 **Table 2.** Means (SD) of respiratory variables for the baseline and dyspnea condition.

	Baseline	Dyspnea
Breathing frequency (f), breaths/minute	13.85 (3.29)	12.03 (3.22)*
Inspiratory time (T _I), s	2.48 (1.10)	3.34 (1.18)*
Tidal volume (V _T), l	0.57 (0.21)	0.54 (0.23)
Mean airflow (V'), l/s	0.26 (0.09)	0.17 (0.05)*
Peak inspiratory mouth pressure (P _I max), cmH ₂ O	-1.45 (0.42)	-6.22 (1.26)*
End-tidal CO ₂ (ETCO ₂), %	4.75 (0.49)	4.94 (0.58)*

2 Note: Asterisks indicate a significant difference between the baseline and dyspnea condition with
3 *p < .001.
4

1 **Table 3.** Probabilities (SD) in percent for accuracy according to signal-detection theory for the
2 baseline and dyspnea condition.

	Baseline	Dyspnea
Hit rate (H)	0.76 (0.10)	0.77 (0.11)
False alarm rate (FA)	0.12 (0.07)	0.12 (0.07)
Recognition accuracy (Pr)	0.64 (0.13)	0.66 (0.13)
Response bias (Br)	0.31(0.13)	0.32 (0.17)

3 Note: Recognition accuracy ($Pr = H - FA$); Response bias ($Br = p(FA)/p(1 - Pr)$)

Table 4. Means (SD) of reaction times for correctly categorized old and new items for the baseline and dyspnea condition.

	Baseline		Dyspnea	
	Old	New	Old	New
Reaction time, ms*	932.29 (126.79)	982.88 (143.32)	922.39 (128.03)	974.10 (142.09)

Note: Asterisks indicate a significant difference between old and new pictures for both experimental conditions with * $p < .001$.

Table 5. Means (SD) in μV of old-new differences in the ERPs for all latency ranges at fronto-central sites for the left and right hemisphere for the baseline and dyspnea condition.

	Baseline		Dyspnea	
	Left	Right	Left	Right
350-500 ms*	0.79 (0.85)	0.31 (0.95)	0.28 (0.87)	0.29 (1.05)
500-800 ms*	1.32 (0.97) ^a	0.65 (1.21)	0.66 (1.05) ^a	0.59 (1.27)
800-1100 ms*	0.83 (0.98)	0.83 (1.15)	0.43 (1.37)	0.43 (1.31)
1100-1400 ms*	0.20 (1.08)	0.68 (1.24) ^b	-0.27 (1.32)	0.21 (1.36) ^b

Note: Asterisks indicate a significant difference between the baseline and dyspnea condition for the corresponding latency window with $*p < .05$. ^a indicates a significant difference for the left hemisphere with $p < .05$. ^b indicates a significant difference for the right hemisphere with $p < .05$.

Table 6. Means (SD) in μV of old-new differences in the ERPs for all latency ranges at centro-parietal sites for the left and right hemisphere for the baseline and dyspnea condition.

	Baseline		Dyspnea	
	Left	Right	Left	Right
350-500 ms	0.03 (0.85)	-0.14 (0.78)	0.05 (0.84)	0.07 (1.16)
500-800 ms	0.72 (0.93)	0.34 (1.02)	0.54 (0.90)	0.50 (1.32)
800-1100 ms	0.26 (1.23)	0.19 (1.21)	0.44 (1.36)	0.38 (1.40)
1100-1400 ms	-0.24 (1.11)	-0.15 (1.14)	-0.15 (1.17)	-0.12 (1.19)

Figure legends

Figure 1. Illustration of the electrode selection used with permission from Electrical Geodesics, Inc. The electrode selection for the fronto-central left hemisphere, fronto-central right hemisphere, centro-parietal left hemisphere, and centro-parietal right hemisphere is marked in ruby, purple, green, and yellow color, respectively.

Figure 2. Grand average waveforms for the baseline and dyspnea condition combined for the left and right hemisphere at fronto-central (upper panel) and centro-parietal sites (lower panel) for old compared to new items.

Figure 3. Grand average waveforms of the old-new difference wave for the baseline and dyspnea condition combined for the left and right hemisphere at fronto-central (upper panel) and centro-parietal sites (lower panel) with the latency windows 350-500, 500-800, 800-1100, and 1100-1400 ms being marked. Scalp topographies represent old-new differences for both conditions (right panel).

Figure 4. Mean (SE) of old-new difference scores for the baseline and dyspnea condition combined for the left and right hemisphere at fronto-central sites for the latency ranges 350-500, 500-800, 800-1100, and 1100-1400 ms. * $p < .05$.