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CONFERENCE PROGRAM

Symposium: Methods in Respiratory Psychophysiology
Chair: *Richard Gevirtz*

Olaf Holz

Panel Discussion:
5.) **Continuous Physiological Monitoring: Methodological and Statistical Implications**
Chair: *Bernhard Dahme on behalf of Michael Coyle*

Workshop 1
6.) **Psychological Treatment for Comorbid Asthma and Panic Disorder**
Paul Lehrer & Jonathan Feldman

Workshop 2
7.) **Internal and External Assessment of Respiratory Mechanics**
Michael Goldman

Workshop 3
8.) **Treatment and Psychological Factors in COPD**
Frank Kannieß, Kai Richter, Hans-Jörg Baumann, Karin Taube, Stephan Schubert-Heukeshoven.

INVITED ADDRESS
Chair: *Bernhard Dahme*
9.) **Hygiene Hypothesis of Asthma**
Helgo Magnussen

Symposium: Symptom Perception in Pediatric Asthma
Chair: *Andreas von Leupoldt*

10.) **Factors that predict sensitivity to inspiratory resistance in children with moderate-to-severe asthma:**
Not the usual suspects
Andrew Harver, Allison McLacklan, Harry Kotses, Lori Thurber, C. Thomas Humphries

11.) **In search of protective processes for children with asthma:**
Does accurate symptom monitoring make a difference?
Daphne Koinis Mitchell, Elizabeth McQuaid, Sheryl Kopel, Jack Nassau, Robert Klein, Marianne Wamboldt, Gregory Fritz

12.) **Psychiatric symptoms and pediatric asthma morbidity:**
The roles of symptom perception and family management
Elizabeth McQuaid, Daphne Koinis Mitchell, Sheryl Kopel, Jack Nassau, Robert Klein, Marianne Wamboldt, Gregory Fritz

13.) **A comparison of resistive loading and in vivo approaches to assessing symptom perception in pediatric asthma**
Gregory Fritz, Sue Adams, Elizabeth McQuaid, Robert Klein, Sheryl Kopel, Jack Nassau, Marianne Wamboldt, Anthony Mansell

14.) **Symptom perception and asthma morbidity in pediatric asthma**
Jonathan Feldman, Gregory Fritz, Elizabeth McQuaid, Sheryl Kopel, Robert Klein, Anthony Mansell, Marianne Wamboldt

INVITED ADDRESS
Chair: *Elizabeth McQuaid*

15.) **Achievements in Understanding the Neurobiology of Breathlessness (1954-2005)**
Abraham Guz

Symposium: Distinct Components and Central Nervous System Processes of Dyspnea
Chair: *Andrew Harver*

16.) **Differentiation between the sensory and affective dimension of induced breathlessness**
Andreas von Leupoldt, Bernhard Dahme

17.) **The perception of sensory and affective components of dyspnea induced by a histamine provocation test.**
Omer Van Den Bergh, Steven de Peuter, Valentine Lemaigre, Geert Verleden, Katleen Bogaerts, Wan LI, Ilse van Dies

18.) **Relief of dyspnea and pleasantness associated with breathing: Similarities and differences - preliminary results**
Claudine Peiffer, N. Costes, P.H. Herve, L. Garcia-Larrea

19.) **The resistive (R) load threshold for respiratory related evoked potentials (RREP)**
Paul W. Davenport, Pei Ying Chan, Yang Ling Chou, Weirong Zhang
Go to Paper

20.) **Respiratory related evoked potential (RREP) measures of respiratory sensory gating**
Pei Ying Sarah Chan - Winner of a Student Award
Pei Ying Chan, Yang Ling Chou, Paul W. Davenport

VivoMetrics INVITED ADDRESS
Chair: *Andreas von Leupoldt*

21.) **Neurophysiology of Dyspnea**
Robert Banzett

Symposium: Association between gas exchange and psychological factors
Chair: *Omer van den Bergh*

22.) **Negative affect and end-tidal pCO2 in healthy individuals: The moderating effect of gender**
Sibylle Petersen, Bernhard Orth, Andreas von Leupoldt, Thomas Ritz

23.) **Depression, state NA, and end-tidal pCO2**
Ansgar Conrad, Marie A. Kramer, Anna Khaylis, Frank H. Wilhelm, Walton T. Roth, C. Barr Taylor

24.) **Psychophysiological Responses to Breathing Instructions**
Anett Mueller, Walton T. Roth, Ansgar Conrad, Sigrun Doberenz, Sunyoung Kim, Alicia Meuret

25.) **Using breathing in Psychophysiological Stress Profiling**
Erik M.G. Olsson, Anna Kinsten, Tores Theorell

Symposium: Emotions, Stress and Asthma
Chair: *Thomas Ritz*

26.) **Impact of blood and wound stimuli on respiratory resistance and ventilation in asthma, blood phobia, and health**
Thomas Ritz, Frank H. Wilhelm, Alicia E. Meuret, Alexander L. Gerlach, Walton T. Roth

27.) **Role of cholinergic pathway and inflammation in the asthmatic airway response to emotional stimuli: A pilot analysis**
Antje Kullowatz, Hans-Jurgen Smith, Frank Kannieß, Helgo Magnussen, Bernhard Dahme, Thomas Ritz

28.) **Stress increases airway hyperresponsiveness and allergic airway inflammation in mice via substance P**
Ricarda A. Joachim, Viktoriya Sagach, David Quarcoo, Thai Dinh, Petra C. Arck, Burghard F. Klapp

29.)**Stressful life events and the course of asthma in children**
Seija Sandberg

POSTER SESSION

30.) **Preliminary results of an uncontrolled 10-week heart rate variability biofeedback treatment of major depressive disorder**
Maria Karavidas, Paul Lehrer, Evgney Vaschillo, Bronya Vaschillo

31.) **Heart rate resonance features do not depend on respiration**
Evgney Vaschillo, Bronya Vaschillo, Marsha E. Bates, Paul Lehrer, Robert Pandina, Sushismita Ray, Tomoko Udo

32.) **Heart rate variability biofeedback:**
Effects of age on heart rate variability, baroreflex gain, and asthma
Paul Lehrer, Evgney Vaschillo, Shou-en Lu, Dwain Eckberg, Bronya Vaschillo, Anthony Scardella, Robert Habib

