Abstracts
Proceedings of the 15th Annual Meeting of the International Society for the Advancement of Respiratory Psychophysiology (ISARP)
Ann Arbor, USA, October 5–7, 2008

The fifteenth annual meeting of the International Society for the Advancement of Respiratory Psychophysiology took place in Ann Arbor, Michigan, USA, on October 5–7, 2008. The meeting continued the longstanding tradition of bringing together an international group of researchers from multiple disciplines, such as psychology, physiology, and medicine, who share interests in the research and therapeutic applications of psychological and physiological aspects of breathing. Symposia and poster presentations on a wide variety of topics provided stimulation for engaging discussions between clinical and experimental faculty and students. The meeting had the following foci:

Perception of respiratory sensations

Unpleasant respiratory sensations are a significant component not only of lung diseases, but also of anxiety disorders and of many functional somatic syndromes. The perception of respiratory symptoms is influenced by multiple factors, including peripheral and central nervous system physiology, as well as psychosocial effects including learning and memory, sex, and culture. A number of papers focused on the various influences on respiratory symptom perception and reporting. The first symposium addressed the effects of gender and culture on respiratory symptoms. Mei Lan Han delivered a review of the influence of gender on chronic obstructive pulmonary disease (COPD) symptoms, including both pathophysiological and psychological processes that differ between men and women with COPD. Melissa Valerio spoke about the biological and psychological factors that impact asthma self-management in women. Jonathan Feldman presented results from his research that compared panic disorder comorbidity and symptom reporting between adult Puerto Rican and African American patients with asthma. Finally, Daphne Koinis Mitchell presented the results of her work on differences in parents’ reports of their children’s asthma symptoms between mainland and island Puerto Ricans, as well as across ethnic groups and subgroups.

The second symposium in this focus area addressed neurobiological and psychological mechanisms of respiratory symptom perception. Andreas von Leupoldt presented data from his study examining similarities and differences in brain regions involved in the processing of pain and dyspnea in healthy subjects using fMRI. Bernhard Dahme explained the impact of lesions in the insula cortex on the perception of dyspnea and pain. Sibylle Petersen used a dimensional-categorical approach to analyze language descriptors of dyspnea. Omer Van den Bergh presented results from his research on the peak-end effect on dyspnea memory. Finally, Paul Davenport provided a review of animal studies on the neural substrates of respiratory sensations.

Heart rate variability (HRV) and HRV biofeedback

Beat-to-beat variability in cardiac interval has been used as index of autonomic nervous system activity, as well as index of cardiovascular, and overall health. Clinicians have more recently capitalized on these associations and developed biofeedback protocols to aid patients with a variety of disorders to voluntarily alter HRV for primary and adjunctive treatment purposes. Gabriel Tan and Donald Moss presented an overview of this complex and sometimes controversial field. Dr. Moss went on to describe applications of HRV biofeedback to the treatment of anxiety and mood disorders. Tam Dao described his study of HRV biofeedback in combat veterans with posttraumatic stress disorder.

Respiration in anxiety disorder

Dysregulated breathing has been implicated in a number of anxiety disorders, most notably panic disorder, and breathing interventions are part of many evidenced-based treatments for anxiety. Thomas Ritz presented recent results from his research showing breathing dysregulation in patients with Blood-Injury-Injection (BII) Phobia during exposure to phobic stimuli. Erica Ayala described behavioral treatments for BII Phobia, including a novel intervention targeting hyperventilation in these patients. Alicia Meuret presented results from her study of the effects of cognitive therapy on CO2 changes in patients with panic disorder. Karleyton Evans showed fMRI data from his examination of the synchronization of limbic and paralimbic activity during breathing. Finally, Johan Bresseleers described his findings of the relationship between anxiety and cerebral blood flow changes during normo-, hyper- and hypocapnia.

A number of mini-symposia were also included, with presentations on many interesting topics, including asthma symptom perception, respiration in meditation, and general breathing behavior. Finally, the ISARP Presidential Address was given by Dr. Elizabeth McQuaid, who spoke on the topic of pediatric asthma management, including results from her significant and impressive research program that has examined the role of cultural factors in this area of growing clinical importance.

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**Gender and chronic obstructive pulmonary disease**

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The prevalence of chronic obstructive pulmonary disease (COPD) in women is increasing, as is hospitalization for COPD. The number of women dying of COPD in the United States now surpasses men. Despite this, research suggests that physicians are still more likely to correctly diagnose men with COPD than women. Increased tobacco use in women likely explains some of the increase in the prevalence of COPD in women, but data suggest that women may actually be at greater risk of smoking-induced lung function impairment, more severe dyspnea, and poorer health status for the same level of tobacco exposure. The degree to which these observations represent biologic, physiologic, or sociologic differences is not known. Nonsmokers with COPD are also more likely to be female. In addition, new evidence is emerging that men and women may be phenotypically different in their response to tobacco smoke, with men being more prone to an emphysematous phenotype and women an airway predominant phenotype. Inasmuch as COPD is a disease of inflammation, it is also possible that sexual dimorphism of the human immune response may also be responsible for gender differences in the disease. More data are still needed on what the implications of these findings are for therapy. In this clinical commentary, we present current knowledge regarding how gender influences the epidemiology, diagnosis, and presentation of COPD in addition to physiologic and psychologic impairments and we attempt to offer insight into why these differences might exist and how this may influence therapeutic management.