33.) **Perception of resistive loads applied for multiple-breaths in males and females**
Sarah Miller, Erin Robertson, Paul W. Davenport

34.) **Effects of an inter-active biofeedback game on anxiety and pain in children with cancer**
Anke Reineke, Erik Sowder, Richard Gevirtz

35.) **Heart rate variability biofeedback for recurrent abdominal pain: A multiple case history study**
Erik Sowder, Anu Kotay, Cassie Cannon, Jenny Murphy, Warren Shapiro, Richard Gevirtz

36.) **Experimental manipulation of intercostal muscle activity:**
Development of an electromyographic feedback procedure and effects on heart rate and dyspnea
Thomas Ritz, Andreas von Leupoldt, Bernhard Dahme

37.) **Awareness of breathing: German language descriptors of respiratory sensations and their relationship with ventilatory adaptation to respiratory challenge**
Sibylle Petersen - Winner of a Student Award
Sibylle Petersen, Thomas Ritz

38.) **Airway inflammation assessment by exhaled nitric oxide:**
Reproducibility and association with lung function, airway hyperresponsiveness, and negative affect
Antje Kullowatz, Frank Kannieß, Bernhard Dahme, Helgo Magnussen, Thomas Ritz

39.) **Psychophysiological treatment for stress-related somatic-complaints:**
A randomized waitlist-controlled study with 6 and 12 months follow-ups

Erik M.G. Olsson, Lennart Melin

40.) **Role of US-expectancy for symptom learning in an odor-CO2 conditioning paradigm**
with 20% CO2 as unconditioned stimulus
Stien Fannes, Ann Meulders, Ilse van Diest, Deb Vansteenwegen, Paul Eelen, Omer van den Bergh

41.) **Catastrophic thinking in asthma: Validation of a questionnaire**
Steven de Peuter, Valentine Lemaigre, An Victoir, Geert Verleden, Omer van den Bergh

42.) **Effects of feedback on the ability of children with asthma to detect inspiratory resistive loads**
Allison McLacklan, Andrew Harver, Harry Kotses, C. Thomas Humphries

43.) **Correlation of breath holding time and other measures of dysfunctional breathing to end-tidal CO2**
Rosalba Courtney, Marc Cohen

44.) **Anxiety Sensitivity, subjective air hunger and ventilatory behavior during repeated hypercapnic stimulation**
Wan Li, Natalie Oyen, Nele Hombroux, Karyl P, van de Woestijne, Ilse van Diest, Katleen Bogaerts,
Omer van den Bergh

ZAN INVITED ADDRESS
Chair: *Gregory Fritz*

45.) **Respiration and Panic: Looking at the Future**
Giampaolo Perna

Symposium: Panic Disorder, Anxiety and Depression
Chair: *Walton T. Roth*

46.) **Measuring respiration in panic disorder**
Daniela Caldirola, Caterina Namia, Giovanna Vanni, Elisa Favaron, Fabiana Lopez, Giampaolo Perna

47.) **Interoceptive fear conditioning to an inspiratory load using 20% CO2 inhalation as an unconditioned stimulus**
Ilse van Diest, Paul Davenport, Omer van den Bergh, Sarah Miller, Erin Robertson

48.) **Clinical anxiety and respiration: Palo Alto studies in progress**
Walton T. Roth, Sunyoung Kim, Eileen Wollburg, Ansgar Conrad, Sigrun Doberenz, Anett Mueller, Alicia E. Meuret

PRESIDENTS ADDRESS

Omer van den Bergh

49.) **Subjective health complaints and respiratory behavior: The role of anticipation.**

Respiratory response to effort, coupled to inhalation and exhalation, for experienced and novice students in breathing therapy

Jan van Dixhoorn

Centre for Breathing Therapy, Amersfoort, Netherlands

Increasing muscle tension naturally couples to inhalation and exhalation tends to facilitate relaxation. This combination is often used in relaxation instruction. However, executing a movement during exhalation tends to improve coordination and reduce unnecessary effort. This effect requires practice and experience.

In this study a specific movement is instructed: pushing both feet in the sitting position to the floor and releasing the effort. The feet are in front of the knees and the movement therefore results in a backward tilt of the pelvis, which is functionally coupled to exhalation. The push is for some time explicitly coupled to exhalation and for some time to inhalation.

After each combination, the subjective response was noted on a checklist of experiences. It contained 12 descriptors of positive breathing response, four of more negative direction and 11 descriptors of location of perceived breathing. The instruction was given to 41 experienced students (ES) of breathing therapy and to 40 novice students (NS), participating in an introductory workshop. ES was experienced in making effort during exhalation, but not familiar with the specific instruction.

ES reported five out of 11 descriptors of breathing movement and NS about two ($p < 0.001$), for both combinations. About 3.5 out of 12 positive descriptors were noted after pushing with inhalation in both groups, but pushing with exhalation increased the number in ES to 4.2 and reduced it in NS to 1.9 ($p < 0.001$).

Negative experiences occurred less frequently, only 0.5 out of 4 descriptors. In ES they were more frequent after inhalation, in NS after exhalation.

It is concluded that for novice students inhaling during effort is easy and influences breathing, but they are less able to obtain a positive response with a more functional coupling of breathing and effort than experienced students.

Dyspnea cycle in COPD: a bio-psychosocial model. Combination of cognitive behavioural therapy and yoga breathing techniques can help

Vijai Sharma, Kandie Hansen

National Emphysema/COPD Association (NECA), Clevleland, TN, USA

Distressing sensory-mechanical aspects of dyspnea have been investigated relatively extensively, but in laboratory conditions. There is extensive data on asthmatic patients to help explain how psycho-emotional factors such as anxiety and depression interact with respiratory distress and which cognitive-behavioral interventions may be effective. Similarities and differences between asthma and Chronic Obstructive Pulmonary Disease (COPD are discussed.

But asthma is not COPD! The interaction of psychosocial aspects with respiratory distress in COPD has been minimally investigated whereas COPD is the 4th largest cause of death in the USA. Incidence of anxiety, panic attacks, depression and social withdrawal is high in COPD. The “anxiety-dyspnea circularity” compounded by depression and beliefs about the “progressive-irrecoverable disease” pose a unique threat for many COPD patients. There is lack of a comprehensive bio-psychosocial (BPS) framework in which appropriate cognitive-behavioral interventions can be fashioned and modified.

We identify problems that need to be addressed in applying the usual cognitive structuring schema of Cognitive Behavioral Therapy’s (CBT) and the existing exposure and breathing techniques of Panic Control Therapy (PCT).

We propose a comprehensive bio-psychosocial framework and treatment design to target major psychosocial aspects of Dyspnea in COPD. Combination of modified CBT and Yoga Breathing Techniques (YBT) specific to COPD dyspnea will be discussed. This “groundwork” is presented in the hope to serve as a springboard for developing evidence-based interventions and testing specific hypothesis regarding the effectiveness of interventions for a population in which less than one third receive any psychotropic or psychological intervention.

Further understanding of BPS model and of corresponding cognitive and breathing interventions will be useful in both clinical and experimental settings.

Short term HRV measures to indicate vagal cardiac output - should we correct for respiratory effects?

Bernhard Dahme (1), Thomas Ritz (1, 2)

(1) University of Hamburg, Germany
(2) Southern Methodist University, Dallas, TX, USA

Root mean square of successive differences (RMSSD) of heart period and the peak valley method in the time domain and the high frequency band (HF) of the HRV power spectrum in the frequency domain are widely used to measure vagal cardiac output in psychophysiological and psychosomatic research.

However, there is ample evidence that respiration rate (RR) and tidal volume (Vt) have a profound influence on HRV, independently from actual changes in cardiac vagal outflow.

We have earlier published a procedure (Ritz et al., 2001) to determine a more valid estimation of cardiac vagal outflow. It will be demonstrated that HRV measurements of vagal tone should be corrected for Vt and Ttot, when comparing for vagal tone in within subjects studies on, e.g. (1) vagal withdrawal provoked by skeletal muscle activation and (2) the autonomous activation during emotional experience.

Ritz, T., et al. (2001). Psychophysiology, 38, 858-862

Monitoring airway inflammation by exhaled breath analysis - methodology and promises

Olaf Holz

Hospital Großhansdorf, Zentrum für Pneumologie und Thoraxchirurgie, Großhansdorf, Germany
The analysis of sputum, exhaled nitric oxide (eNO) and exhaled breath condensate (EBC) are noninvasive procedures for the assessment of airway inflammation. Both sputum and eNO are well validated tools, but only eNO yields a read-out without time delay.

Nitric oxide (NO) is produced by NO-Synthases (NOS), which use L-Arginine as substrate. The major part of NO in the airways is considered to be produced by inducible NOS, which is known to be expressed in e.g. epithelia cells and macrophages. NO plays an important role in vasodilatation, but also as a host defence mechanism, which could be one reason for the very high concentrations of NO within the nasal cavities.

The levels of eNO is increased in patients with asthma and in allergic subjects exposed to allergen, but the exact mechanism behind increased eNO during allergic airway inflammation is not known, despite a large number of studies.

The concentration of eNO depends, among a number of minor factors, on the flow rate of exhaled air, the airway calibre and the extend of mucus within the airways. Exhaling against a low resistor will close the nasal vellum and avoids contamination with nasal NO.

The analysis of other compounds of exhaled air, particularly those of exhaled breath condensate (EBC), offers fascinating perspectives, however, the reliable detection of inflammatory mediators in EBC is difficult, due to the very high and often variable dilution with water vapour.

VivoMetrics PANEL DISCUSSION:

Continuous Physiological Monitoring: Methodological and Statistical Implications

Michael Coyle

Harvard School of Public Health, Department of Environmental Health, Boston, MA, USA

Past research focusing on human subjects stayed in the laboratory to assess treatment effect in order to minimize sources of variability that could potentially mask treatment effect. The question remained, however, as to how the patient might respond to the treatment in a more naturalistic and less controlled environment.

Many studies are executed over a period that is conducive to multiple lab visits per patient. In order to conserve laboratory resources and supplies, laboratory-based patient assessments have been reduced to the minimum necessary number to generate a reasonable data set.

Experimental designs employing specific time point assessments have, thus, become a standard by which treatment effect and group mean differences are evaluated. This type of design, however, is not without limitations.

Specific challenges to time point assessment designs are (1) the results of the study are relegated to “buckets” or “bins” of time and (2) treatment group means are a function of the (a. priori) selection of the time period.To augment laboratory measurements, as well as to “fill in the gaps” between laboratory visits, patient self-report data was included in study designs.

The peer-review literature is now replete with studies that focus on patient reported outcomes, as subjective data are seen as an essential component to most therapeutic-specific clinical trials and NIH grant submissions. It is well known, though, that patient compliance is poor and patients either retrospectively/prospectively complete the questionnaires or completely disregard the questionnaires- strategies that eliminate any possibility of providing key secondary outcome variables and, furthermore, add bias and variance to the data set. This panel will review and discuss the important methodological aspects of continuous physiological monitoring and its implications for increased study power and reduced measurement variance in hopes of answering the following questions: What are the advantages/disadvantages of continuous physiological monitoring? What is the relationship between study power, effect size, variance and continuous monitoring? What methodological constraints should be adopted?

*Organised and supported by VivoMetrics, Inc. / M. Coyle was formerly employed by VivoMetrics, Inc. as Principal Scientist.

Psychological Treatment for Comorbid Asthma and Panic Disorder

Paul Lehrer (a) and Jonathan Feldman (b)

(a) UMDNJ-Robert W Johnson Medical School, Piscataway, USA
(b) Ferkauf Graduate School of Psychology/Yeshiva University, Bronx, USA

Attendees will learn issues involved in treating the common comorbidity of asthma and panic disorder.

We will cover research evidence and clinical experience related to comorbidity, etiology, and principles for treatment.

We will present a manual for training, incorporating elements of Barlow's Panic Control Therapy, the National Asthma Education Program (of the National Heart, Lung, and Blood Institute, NIH), and interventions targeted at specific comorbidity issues.

We also will present preliminary data on effectiveness of the intervention.

Internal and External Assessment of Respiratory Mechanics

Michael D. Goldman

University of California, Los Angeles, USA

Current technologically-advanced continuous physiological monitoring provides insight into a number of manifestations of interest to respiratory psychophysiologists.