**Ethnic and gender differences in asthma–panic disorder comorbidity**

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Numerous studies have shown that there is substantial comorbidity between panic disorder (PD) and asthma. It is also important to examine whether ethnic or gender differences exist in the prevalence and types of panic symptoms reported by comorbid patients. The goals of this study were to compare the prevalence of PD between Puerto Rican and African American asthma patients, and to examine the types of panic symptoms reported by women versus men. Participants were 304 adult patients with asthma (aged 18–89 years, M = 44.6 years) recruited from an emergency room and asthma clinic at an inner-city hospital in the Bronx NY. Clinical psychology graduate students assessed PD with a clinical interview using the Prime–MD Patient Health Questionnaire, and follow-up questions to specifically tease apart asthma versus panic attacks. Participants were asked to identify their primary ethnicity. Thirty percent of the sample reported experiencing a panic attack during the last four weeks, and 16.4% of the entire sample met criteria for PD. The two most common symptoms were shortness of breath (91.2%) and heart pounding (92.4%) among asthma-PD patients. Puerto Ricans (21.1%) were more likely to meet criteria for PD than African-Americans (6.3%; p = .002). This effect remained significant after controlling for age. No difference was found between women (17.4%) and men (14.4%) on the prevalence of PD. However, women (M = 3.4) reported more somatic symptoms (e.g., shaking, nausea, dizziness) of panic versus men (M = 2.5), after controlling for age (p = .012). Puerto Rican patients with asthma are at increased risk for having PD. Women appear to be more likely to report somatic symptoms of panic than men among comorbid patients. It is important to develop interventions that are tailored to the specific needs of inner-city, asthma-PD patients.

**Influence of sex and gender on asthma symptoms**

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Recent research related to sex and gender role influences on asthma in women is summarized. Implications for enhancing women’s self-regulation and ability to manage asthma effectively are discussed.

**Recent Findings:** Studies in the past year have indicated that asthma is a significant burden on women and emphasized the importance of control, especially during pregnancy. The significance of hormonal variation in symptoms and severity has been noted. An association between weight and asthma has been observed. Evidence suggests that hormonal changes contribute to the asthma prevalence shift from men to women in adolescence. One study showed positive results of focusing on sex-related and gender-related factors in self-regulation education for women. Recent findings imply that enhancing self-regulation and effective management of asthma in women requires attention to sex and gender role influences in clinical counseling and intervention research.

**Summary:** Clinicians may help female patients with asthma by incorporating sex and gender role related considerations into their clinical consultations. Evidence-based asthma education interventions to assist women with their particular asthma management challenges are needed.

**Ethnic differences in caregivers’ report of children’s asthma symptoms part ii: What do they see, what do they hear, and what do they do?**


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Identifying the mechanisms underlying asthma health disparities among children from specific ethnic groups has been the focus of much research over the past several years. Latino children, and Puerto Rican children in particular, remain at high risk for experiencing asthma morbidity. How individuals’ recognize and report on asthma symptoms has been addressed in previous work; however, less attention has been paid to ethnic group and subgroup differences in how children and parents experience specific asthma symptoms, and how this may be associated with asthma morbidity. This study will describe differences in how parents report on children’s asthma symptoms observed during typical exacerbations across two sites (Mainland Rhode Island and Island Puerto Rico) and across ethnic groups and subgroups (Puerto Rican, Dominican, and Anglo). How these reports differ by level of
The perception of dyspnea and pain involves similar limbic brain structures

A. von Leupoldt, T. Sommer, S. Kegel, H. Jörg Baumann, H. Klose, B. Dahme, C. Büchel

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A dimension–categorical approach to the language of dyspnea

S. Petersen, A. von Leupoldt, T. Ritz

The impact of right insular cortex lesions on the perception of breathlessness and pain

B. Dahme, D. Schör, M. Rosenkranz, J. Regelsberger, C. Büchel, A. von Leupoldt

Recent work has emphasized that dyspnea and pain share many characteristics. Both are subjectively perceived physiological sensations with a similarly alarming and unpleasant character, which signals physical threat. Moreover, similarities in the cortical processing of both sensations have been assumed including activations of the limbic system, but not yet tested. Therefore, this study examined the similarities and differences in the cortical processing of dyspnea and pain by using functional magnetic resonance imaging in fourteen healthy volunteers.

Dyspnea was induced by resistive load breathing. Heat pain was induced with a contact thermode placed below the sternum on the skin surface. The blood oxygen level dependent contrast was measured as an index of brain activity while volunteers received either conditions of dyspnea or pain. Respiration was continuously monitored.

The results showed similar activations of the insula, anterior cingulate cortex, amygdala and medial thalamus during the perception of both dyspnea and pain. Specific activations during resistive load breathing were observed in the sensorimotor cortex and in further areas of the anterior cingulate cortex. Activation of the periaqueductal grey was specific during induced heat pain.

Our findings show that – beside distinct brain activations during perceived dyspnea or pain – the perception of both sensations is associated with prominent activations of a common limbic brain network. The well-known role of the limbic system in emotion processing suggests that this network is underlying the processing of the affective unpleasantness of both dyspnea and pain.

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We found cluster affiliations of single descriptors to vary between subgroups of participants, whereas dimensions of dyspnea provided a more reliable picture of the structure of dyspnea report. Results found with Preference Mapping showed that these dimensions of dyspnea contributed simultaneously to the experience of discomfort related to breathlessness in younger individuals with and without reported respiratory disease, but not in older individuals. Our results suggest that latent dimensions of dyspnea could help to explore the affective evaluation of sensation descriptors and to assess comparability of sensation report between groups.

Memory for dyspnea and how to make it less unpleasant

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Objective: Human memory of the unpleasantness of an experience is dominated by unpleasantness at the peak and at the end and by relative neglect of its duration (peak-end effect). This predicts that remembered dyspnea is less unpleasant by making it ending better, even if it would last longer.

Methods: A group of healthy participants (N = 61) went through two subsequent rebreathing trials consisting of a baseline (60 s room air breathing) and a rebreathing phase (150 s), which gradually increased ventilation, PaCO2 and dyspnea. In one trial, the breathing system (mouthpiece) was removed immediately after peak dyspnea. In the other trial, breathing was switched to room air after peak dyspnea and continued in the breathing system for 150 s. Respiratory behavior was continuously monitored and dyspnea was rated every 10 s by half of the participants.

Results: Two-thirds of the participants preferred to repeat the longer trial, confirming the peak-end rule for dyspnea.