Initial analyses of data focus on changes in mean/variance of parameters over defined periods of time, often in association with psychological interventions. More detailed parameter analysis has demonstrated dramatic effects of paced breathing on the relation between cardiac and respiratory frequencies, and longer term effects of paced breathing on a number of psychophysiological parameters.

More sophisticated temporal pattern analyses permit recognition of significant respiratory events, such as objectively identifying spontaneous coughing or onset of increased airflow obstruction in patients with respiratory disease.

The present work focuses on ‘local’ analysis of respiratory parameters, as manifested by ‘real time’ within-breath relationships of the mechanical effects of respiratory muscle actions.

At the entrance to the respiratory system, upper airway muscles including the vocal cords may be evaluated by continuously measuring pressures and flows resulting from added pulses of pressure to either the nasal or oral airway during normal resting breathing.

Within-breath patterns of airflow resistance have been evaluated in normal subjects and those with lung disease and so-called ‘paradoxical vocal cord dysfunction,’ (VCD).

Characteristic patterns of resistance in inspiration and expiration have been identified in patients with lung disease that are not unlike those seen in VCD.

At the ‘exit’ of the respiratory system, (thoracoabdominal wall), within-breath patterns of thoracic and abdominal movements may be used to calibrate these movements in terms of respiratory airflow, and to infer actions of thoracic and abdominal respiratory muscles.

Sleep apnea, airflow obstruction, and changes in respiratory drive with volition and neurochemical stimuli, both psychological and metabolic, are inferred from within-breath relations between thoracic and abdominal movements.

It is concluded that upper airway and thoracoabdominal respiratory muscle 'signatures' within the breathing cycle provide useful physiological interpretation of responses to psychological and physiological respiratory stimuli.

Treatment and Psychological Factors in COPD

Frank Kannieß (1), Kai Richter (2), Hans-Jörg Baumann (3), Karin Taube (4), Stephan Schubert-Heukeshoven (4)

(1) Pulmonary Research Institute at Hospital Großhansdorf, Germany
(2) Pulmonary Research Institute at Hospital Großhansdorf/Hamburg Side, Germany
(3) University Medical Center Hamburg-Eppendorf, Germany
(4) Atem-Reha GmbH, Hamburg, Germany

Prevalence of obstructive airway diseases like bronchial asthma or COPD is increasing world-wide. Especially for chronic obstructive bronchitis and lung emphysema, summarised as COPD, the economic burden is enormous, due to costs for medical treatment, rehabilitation programs, days off from work etc. Like for most chronic diseases, patients with COPD are reminded on their disease every day. Therefore the psychological impact on health related quality of life (HRQoL) is a very important issue in all fields of treatment, irrespective if its pharmaceutical treatment or non-pharmaceutical treatment of acute and chronic symptoms.

Beside all progress in diagnosis and symptomatic treatment of COPD and increased knowledge in understanding the biology of the disease, it is well known and agreed that psychological disorders play an important role in daily life of patients with advanced COPD. It has been found for example in more than 12000 patients that smokers with respiratory symptoms show higher levels of depressive mood than smokers without symptoms and other chronic disesaes like CHF. The relationship between depression and medical state of the patients is part of many running trials.

The first chapter of this workshop is aimed to give an overview about pathophysiology and pharmaceutical options to treat COPD. It is important to know about the biology of the disease and the medical options to treat this disease using bronchodilators for acute symptoms relief and anti-inflammatory drugs for prevention of symptoms.

The second chapter will give insight into the non-pharmaceutical interventions for patients with COPD: non-invasive ventilation and the options and benefits of in-house and ambulant pulmonary rehabilitation. Whereas non-invasive ventilation is a relatively new method the treat patients with very severe end-stage COPD, the results of long-term follow up of these patients are very promising. The same is true for data from in-house and ambulatory pulmonary rehabilitation.

The third chapter will discuss the different aspects of psychological disorders that are observed in patients with advanced COPD and the options for psychological intervention in those severely ill patients.

Hygiene Hypothesis of Asthma

Helgo Magnussen

Center for Pulmonology and Thoracic Surgery, Großhansdorf, Germany

No abstract available

Factors that predict sensitivity to inspiratory resistance in children with moderate-to-severe asthma: not the usual suspects

Andrew Harver, Allison McLacklan, Harry Kotses, Lori Thurber, C. Thomas Humphries

UNC Charlotte, Ohio University, Asthma & Allergy Specialists, PA, USA

Background: Although some investigations have demonstrated that the ability of individuals to detect airflow obstruction is normally distributed, no characteristics of "good perceivers" of asthma have been identified.

The purpose of the present study was to determine variables that serve to predict the ability of children with moderate-to-severe persistent asthma to detect added inspiratory loads.

Method: Twenty-six children with asthma (M = 10.3 yrs) enrolled in a pediatric asthma education research program participated in a threshold resistance task.

In the task, subjects breathed on a mouthpiece and one of 10 loads was added to inspiration (range: 0.20-7.58 cmH2O/l/sec), once every 3 to 6 breaths. Each load was presented 10 times for a total of 100 load presentations. We used modified signal detection analyses (A prime) to calculate sensitivity to added loads.

A comprehensive set of measures including asthma severity, sociodemographic, and healthcare utilization variables - was used to predict individual A prime values.

Results: Four variables accounted for 66% of the variance (Multiple R = 0.81, $p < .05$) in load sensitivity in children including: household SES, medication compliance, peak flow meter ownership, and nighttime awakenings.

The correlation between actual and predicted A prime values was robust, and statistically significant ($r = 0.81$, $p < .05$).

Measures of healthcare utilization and perceived asthma severity were highly interrelated but did not make reliable contributions to the prediction equation.

Discussion: Household resources, medication adherence, asthma monitoring, and frequency of nighttime awakenings may relate, in part, to a range of environmental and behavioral factors that influence symptom recognition.

Supported by NIH/NHLBI R01HL068706

In search of protective processes for children with asthma: does accurate symptom monitoring make a difference?

Daphne Koinis Mitchell (1), Elizabeth McQuaid (1), Sheryl Kopel (1), Jack Nassau (1), Robert Klein(1), Marianne Wamboldt (2), Gregory Fritz (1)

(1) Brown Medical School, Providence, RI, USA
(2)University of Colorado Health Sciences Center, Denver, Colorado, USA

Background: Children with severe asthma are at an increased risk for experiencing functional impairment. Research has begun to identify processes that ameliorate children's exposure to stressors associated with managing asthma's complex treatment regimen. Focusing on modifiable protective processes within the child may help to maintain optimal asthma control.

Accurate symptom perception has been linked with less functional morbidity. Whether perceptual accuracy may function as a protective factor against asthma severity remains unclear. This study examines the potential

moderating role of accurate symptom perception in the relation between asthma severity and functional morbidity in children.

Method: Two-hundred parent-child (aged 7-17) dyads participated in this study. A range of asthma severity levels was represented (NHLBI, 1997). The Asthma Functional Severity Scale (AFSS) assessed children's functional impairment (Rosier et al., 1994). The Asthma Risk Grid was used to compare patients' subjective estimates of symptoms (peak flow guess) with objective lung function data (actual PEFR).

Results: Asthma severity level (= .35; p<.001; R2 = .12) and accurate symptom perception (= -.22; p<.001; R2 = .6) each accounted for a portion of the variance in functional morbidity. The interaction between severity level and accurate symptom perception on functional morbidity approached significance (= .19; p<.06; R2 = .18).

Simple regressions were conducted for children with more persistent asthma. For children with mild persistent asthma, accurate symptom perception accounted for 5% of the variance in functional morbidity (= -.23; p<.001).

For children with moderate and severe asthma, accurate symptom perception accounted for 7% of the variance in functional morbidity (= -.25; p<.05).

Discussion: Despite the level of asthma severity, accurate symptom monitoring may exert a protective function against increasing levels of functional impairment. These findings underscore the importance of children's symptom monitoring as a necessary component of effective asthma control for children with more severe asthma.

Psychiatric symptoms and pediatric asthma morbidity: the roles of symptom perception and family management

E.L. McQuaid (1), D. Koinis Mitchell (1), S.J. Kopel (1), J.H. Nassau (1), R.B. Klein (1), M.Z. Wamboldt (2), G.K. Fritz (1)

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(2) University of Colorado Health Sciences Center, Denver, Colorado, USA

Background: Psychiatric symptoms are associated with asthma morbidity. This study evaluates the associations among anxiety, depression, attention problems and pediatric asthma morbidity, and investigates whether these associations are mediated by asthma symptom perception and family management.

Method: 110 children with asthma (ages 7-17) and a parent participated. Children completed the Children's Depression Inventory (CDI), the Multidimensional Anxiety Scale for Children (MASC), and a continuous performance test (Connors CPT). Parents completed Connors Parent Report (CPRS-R) regarding child ADHD symptoms, and an asthma morbidity questionnaire.

Perception of asthma symptoms was assessed over five weeks using an electronic spirometer that prompted children to guess their PEFR prior to objective measurement. An error grid was used to determine children's perceptual accuracy.

Asthma management was assessed with the Family Asthma Management System Scale (FAMSS).

Results: Anxiety and depression were unrelated to asthma morbidity (all p's > .05).

Parent report indices of child ADHD symptoms were related to morbidity (r's .21 - .29, all p's < .05).

Poor CPT performance was associated with morbidity, r = .29, p < .01.

Regression models demonstrated that the association between parent report of ADHD symptoms and morbidity was mediated by family asthma management and partially mediated by symptom perception. The association between inattentiveness (as measured by the CPT) and morbidity was mediated through family management.

Discussion: In this study, attention problems, but not anxiety and depression, were linked to asthma morbidity. Results indicate that the association between ADHD symptoms and asthma morbidity may operate through deficiencies in both individual symptom perception and general family asthma management.

A comparison of resistive loading and in vivo approaches to assessing symptom perception in pediatric asthma

Gregory K. Fritz (1), Sue Adams (1), Elizabeth L. McQuaid (1), Robert Klein (1), Sheryl Kopel (1), Jack Nassau (1), Marianne Wamboldt (2), Anthony Mansell (1)

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(2) University of Colorado Health Sciences Center, Denver, Colorado, USA

Introduction: There is increasing recognition that inaccurate symptom perception is a contributing factor in asthma morbidity and mortality. Over the past two decades, a variety of methods have been developed to assess perception of respiratory sensation and dyspnea. Few researchers, however, have compared two or more approaches in the same group of subjects.

The present study was undertaken to compare two highly evolved protocols, resistance loading and in vivo symptom perception, for assessing symptom perception in a large number of children with asthma to determine which method was most predictive of asthma morbidity.

Method: Linear regression analyses were used to examine the independent contribution of the primary study variables: 1) laboratory resistance loading threshold, and 2) in vivo symptom perception obtained with a programmable home spirometer, to the prediction of variation in asthma morbidity.

Participants in this study were 78 children aged 7 – 16 years (M = 11.4); recruited for participation in Rhode Island (N = 42; 54% of sample) and Texas (N = 36; 46% of sample). The participant group from Texas was ethnically more diverse than the Rhode Island sample but the two groups were otherwise comparable. The majority of participants (57%) had mild persistent asthma.

Results: With the in vivo protocol, the accurate zone score significantly predicted baseline asthma morbidity (ß = -.29, p<.01), whereas the danger zone score (ß = .20, p =.06) and symptom magnification score (ß = .20, p= .07) were marginal predictors of morbidity.

In contrast, neither of the two resistive-loading thresholds approached predictive significance.

Discussion: We conclude that, despite its advantages in standardizability and rapid administration, a resistive load detection paradigm has minimal utility as a measure of children's perceptual ability in asthma.

Symptom perception and asthma morbidity in pediatric asthma.

Jonathan Feldman (1), Gregory Fritz (2), Elizabeth McQuaid (2), Sheryl Kopel (2), Robert Klein (2), Anthony Mansell (2), Marianne Wamboldt (3)

(1) Ferkauf Graduate School of Psychology/Yeshiva University, New York, NY, USA
(2) Rhode Island Hospital/Brown Medical School, Providence, RI, USA
(3) The Children’s Hospital, Denver, CO, USA

Background: The ability to detect changes in respiratory compromise may have important clinical implications for self-management of asthma. This study examined the relationship between symptom perception and asthma morbidity, and assessed whether this association was stronger using PEFR or FEV1 as the objective marker.

Methods: Participants were 211 children with asthma (aged 7 – 16 years, mean = 11.8 years) from two sites. Asthma severity was rated using NHLBI guidelines.