Conclusion: Investigations and interventions causing dyspnea should take care to let dyspnea diminish gradually rather than abruptly, even when this makes the dyspnea episode last longer.

Neural substrates for respiratory sensation—Findings from animal studies

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Respiratory sensations motivate humans to behaviorally modulate their breathing and are the sensory urge component of the respiratory motivation-to-action neural system. Human and animal studies have provided evidence for the neural substrate for afferents in the respiratory tract and muscles to project to the cerebral cortex. What can animal studies tell us about respiratory cognitive sensations and dyspnea? By definition, dyspnea is a cognitive sensory process which requires activation of sensory neural systems to elicit the sensation. Animals and humans have the same respiratory related afferents. In addition, animals have behavioral responses consistent with conscious awareness of respiratory stimuli that are aversive, i.e. hypocapnia and respiratory loads. These are the same stimuli that elicit cognitive respiratory sensations in humans. Thus, animals have similar respiratory related sensory systems and behavioral responses as humans. The advantage of animal studies is the ability to perform specific invasive investigations of neural mechanisms. These studies have provided unique insight into the subcortical and cortical neural mechanisms mediating respiratory sensations. Respiratory afferents transduce breathing pattern into a sensory neural code. This neural code is transmitted to a subcortical gating area. Respiratory sensory information is then transmitted by respiratory modality specific convergent and divergent subcortical pathways to the cerebral cortex. There are two primary cortical pathways: (1) the discriminative pathway related to respiratory proprioception, (2) the affective pathway related to the qualitative assessment of breathing. The significance of respiratory sensory information processing is the fundamental intersensory perception of ventilatory status.

Overview of heart rate variability (HRV) and HRV biofeedback

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HRV is a measure of beat-to-beat variations in heart rate, usually calculated by analyzing a time series of beat-to-beat intervals from ECG. Measures include time domain measures (SDNN, rMSSD and pNN50); frequency domain measures: HF (0.15–0.4 Hz), LF (0.04–0.15). Respiratory sinus arrhythmia (RSA) is the natural cycle of arrhythmia that occurs through the influence of breathing on the flow of sympathetic and vagus impulses to the sinoatrial node. Rhythm of the heart is controlled by the vagus nerve; vagus nerve is impeded when we inhale resulting in increased HR; reverse occurs when we exhale; fluctuation is controlled by regular impulses from baroreceptors in the aorta and carotid arteries. HRV is important because it provides a window to observe the heart’s ability to respond to normal regulatory impulses that affect its rhythm. Several prospective studies have shown that HRV independently predicts mortality within two years following a heart attack. HRV decreases with age and is lower among people who have an inactive lifestyle and among those with medical conditions such as coronary heart disease, HTN, and diabetic neuropathy. HRV has also been shown to be depressed among those with anxiety disorders, PTSD, depression, asthma, and fibromyalgia.

RSA can be enhanced through biofeedback to reinforce the natural feedback activity of the baroreceptors through breathing at resonant frequency.

Breathing dysregulation in blood-injury-injection phobia during exposure

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For some time, blood-injury-injection phobia (BIIP) has been known to be linked to fainting. However, little progress has been made in elucidating triggers and mechanisms that contribute to fainting behavior in patients during exposure to feared stimuli. A number of studies have explored autonomic adjustments to exposure, revealing a typical vasovagal response pattern with sharp decreases in blood pressure and heart rate. Until recently, little was known about the accompanying respiratory adjustments. In an initial study, we found evidence for phasic hyperventilation in patients during exposure to surgery films, with values of end-tidal pCO2 dropping below 30 mmHg, in comparison to other emotional film material as well as to healthy controls. Because hypocapnia leads to cerebral vasoconstriction, low pCO2 may pose a risk factor for developing a fainting response. In a new study, we sought to replicate these initial findings, explore how long hypocapnia is
sustained, and compare patients’ responses to surgery films with disgusting film material. Sixty BII patients viewed film clips inducing happiness, sadness, anger, disgust, and a neutral emotional state, as well as a surgery film. Respiration, including end-tidal pCO2, was measured continuously during films and their subsequent 1 min recovery periods; for surgery films, recovery measurements were extended across 5 min. As expected, patients showed significantly lower pCO2 during the surgery film compared to other films, with pCO2 dropping below 30 mmHg for 30 patients. pCO2 levels were also reduced during the disgust film but tended to be lower during the surgery film. Patients’ pCO2 recovered readily after the disgust films, whereas for surgery films, low pCO2 continued throughout the 5 min recovery period. Thus, hyperventilation is common in BII during exposure to feared stimuli and sustained for a considerable time period afterwards. More research is warranted exploring the contribution of hyperventilation to vasovagal fainting in BII patients.

Behavioral treatments for blood-injury-injection phobia: Current evidence and a novel approach targeting hyperventilation

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Blood-injury-injection (BII) phobia is unique in its physiological response pattern, with a great number of sufferers reporting a history of fainting when exposed to BII-relevant stimuli. The current treatment recommendation is applied tension (AT), a technique aimed at counteracting a biphasic response (fainting) by increasing venous return to the heart and brain through tension of the skeletal muscles. However, clinical outcome research is limited to five studies, all from the same research group, with results yielding superiority to AT compared to other approaches such as applied relaxation (Ayala et al., submitted for publication). The present ongoing study sought to replicate and extend previous research by demonstrating the efficacy of a single session of AT in comparison to a technique specifically aimed at reducing hyperventilation. Hyperventilation, as indicated by low levels of pCO2, has been found to be prevalent in patients with BII phobia during exposure (Ritz et al., 2005). Because hyperventilation constricts cerebral vessels, it may be a critical factor in developing a fainting response to BII-relevant stimuli. Fifty-eight BII patients were randomly assigned to learn one of the following techniques: AT, a counter-hyperventilation technique (BRT), or relaxation (R). We examined each technique’s effect on anxiety, disgust, end-tidal pCO2, and symptom levels during exposure to film clips selected to elicit different emotions, including a phobic response to surgical films. Significant group differences emerged for both the ability to apply the technique and its usefulness; although participants in the AT group reported the highest success in application, BRT was viewed as equally helpful in reducing the phobic response. Overall, the techniques resulted in strong reductions in anxiety, disgust, and physical symptoms such as faintness, lightheadedness, and dizziness, as well as an increase in feelings of control. Patients undergoing BRT reached higher levels of pCO2 during exposure to a BII-related test film than the other groups. Group differences in reductions in anxiety approached significance, with AT and BRT performing similarly compared to R, which showed minimal improvement. No other significant differences were found between the groups. Preliminary findings suggest that BRT may be a useful treatment for BII phobia. Further research should explore the potential of BRT in preventing fainting responses in BII phobia patients under in vivo exposure.

References


Event-related fMRI reveals synchronized limbic and paralimbic activity with each breath

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Limbic and paralimbic circuitry has been implicated in several recent neuroimaging studies of respiratory provocation in humans. Stimulation of this circuitry in animals and humans results in dramatic changes in tidal volume (VT) and respiratory rate (RR). Yet the extent of resting state limbic involvement in humans is unknown. The present blood oxygen level dependent functional magnetic resonance imaging (BOLD-fMRI) study sought to probe limbic, paralimbic and brainstem circuitry for neural activity synchronized with resting spontaneous breathing.

Fourteen healthy subjects underwent BOLD-fMRI with simultaneous physiological monitoring (heart rate (HR), RR, VT, end-tidal CO2 (pCO2)) during resting spontaneous breathing. Imaging data were analyzed with SPM5. Each respiratory phase transition served as the independent input variable for event-related fMRI time-series analyses conducted with stringent regional thresholds (reflecting Bonferroni-type correction).

The group mean physiological data were consistent with published data: HR = 60.8 ± 9.1 beats/min, RR = 14.6 ± 2.7 breaths/min, VT = 0.41 ± 0.18 l/breath and pCO2 = 39.44 ± 0.75 mmHg. Voxelwise, group image analyses demonstrated significant neural activation during respiratory transitions within amygdala, anterior cingulate, anterior insula, thalamus, basal ganglia, cerebellum, midbrain andpons. Respiratory synchronized activity was also observed in the medulla however only at an exploratory, uncorrected threshold.

The present findings provide the first evidence for synchronized neural activity across a distributed network of limbic, paralimbic and brainstem regions during resting spontaneous breathing in humans. Further, the present findings extend earlier stimulation studies and are supported by recent neuroanatomical tract-tracing observations of reciprocal connections between the brainstem and limbic/para-limbic circuits. Taken together with other emerging neuroimaging findings, we speculate that the identified limbic/paralimbic circuitry plays a significant role in cognitive and affective influences on breathing in healthy individuals as well as in patients with cardio-pulmonary and anxiety disorders.

Changes in panic cognitions, perceived control, and respiratory physiology in cognitive versus respiratory therapy: Specificity and temporality

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Various theories in panic disorder suggest different pathways of treatment success. Among the most prominent psychological
mechanisms for treatment success is the presumed change of maladaptive cognition, whereas prominent biological theories suggest the corrections of maladaptive biological markers, such as respiration. However, little is known about why certain treatments work and whether the assumed change is related to the proposed mechanism of a specific theory.

Here we report on a study that was aimed at assessing changes over time in physiology (pCO₂, respiration rate), panic related cognitions (anxiety sensitivity, misappraisal of bodily sensations), perceived control, and overall panic severity. Changes were measured continuously throughout a 4-week treatment aimed at exclusively changing cognitions (CT: N = 20) or respiration (such as hypocapnia and respiration irregularities; BRT: N = 21).

Treatment was equally successful in both treatments, with significant reduction on all psychological measures. BRT led to a correction of initial hypocapnia to normocapnic levels; CT, however, did not. In BRT, changes in pCO₂ mediated and preceded changes in panic related cognitions, perceived control, and panic severity for patients who reported high levels of symptoms at pretreatment. In CT, changes in misappraisal were associated with, but did not precede, changes in perceived control. Surprisingly, neither changes in panic related cognitions nor changes in perceived control were generally associated with changes in panic severity.

This is the first study to examine mechanisms of change in core aspects of panic symptoms in theoretically different interventions. Changes in pCO₂ confirmed the importance of respiratory pathways in our BRT treatment for PD. Only limited evidence was found for a cognitive pathway of change in PD treatment.

**Anxiety and cerebral blood flow in normo-, hyper- and hypocapnia**

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Only a few studies have investigated the link between anxiety and global cerebral blood flow (CBF), leading to conflicting results. Anxiety has been found to have either no effect, or to cause an increase or a decrease in CBF. Furthermore, different studies applied different anxiety manipulations, often using a stimulus which influences CBF on its own (such as CO₂). A possible mechanism in the relationship between anxiety and CBF is through the sympathetic nervous system. Sympathetic activity has been found to decrease CBF, especially under hypcapnic conditions.

In the present study we aimed to investigate the effect of anxiety on CBF under different levels of CO₂. Anxiety was manipulated using threat-of-shock: participants were told that they could receive multiple shocks. In fact, only one shock was given in the first two threat trials, near the end of the trial. The experiment consisted of three types of trials. A room-air breathing trial, a 7.5% CO₂-inhalation trial, and a hypocapnic trial in which participants were instructed to breathe as deep as possible at a rate of 30 breaths/min. Each participant received the three breathing trials in both the safe and the threat-of-shock condition. The order was counterbalanced. Anxiety was measured after each trial with the STAI-S and an ad hoc rating scale. A pneumotachograph and an infrared capnometer were used to measure breathing parameters and end-tidal CO₂. CBF velocity was measured using a Transcranial Doppler.