Participants were instructed to use a programmable electronic spirometer that prompted them to guess their PEFR prior to exhalation. Each subjective guess was classified as being in an Accurate Zone (AZ), danger zone (DZ; under-perception), or symptom magnification zone (SMZ) based upon the corresponding measurement of PEFR or FEV1. Data on symptom perception were collected over 4-6 weeks.

An index of functional morbidity was collected by parent report at baseline and across 1-year follow-up.

Results: FEV1 was a more sensitive indicator of decline in pulmonary function than PEFR, as indicated by a greater percentage of DZ blows (20.5% vs. 8.3%, $p < 0.001$) and less AZ blows (60.5% vs. 72.7%, $p < 0.001$).

After controlling for asthma severity, age, and race/ethnicity, the DZ ($r2 = 5\%$, $p = 0.001$) and AZ ($r2 = 4\%$, $p < 0.01$) both explained a significant proportion of variance in functional morbidity at baseline when using PEFR as the objective measurement. No zone of symptom perception calculated with FEV1 was associated with functional morbidity at baseline.

The AZ using PEFR and FEV1 ($r2 = 3\%$, $p < 0.05$) and the SMZ using FEV1 ($r2 = 3\%$, $p < 0.05$) contributed a significant proportion of variance in functional morbidity across 1-year follow-up, after controlling for site, asthma severity, age, and race/ethnicity.

Discussion: Calculating symptom perception using FEV1 is a more sensitive marker for measuring under-perception of asthma symptoms. However, symptom perception measured with both FEV1 and PEFR during baseline period was associated with asthma morbidity across one year.

Achievements in understanding the neurobiology of breathlessness (1954 / 2005)

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Breathlessness is Dyspnoea in Greek. There have been studies from the understanding of this symptom since the days of Hippocrates and perhaps before. I have chosen 1954 as a significant date to begin a review of ‘modern’ times because of a now classic paper by George W. Wright and Ben Branscombe that appeared in that year.

These physicians used the tools of accurate ‘medical history taking’. They concluded that `the sensation of breathlessness is likely to reflect the state of activity of the medullary respiratory centre` and that `the influence of the act of inspiration on the sensation is not humoral but neurogenic`. Relief is immediately obtained in spite of inhaling pure nitrogen!

The authors speculated on the relevance of the classical Herring / Breuer mechanism of lung stretch receptor discharge with lung inflation. When such discharge is abnormally weak, i.e. a small breath or the presence of areas of lung collapse, might not result in ‘adequate neutralising inspiratory impulses of a normal intensity generated in the brain stem’.

This paper appeared in the Trends Am Association of Physicians 1954 pp 116-125, having been presented in the Association’s meeting of that year. It caused the sensation in some respiratory clinical circles it was hardly known among scientists!

Thus the famous and challenging review by Julius H. Comroe that appeared in Mod. Concepts of Cardiovascular Disease vol. 25, number 9, Sept 1956, did not mention the Wright and Branscombe paper of 1954.

However, Comroes’s review created a widespread interest in the subject and influenced many workers, including myself to focus.

It is my intention in this Lecture to focus firstly on the work that our group did in the early 1970's, and secondly, to show how the use of new technology – particularly brain imaging – has moved the subject forward.

Differentiation between the sensory and affective dimension of induced breathlessness

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Breathlessness or dyspnea is the subjective experience of breathing discomfort and a symptom in various respiratory and other disorders. Like pain, this experience results from multiple physiological, psychological, and other factors and their interactions. Both dyspnea and pain are unpleasant, alarming physical sensations which seem to have similarities in their cortical processing.

Because of these similarities recent work has suggested to adopt successful methods from pain research for investigations into dyspnea. A key contribution in pain research has been the realisation of the difference between sensory and affective aspects of pain. Although first data seem to suggest a similar multidimensionality of perceived breathlessness, this issue has received limited attention.

In the present study we examined whether healthy volunteers can differentiate between the sensory dimension (intensity) and the affective dimension (unpleasantness) during induced dyspnea.

Dyspnea (i.e. increased work/effort of breathing) was induced by breathing through inspiratory resistive loads of increasing magnitude (0.99 to 2.33 kPa/l/s) for 1 min epochs, alternating with 1 min epochs of unloaded breathing. Following each condition participants rated the experienced intensity and unpleasantness of breathlessness on separate visual analog scales (VAS).

Results showed that with increasing dyspnea the ratings for experienced unpleasantness increased stronger than for experienced intensity. The findings are supported by first data from a pilot study in which the perceived unpleasantness of induced breathlessness decreased due to distraction while the experienced intensity of the sensation remained constant.

The results suggest that healthy volunteers are able to distinguish between the sensory and affective dimension of breathlessness and that these dimensions might be manipulated differentially. The findings provide further evidence for the multidimensionality of the sensation of dyspnea.

The perception of sensory and affective components of dyspnea induced by a histamine provocation test.

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Aim: This study aimed to differentiate between sensory and affective components of subjective dyspnea in a standard histamine provocation test.

Methods: Patients with asthma (N=25) underwent a histamine provocation until a 20 % fall in forced expiratory volume in 1 sec (FEV1) was reached. After each dose level, the intensity of 12 symptoms was rated.

Individual sensitivity was determined by the slope of the linear regression between the fall in FEV1 and the increase in symptoms for the total symptom scores, and for affective and sensory symptoms separately (Bijl-Hofland et al., 1999).

Trait anxiety, state anxiety at baseline, daily asthma symptoms and catastrophizing during an asthma exacerbation were also assessed.

Results: Sensitivity was unrelated to physiological indices of disease severity (i.e. baseline FEV1 and histamine dose level at 20% fall in FEV1), whereas it was positively related to trait anxiety, state anxiety, daily asthma symptoms and catastrophic thinking during an asthma exacerbation in daily life. These relationships were overall much stronger for affective than for sensory symptom slopes.

In stepwise multiple regressions, state anxiety was the best predictor of the affective symptom slopes, whereas catastrophic thinking during an asthma exacerbation was the best predictor for the sensory symptom slopes.

Conclusions: Subjective dyspnea is more determined by affective than by sensory components. Both components are related to different psychological variables.

Relief of dyspnea and pleasantness associated with breathing: similarities and differences - preliminary results

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Daily clinical observation shows that dyspnea relief (DR) i.e. the specific sensory experience of breathing becoming easier is often associated with a sensation of pleasure.