Under normocapnia, a significant but small CBF increase was found during threat-of-shock. Because threat-of-shock did not increase anxiety in the hypocapnic trials, a regression analysis was used, which showed a different effect of anxiety on CBF under hypocapnic conditions. Whereas anxiety increased CBF under normocapnia, it decreased CBF under hypocapnia. Because these last results are correlational, further research on this matter is needed.

**Effects of feedback on the detection of inspiratory resistive loads in children with persistent asthma: An ROC approach**

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The purpose of the present paper was to evaluate receiver operating characteristics (ROC) graphs in children with asthma 8–15 years of age who were assigned randomly to one of two resistive load training conditions in a signal detection paradigm: training with immediate performance feedback or training with no performance feedback. An ROC graph is a way to depict performance in a task based on the tradeoff between hit rates and false alarm rates.

Thirty-nine children were assigned randomly to training with feedback and thirty-one to training without feedback. In each of three separate sessions, children participated in a signal detection task comprised of 100 trials. Each session consisted of 50 signal (resistive load present) and 50 non-signal (no resistive load) trials. Children were asked to determine if an increase in the resistance to breathing occurred on each target inspiration. The children assigned to the feedback condition were given immediate feedback regarding the accuracy of their responses. The children assigned to the no feedback condition were treated similarly except they were not given information regarding the accuracy of their responses. After each trial, the child was asked to select the level of confidence, on a five-point scale (very confident, mostly confident, somewhat confident, not really confident, not at all confident), that most closely characterized the child’s judgment.

We determined ROC graphs for both groups based on hit and false rates for each level of confidence for each trial for all sessions. In separate analyses, the area under the ROC curve (AUC) was used as a common scalar to compare performance in the two groups. Children in the feedback condition exhibited greater sensitivity to added resistive loads compared to children in the no feedback condition but children in both conditions exhibited performance considered “conservative” (i.e., true positive decisions were based on strong evidence for the presence of a signal).

Feedback training results in improved sensitivity to increases in airflow obstruction in asthmatic children. The improvement occurred despite the reluctance of children to identify a signal in the absence of any but the strongest evidence of its presence. Supported by NIH/NHLBI R01HL068706.

**Inaccurate perception of asthma symptoms during a modified histamine challenge test**

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Low congruence of asthma symptoms and objective measures of lung function is often found in asthma and is considered an important factor in asthma morbidity. Expectancy and affective variables appear to play an important role. In a modified histamine challenge test, we assessed the influence of contextual variables on the perception of
asthma symptoms in order to identify persons with a tendency towards inaccurate perception of asthma symptoms. Participants were patients referred for a histamine challenge test to confirm asthma diagnosis. They underwent a modified histamine challenge protocol. After inhaling doubling dosages of histamine until 20% decrease in FEV1 was observed, an identical inhalation containing albuterol followed, which was not told to the participants. Therefore, a placebo inhaler was given – which was described as a typical albuterol inhaler – in order to restore symptom levels. After each inhalation, we assessed lung function and both the intensity and valence of the perceived respiratory distress. Before the histamine challenge, patients filled out questionnaires measuring trait negative affectivity (NA) and asthma symptoms in daily life.

Differences in perceptual sensitivity to histamine (sensitivity slopes) were not related to differences in NA. There was a trend towards an influence of NA on overall differences in symptom perception ($p = .15$). Specific tests for the influence of the masked albuterol inhalation on symptom levels show a moderating effect of NA on this relationship ($p < .05$). No significant results were obtained in response to the placebo inhaler.

Preliminary results suggest that the modified histamine challenge test may be used during the assessment of asthma to routinely detect inaccurate perception of asthma.

### Meditation for health purposes: On the importance of breathing

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Emphasis on respiration is central to most forms of meditation. Some deliberately employ undisturbed breathing pattern as object of investigation (e.g. mindfulness), others aim to actively or passively modify ventilatory parameters (Yoga or mantra meditation). Whatever the form of orientation to breathing, meditation practices appear to influence specific respiratory variables, psychological parameters and physiological patterns of central nervous system activity and of autonomic traffic to the periphery. Reviewing my own research findings and those of others, this presentation provides empirical evidence of such alterations. Respiratory effects include decreased respiration rate and greater tidal volume and regularity, whereas autonomic consequences appear to comprise enhancement of cardiac vagal responsiveness and reduction of sympathetic nerve traffic. Psychological benefits of meditative orientation to breathing appear to be improved mood and reduced anxiety. These findings suggest that respiratory processes may play a central role in mediating those positive health improvements sometimes attributed to meditative practices.

**Every breath you take: event-related fMRI identifies cortico-limbic-bulbar circuity modulation with breathing during meditation**


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Mindfulness meditation (MMED) involves focused awareness, often attention to breathing. Dramatic decreases in respiratory rate (RR) have been reported during MMED, and are thought to be mediated via the limbic system. Recent neuroimaging studies have implicated limbic neural circuity during meditative states. We have previously identified greater thickness of the insular cortex in MMED practitioners compared to controls, where the magnitude of thickness correlated with years of MMED practice. Given these findings, together with the established pontine role in bradypnea, we sought to use blood oxygen level dependent functional magnetic resonance imaging (BOLD-fMRI) to test a hypothesis of cortico-limbic-bulbar breathing modulation during MMED.

Nine MMED practitioners underwent BOLD-fMRI with physiological monitoring (heart rate, RR, airflow, end-tidal CO$_2$) during MMED, and a control condition of paced breathing (PACE, cued to MMED RR). Imaging data were analyzed with SPM5. Each respiratory phase transition served as the independent input variable for event-related fMRI time-series analyses conducted with stringent regional thresholds (reflecting Bonferroni-type correction). Mean RR was not different between MMED and PACE conditions, yet slower than the MMED subjects’ resting breathing. Potentially confounding variables (e.g. $p_{CO_2}$ heart rate) were not different across conditions. Voxel-wise $t$-tests demonstrated differential activation (MMED > PACE) within the anterior insula, motor cortex, parietal cortex (precuneus) and pons during respiratory transitions.

This is the first neuroimaging study to implicate respiratory synchronized cortico-limbic-bulbar activity during MMED. The insular cortex has been previously implicated in respiratory sensation. Simultaneous insular-bulbar activity has been observed during volitional breath-hold. The parietal/precuneus regions seen here have not previously been associated with respiratory control but have been implicated in MMED. Taken together the present findings of exaggerated cortico-limbic-bulbar activity synchronized with respiratory transitions during MMED suggests this circuity modulates bradypneic breathing during MMED.

### Pediatric asthma management: Culture and context ISARP presidential address, 2008

**E.L. McQuaid**

**Brown Medical School/Rhode Island Hospital, United States**

**Background:** Management of pediatric asthma occurs within the family context. Families of varying demographic backgrounds bring cultural attitudes and beliefs toward illness that may exert effects on how they perceive and manage illness. Key findings from a program of research and clinical intervention that has examined the role of cultural factors in pediatric asthma management is provided.

**Method:** Studies from the Childhood Asthma Research Program are reviewed. These include clinical data from an asthma education program ($N = 677$), and data from a cross-site study (RI and PR) of asthma disparities ($N = 802$; the RPRAC study).

**Results:** Data indicate that, relative to African Americans and non-Latino whites (NLWs), Latinos express more fear regarding asthma, despite similar levels of asthma control ($F = 6.94$, $p < .001$). When evaluated using a standardized symptom perception paradigm, Latino children report a greater degree of asthma symptoms relative to objective lung function than NLW children ($F = 27.53$, $p < .001$). Latino parents also express different beliefs about the efficacy of asthma medication and concerns about medication safety, with Island PR parents expressing the least favorable attitudes (low medication necessity, high concern), followed by RI Latino parents, and NLW parents having the most favorable attitudes ($F = 29.43$, $p < .001$). Objective data regarding adherence to controller medications follows a similar pattern, with Island PR families demonstrating the lowest use of medication,
followed by RI Latino families, with NLW families using medications most frequently ($F = 10.12$, $p < .01$).

Conclusions: Research programs investigating chronic illness management will increasingly need to account for cultural differences in attitudes toward symptoms, medication, and disease. Differences in disease management by culture should be interpreted within the context of the family, their economic resources, and the health care system.

Nijmegen Questionnaire—revisited

J. van Dixhoorn

The Nijmegen Questionnaire NQ is a short questionnaire (16 items, score range 0–64) that is being used to assess hyperventilation complaints and/or ‘dysfunctional breathing’. However, its validity is questionable, since there is no independent criterion to assess either hyperventilation complaints or dysfunctional breathing.

It will be argued, that NQ is valid as a tool to assess complaints that result from excess tension, particularly in the respiratory system. First, normal values have been established, which range from 10 to 12 (standard deviation about 6). Second, patients with complaints that have no apparent specific cause, but are related to tension and anxiety, have markedly elevated scores. Thirdly, when such patients are treated with tension reducing techniques, centering around breathing (‘breathing and relaxation therapy’), the scores normalize when treatment is successful to solve the problem. However, when external causes appear to exist, that block successful treatment by such treatment, scores lower somewhat, but do not normalize. That constitutes a reason for further diagnostic and therapeutic procedures. Data will be presented from more than 500 patients to support this.

It is concluded that NQ is useful as a screening tool to detect complaints that may be due to excess tension. Breathing and relaxation therapy can confirm or reject that possibility and NQ is useful to evaluate treatment outcome.

The effect of mental stress on sigh rate and respiratory variability


Background: Physiologically, sighing is assumed to prevent atelectasis and restore lung compliance. Its psychological functions are unknown. Paradoxically, sighing has been related both to stress and anxiety, and to relief and relaxation. The hypothesis that sighing relieves tension predicts that sighing is increased (a) following brief periods of stress, and (b) during more sustained stress periods as an attempt to reduce tension. Previous experiments (Vlemincx et al., 2009) have confirmed that sighing occurred more frequently during brief periods of relief compared to brief periods of stress. The present study aimed to examine the occurrence of sighing during sustained periods of stress.

Method: Participants ($N = 43$) went through a 6 min baseline trial, followed by three trials (presented in randomized order) consisting of a 6 min task followed by a 6 min recovery phase. The three tasks consisted of two mental arithmetic tasks (MAT, involving 3-digit number calculations) and one postural task (PT, indicating the largest number in a series with a mouse). One of two MAT was followed by the instruction to sigh within the next 20 s. Respiration was recorded using the LifeShirt System.

Results: MAT elicited increases in respiration rate (RR) and more ribcage breathing compared to the subsequent recovery phases and baseline, suggesting that stress was successfully induced. Compared to baseline, more sighing occurred during MAT and during recovery after PT. Whereas MAT was characterized by increased coefficient of variation (CV) and low autocorrelation of RR, PT was marked by lower CV of RR compared to baseline.

Conclusion: Increased sighing was found (a) following phases during which respiratory variability was low, possibly to restore effects of atelectasis, and (b) during sustained stress (which was marked by high respiratory instability) possibly to reduce tension. Further analyses will clarify how respiratory dynamics change preceding and following individual sighs.

Reference


Threats from within the body: Interoceptive conditioning of fear to respiratory cues

M. Pappens, I. Van Diest, D. Vansteenwegen, S. De Peuter, O. Van den Bergh

Department of Psychology, University of Leuven, Belgium

Background: Interoceptive fear conditioning to respiratory cues in humans has hardly been investigated, despite its great potential to understand the relationship between respiration and fear, particularly panic. We investigated whether loaded breathing can be applied to establish interoceptive conditioning of fear.

Methods: The interoceptive aversive US consisted of 30 s of restricted breathing as induced by adding a resistive load of 40 cmH2O/l/s to the breathing circuit. This US was consistently preceded by a 8 s picture in one group (extero–intero pairing), and by a weak load (8 s, 10 cmH2O/l/s; interoceptive CS) in another group (intero–intero pairing). Control groups received the same amount of CSs and USs in an unpaired fashion. Self-reported fear, electrodermal responses and startle blink EMG responses were assessed during 6 acquisition and 6 extinction trials.