We therefore assessed this specific component of DR, by the score of pleasantness associated with breathing (PBSc), together with the global score of DR (DRSc) and the subjects' choice of specific word descriptors of DR (of positive or neutral valence) in 10 healthy volunteers at the occasion of a functional brain imaging study of DR.

We found a significant relationship between DRSc and PBSc for the study group as a whole and in most individual subjects.

Overall variance of sensation scores explained by respiratory parameters was lower in PBSc than in DRSc, suggesting that the determination of perceived intensity by non-sensory parameters may be higher in sensation of pleasantness associated with breathing (PB) than in DR.

Furthermore, respiratory determinants differed qualitatively between PBSc and DRSc. Indeed, DRSc was predominantly determined by the decrease in an index of motor command and/or of neuro-mechanical uncoupling, whereas in PBSc, an index of execution of motor command alone (VE) and PetCO2 had the greatest relative contribution.

Both DRSc and PBSc were significantly and positively related to the total number of selected DR descriptors and to those with a positive valence and inversely related to descriptors with a neutral valence. However, these correlations were stronger in PBSc than in DRSc.

These preliminary results suggest that despite similarities between the sensations of pleasantness associated with breathing and relief of dyspnea (which includes all dimensions of the sensation), PB may have some specificity in terms of underlying determinants. However, these results need to be confirmed in a much larger number of subjects.

The resistive (R) load threshold for respiratory related evoked potentials (RREP)

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The amplitudes of the RREP peaks increase with increasing load magnitude for detectable R loads. However, the R threshold for eliciting the RREP is unknown. It was hypothesized that the RREP peaks would only be elicited by R loads above the detection threshold.

The R detection threshold was measured in healthy subjects. RREP's were recorded from the same subjects using R loads that spanned their detection threshold (Ro=0, R1=0.8, R2=4.7 and R3=21.0 cmH2O/l/s). The subjects signaled detection of the inspiratory R during the attend session.

The subjects watched a video movie during the ignore session.

In each session, each load was presented 50 times in a randomized block design. RREP peaks Nf, P1, N1 and P300 were identified. The R load detection threshold was 2.67±1.09 cmH2O/l/s. The Nf, P1 and N1 peak amplitudes were significantly greater for the R3 than R2. The P300 peak was present only in the R2 and R3 loads during attend trials. No RREP components were found with the Ro and R1 loads for both attend and ignore trials. There was no significant difference in peak latencies.

The results demonstrate that the R load must be above the detection threshold for the RREP peaks to be observed. There is a relationship between the R load magnitude and the amplitude of the Nf, P1, N1 and P300 peaks. The P300 peak is only present if the short latency peaks are present and if the subject attends to the stimulus. Thus, there is a direct relationship between R load detection threshold and the expression of the RREP.

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Respiratory related evoked potential (RREP) measures of respiratory sensory gating

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The S2/S1 ratio of the N100 peak amplitude with application of paired somatosensory stimuli is less than 0.5 when the stimuli are separated by 500 msec. The reduced N100 amplitude of the second stimulus (S2) is due to central neural sensory gating.

It was hypothesized that application of paired occlusions will result in reduced amplitude of the S2 RREP N1 peak due to gating of respiratory information.

Subjects were studied with: 1) paired occlusion RREP, 2) paired mouth air puff EP (MEP) and 3) paired air puff stimulation of the hand (SEP).

Paired occlusions were delivered in a single inspiratory phase. Pairs of mouth air puffs were delivered during inspiration. Pairs of air puff stimulations were delivered to the subject's hand.

The N100 peak amplitude for the first stimulus (S1) and S2 and the S2/S1 ratio was measured. The S1 RREP N100 peak was significantly greater than the S2 N100 peak and the S2/S1 ratio was 0.37. The S1 MEP N100 peak was significantly greater than the S2 N100 peak. The S1 SEP N100 peak was significantly greater than the S2 N100 peak. The S1 RREP N100 peak was not significantly different from the RREP N1 peak elicited by a single occlusion at the same time in the breath as S2 during the paired protocol.

These results demonstrate that the RREP S2 amplitude is reduced with paired occlusion, consistent with central neural gating of respiratory afferent input. The decreased S2 N100 amplitude is not due to occlusions delivered late in the breath. The RREP gating response is similar to somatosensory mechanoreceptor gating.

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Neurophysiology of dyspnea

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This presentation will review the afferent and cerebral pathways of dyspnea. Three distinguishable sensations that are categorized under the general term dyspnea will be described: air hunger, work/effort, and tightness. Our current understanding of their separate afferent pathways will be discussed.

Air hunger, the uncomfortable urge to breathe, is subserved by integration of chemoreceptor and pulmonary stretch receptor information. Perception of corollary discharge arising from reflex drive from medullary respiratory motor centers is probably involved.

The sensation of respiratory **work/effort** is subserved by respiratory muscle afferents and corollary discharge from cortical centers of voluntary respiratory drive.

The sense of **tightness**, unique to asthma, probably arises from pulmonary receptors stimulated by bronchoconstriction.

The likely role of limbic system structures such as insula and anterior cingulate in perception of dyspnea as shown by PET and fMRI will also be discussed.

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Negative affect and end-tidal pCO2 in healthy individuals: the moderating effect of gender

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Background: Studies have suggested a systematic association between negative affect (NA) and end-tidal pCO2 levels, however, controversial findings have been reported regarding the direction of this association.

It has also been assumed that feelings of discomfort or dyspnea due to measurement procedures, and menstrual cycle through progesterone in women, can influence pCO2 levels and may therefore mask the true relationship between trait NA and pCO2.

Therefore, we studied the relationship between trait NA and pCO2 controlling for these factors.

Methods: Ninety-eight participants (71 women) participated in a laboratory protocol that included baseline pCO2 measurements, after which ratings of dyspnea and feelings of unpleasantness during the measurement were collected.

In addition, participants completed the trait and state versions of the Positive and Negative Affect Schedule, and women also reported on their menstrual cycle and the use of oral contraceptives.

Results: Trait NA and pCO2 showed a positive correlation in women, while in men a significant negative correlation was found. The difference between the correlation coefficients was significant.

In a hierarchical multiple linear regression the association for women was not significant after controlling for hormonal phase, unpleasantness of the experimental situation and dyspnea.