Results: The interoceptive CS evoked overall larger electrodermal responses than the exteroceptive CS. Conditioning of electrodermal responses (paired > unpaired), however, occurred for the extero–intero, but not for the intero–intero pairings. Startle blinks were larger throughout the entire experiment in the unpaired compared to the paired conditions. Intragroup comparisons showed that blinks during CS presentations were enhanced relative to intertrial intervals (ITI’s). This was more the case for the paired compared to the unpaired group, and for the exteroceptive compared to the interoceptive CS.

Conclusion: Fear conditioning was established with the extero–intero, but not with the intero–intero pairings.

Can neuropsychological complaints and a decrease in cerebral blood flow be learned? A conditioning study

J. Bresseleers, I. Van Diest, P. Verhamme, O. Van den Bergh

Background: Neuropsychological complaints such as lightheadedness are prominent in various syndromes, such as panic disorder and in functional syndromes, such as idiopathic environmental illness. The

Method: Participants ($N = 43$) went through a 6 min baseline trial, followed by three trials (presented in randomized order) consisting of a 6 min task followed by a 6 min recovery phase. The three tasks consisted of two mental arithmetic tasks (MAT, involving 3-digit number calculations) and one postural task (PT, indicating the largest number in a series with a mouse). One of two MAT was followed by the instruction to sigh within the next 20 s. Respiration was recorded using the LifeShirt System.

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Conclusion: Increased sighing was found (a) following phases during which respiratory variability was low, possibly to restore effects of atelectasis, and (b) during sustained stress (which was marked by high respiratory instability) possibly to reduce tension. Further analyses will clarify how respiratory dynamics change preceding and following individual sighs.

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Results: The interoceptive CS evoked overall larger electrodermal responses than the exteroceptive CS. Conditioning of electrodermal responses (paired > unpaired), however, occurred for the extero–intero, but not for the intero–intero pairings. Startle blinks were larger throughout the entire experiment in the unpaired compared to the paired conditions. Intragroup comparisons showed that blinks during CS presentations were enhanced relative to intertrial intervals (ITI’s). This was more the case for the paired compared to the unpaired group, and for the exteroceptive compared to the interoceptive CS.

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Background: Neuropsychological complaints such as lightheadedness are prominent in various syndromes, such as panic disorder and in functional syndromes, such as idiopathic environmental illness. The
considerable overlap with symptoms of hyperventilation gave rise to the clinical working model that stress-induced hyperventilation may cause these complaints through cerebral vasocostriction. However, the model has been partly discredited after it was found that reductions in PaCO2 did not temporarily coincide with symptom reports (Hornsveld et al., 1996). The current study aimed to replicate the finding that lightheadedness can be learned as a result of episodes of hyperventilation (Van Diest et al., 2006). Furthermore, we wanted to investigate whether conditioning of cerebral vasocostriction to hyperventilation was possible.

Method: Diluted ammonia and acetic acid were used as conditional stimuli (CS) in a differential conditioning paradigm. One odor was paired with three hypocapnic overbreathing trials ("hyperventilating"; CS+), the other odor was paired with three normocapnic overbreathing trials (CS−) during which CO2 was added to the breathing circuit to keep individual end-tidal CO2 levels within the normocapnic range. In the test trials, both odors were presented once in a normocapnic overbreathing trial and once in a spontaneous breathing trial.

Results: In the test phase, participants rated higher levels of lightheadedness after both CS+ trials compared to CS− trials. Participants experienced lightheadedness sooner in the normal breathing CS+ trials and tended to experience lightheadedness sooner in the overventilation CS+ trial compared to the corresponding CS− trials. In the overventilation CS+ trial, participants also rated higher maximum levels of lightheadedness compared to the overventilation CS− trial. However, no differences were found in the test phase on cerebral blood flow, suggesting that learned lightheadedness is mainly the result of symptom perception processes.

Conclusions: This study shows that lightheadedness can be conditioned after only three learning episodes. This finding supports a learning model of neuropsychological complaints.

References

Preliminary investigation of a measure of dysfunctional breathing symptoms: The Self Evaluation of Breathing Questionnaire (SEBQ)

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Introduction: Dysfunctional Breathing (DB) is sometimes defined by the presence of unexplained breathing symptoms however validated questionnaires to comprehensively evaluate all dimensions of breathing symptoms proposed to be associated with DB have not been extensively developed. This paper discusses the development and exploration into the dimensions of a preliminary questionnaire, the Self Evaluation of Breathing Questionnaire whose items are derived from a popular Internet questionnaire for evaluating breathing functionality and breathing symptoms proposed in the scientific literature to be discriminative for DB. Method: The 17 item SEBQ was administered to 83 adults. Exploratory Factor Analysis was performed and correlations made between the SEBQ and the Nijmegen Questionnaire (NQ), which is a validated questionnaire for hyperventilation syndrome. Results/Discussion: Two dimensions were found in the SEBQ. One dimension named “lack of air” appears to reflect sensations of air hunger that may relate more to chemoreceptor aspects of breathing sensation. The other dimension named “perception of inappropriate or restricted breathing” appears to reflect sensations and observations about the work of breathing may relate more to the biomechanical aspects of breathing sensation. The correlations of agreement between the SEBQ, which assesses respiratory symptoms, and the NQ, which assesses respiratory and somatic symptoms of Hyperventilation were 0.6 when for the 17 item SEBQ and 0.3 for the final 12 item SEBQ which contained the strongest items of the two dimensions. Conclusion: Breathing symptoms associated with dysfunctional breathing arising from predominately biomechanical aspects of breathing might be distinguishable from symptoms arising from factors reflecting chemoreceptor input. The two dimensions of the SEBQ may represent related but distinct aspects of dysfunctional breathing symptoms that appear different to those assessed by the Nijmegen Questionnaire. The SEBQ may be a useful clinical assessment tool that can impact on the assessment and treatment of DB. The results of this study may be used to inform future development of a questionnaire to assess dysfunctional breathing.

Effects of feedback on the correspondence between estimated and actual PEFR in children with persistent asthma

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The correspondence between subjective and objective indicators of asthma varies widely in both children and adults. We include as part of a large-scale pediatric asthma education program (Project On TRAC: Taking Responsibility for Asthma Control) a rigorous test of the effects of asthma home monitoring on the correspondence between actual and estimated peak expiratory flow rate (PEFR) in children ranging between 8 and 15 years of age with moderate to severe persistent asthma. In this paper we report on results obtained from an initial cohort of program participants who measured PEFR values for 15 days or longer.

Patients completed symptom diaries and recorded both estimated and actual peak flow on an electronic meter (Jaeger, AM2+) in the morning and in the evening, for 30 consecutive days, following three sessions of asthma education. Participants were assigned randomly to one of two peak flow monitoring conditions: half the children (n = 44) were provided meters that recorded and displayed both estimated and actual peak flow scores each day (feedback group); the remaining children (n = 43) were provided meters that recorded both estimated and actual peak flow scores but displayed only estimated values to participants (no feedback group).

In each group recorded PEFR values for essentially identical numbers of days (25.68 and 25.60 in the feedback and no feedback groups, respectively). Using normalized correlation coefficients, we observed significantly greater levels of correspondence (r(85) = 2.75, p = .007) between estimated and actual peak expiratory flow rate in the feedback group (M = 0.32) compared to the no feedback group (M = 0.12).

We conclude that daily monitoring of peak flow results leads to greater levels of correspondence between estimated and actual indicators of lung function than does recording PEFR without knowledge of results.

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Implicit negative evaluation of asthma-related words in asthma patients and healthy individuals: The role of self-categorization and negative affect

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Background: We explored the implicit evaluation of asthma-related cues via reaction times in individuals suffering from asthma and healthy individuals. Furthermore, we explored the role of the degree of self-categorization as asthma patient in the association of implicit evaluation of asthma-related stimuli with negative affect.

Methods: Participants were individuals suffering from asthma and healthy controls. We assessed implicit attitudes towards asthma cues in a Single Target Implicit Association Test. Furthermore, we asked our participants to complete questions on asthma-specific coping strategies, beliefs about medication, degree of self-categorization as asthma patient and negative affect.

Results: Individuals reporting an asthma diagnosis evaluated asthma-related word stimuli significantly more negative than individuals without any reported chronic disease. Implicit negative evaluation of asthma-related word stimuli by participants reporting asthma was positively related to the report of concerns about medication, worries about asthma, and ignoring asthma. Implicit negative evaluation of asthma-related word stimuli was negatively related to self-categorization as asthma patient and positively to trait negative affect. Furthermore, trait negative affect was negatively related to degree of self-categorization.

Conclusion: These findings confirm results of studies which found reaction times to asthma-related word stimuli to be related to self-reported compliance with asthma medication and coping behavior. Furthermore, our results suggest that degree of self-categorization as patient might play an important role in the relationship between negative affect and reported disease management.

No peak-end effect in patients with medically unexplained dyspnea

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Objective: Remembered dyspnea is less unpleasant if the dyspneic episode is ending gradually compared to abruptly, even if it lasts longer (peak-end effect). We investigated whether patients with medically unexplained dyspnea (MUD) also showed this typical memory bias.

Methods: The Rebreathing test was administered to a clinical sample with MUD and a matched healthy control group (total \( N = 58 \)). All participants received two subsequent rebreathing trials consisting of a baseline (60 s room air breathing) and a rebreathing phase (150 s), which gradually increased ventilation, \( \text{PaCO}_2 \) and dyspnea. In one trial, the breathing system (mouthpiece) was removed immediately after peak dyspnea. In the other trial, breathing was switched to room air after peak dyspnea and continued in the system for 150 s. Respiratory behavior was continuously monitored and dyspnea was rated every 10 s.

Results: Patients with MUD showed deficient recovery of self-reported dyspnea compared to controls that could not be explained by differences in respiratory behavior. Whereas two-thirds of the healthy group preferred to repeat the longer trial (peak-end effect), patients with MUD did not show such preference.

Conclusion: Both effects, slowed recovery in perceived dyspnea and absence of the peak-end effect, suggests important differences in perceptual and cognitive processing of dyspnea in patients with MUD compared to healthy controls.

The unpleasantness of dyspnea is processed in the human anterior insula and amygdala

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Recent research has demonstrated that the subjective perception of dyspnea consists of sensory (intensity) and affective aspects (unpleasantness). However, little is known about the brain areas that process these distinct aspects of perceived dyspnea. Therefore, we examined the cortico-frontal areas associated with the processing of the affective unpleasantness of perceived dyspnea by using functional magnetic resonance imaging (fMRI) in fourteen healthy volunteers.

While volunteers laid supine in the scanner, dyspnea was induced by inspiratory resistive load breathing with concomitant positive and negative emotional stimulation by viewing emotional picture series (Lang et al., 1999). The blood oxygen level dependent contrast (BOLD) was measured as an index of local neuronal activity while respiration was continuously monitored.

Negative emotional stimulation during resistive load breathing was associated with higher unpleasantness of perceived dyspnea when compared to resistive load breathing with concomitant positive emotional stimulation (47.4 vs. 32.9, \( p < 0.05 \)). The intensity of perceived dyspnea, resistive load magnitude and respiratory responses were similar between both conditions. Higher unpleasantness of dyspnea was related to neuronal activations in the right-hemispheric anterior insula and in the right-hemispheric extended amygdala (\( p < 0.05 \)).

Our findings are in line with previous theoretical assumptions suggesting that the affective unpleasantness of perceived dyspnea is related to activations of limbic system structures such as the right anterior insula and amygdala.

Reference