Exploratory multiple regression analysis for men showed that the association remained significant after controlling for unpleasantness of the experimental situation.

Bivariate correlations for both sexes showed that trait NA was indeed associated with ratings of unpleasantness and dyspnea, but these ratings were not associated with pCO2.

Conclusion: Gender has a moderating effect on the trait NA-pCO2 relationship, whereas measurement procedures do not have an impact on this relationship. Negative affect and end-tidal pCO2 in healthy individuals: the moderating effect of gender

Depression, state NA, and end-tidal pCO2

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While reduced end-tidal pCO2 has repeatedly been associated with stress and anxiety in healthy subjects and panic patients, less information is available on the relationship of state and trait positive and negative affect (PA, NA) with end-tidal pCO2.

We assessed end-tidal pCO2 for 5 min in 48 depressed and 20 non-depressed individuals, 55 years or older and at risk for cardiovascular disease (CVD), before the administration of a psychological stress test.

After the baseline assessment, participants completed the state version of the PANAS (Watson, Clark, and Tellegen, 1988).

While depressed and nondepressed individuals did not differ in age, gender, or cardiovascular risk and medication, depressed patients reported greater state NA and lower state PA than nondepressed subjects.

A three-way ANOVA with the factors group (depressed vs. nondepressed), state NA (high vs. low), and gender (male vs. female) indicated that participant with high state NA differed significantly from subjects with low state NA in end-tidal pCO2 ($p < 0.001$), while none of the other factors or interactions reached significance.

State NA was inversely correlated with end-tidal pCO2 in nondepressed women ($p = 0.03$) and men ($p = 0.008$), and in depressed men ($p = 0.03$), but surprisingly not in depressed women.

In conclusion, state NA is negatively related to expiratory CO2 in nondepressed patients at risk for CVD. Among depressed patients, men follow this pattern while women do not, suggesting gender differences in the interaction of physiological and psychological variables in depression.

Psychophysiological responses to breathing instructions

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Breathing instructions are commonly included as advice to people with panic disorder or other anxiety disorders and to people with generic stress and tension. Goals are to reduce hyperventilation or facilitate a meditative or relaxed state. The effect of such advice on respiration has rarely been measured.

We are testing the effects of different breathing instructions in three groups of subjects: those with panic disorder, those complaining of daily tension, and those self-described as calm.

The procedure is the following: Participants are instructed to relax for 8 minutes. Then, in randomized order for 4 minutes each, they are asked to (A) to count their breaths while inhaling and think “relax” while exhaling, (B) to breathe at a slower pace than usual, (C) to breathe shallower than usual, and (D) to breathe both shallower and at a slower pace than usual.

End-tidal pCO2 is measured from a nasal cannula, and tidal volume (TV) and rate, from bands around the chest and abdomen.

Preliminary data from 10 calm participants showed that compared to the initial relaxation period, instructions A raised TV and lowered rate slightly without changing pCO2. Instructions B raised TV by 260 mm and lowered rate by 2.8 c/min without changing pCO2. Instructions C lowered TV by 120 ml and lowered pCO2 by 5 mmHg instead of increasing it, presumably because of a compensatory rate increase of 5.7 c/min. Instructions D lowered TV by only 60 ml, and contrary to these instructions raised the rate by 1.8 c/min without changing pCO2.

We conclude that in calm people breathing instructions that might be expected to raise pCO2 levels fail to do so. Feedback of end-tidal pCO2 may be a superior way of teaching people not to hyperventilate.

Using breathing in psychophysiological stress profiling

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Brief background: Internationally, many different types of psychophysiological procedures are used to evaluate stress response and relaxation capacity, often called psychophysiological stress profiles (PSP). Most used are cardiovascular measures. Since physiological systems respond differently, the demands on a multimodal stress profile is high.

Our hypothesis is that the breathing parameters respiration rate (RR), end-tidal CO2 (ETCO2) and Oxygen saturation (SpO2) work well in PSP.

Study method: Subjects were nineteen female students (19-33 yrs). The procedure contained 5 minutes of adaptation, 4 minutes of silent reading baseline, 2 minutes math-stress, 2 minutes of silent reading baseline, 2 minutes of active relaxation, and 2 minutes of slow breathing.

Results: Data show that respiration rate and ETCO2 are sensitive to both stress and relaxation and that SPO2 is sensitive to stress during such time limited conditions.

Discussion: Pros-and cons of different PSPs are discussed and a suggestion is made.

*E. Olsson is part time employee of PBM Stress Medicine Systems. The company is selling psychophysiological equipment used in the research being presented.

Impact of blood and wound stimuli on respiratory resistance and ventilation in asthma, blood phobia, and health

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We observed previously that asthmatics show more arousal and greater increases in respiratory resistance to blood and wound stimuli, perhaps because of greater sensitivity of vagally controlled airways. Vagal excitation is also prevalent in blood phobia patients when confronted with blood and wound related stimuli; however, it is not known how the airways of blood phobics respond when exposed to such stimuli.

Asthmatics, blood phobics, and healthy controls were shown 10 films, two in each of 5 categories: pleasant, unpleasant, neutral, blood phobia-related (surgery), and asthma-related (portraying labored breathing).

For one subset of films (one film from each category) the instruction was simply to view the film, and for the other subset, to view the film while tensing the leg muscles. Because skeletal muscle contraction is known to dilate airways, we wanted to test this effect during emotional film viewing.

Oscillatory resistance (Ros), respiration, cardiovascular activity, skin conductance level, leg electromyogram, and self-report of symptoms and emotion were measured for each film.

Results showed that Ros was higher during emotional and disease-relevant films than neutral films, and that surgery films had the strongest effect. No group differences in airway response were observed.

In addition, blood phobia patients showed strong increases in ventilation to surgery films. Leg muscle tension during film viewing increased ventilation, heart rate and skin conductance, but did not substantially alter Ros.

We conclude that airways are particularly sensitive to blood and wound stimuli, but that this sensitivity is not limited to asthma.

Role of cholinergic pathway and inflammation in the asthmatic airway response to emotional stimuli: a pilot analysis

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Background: Previous studies showed that experimentally induced emotions induce an increase of respiratory resistance. However, it is not known where the changes in the respiratory tract are located.

We used a pharmacological blockade of the cholinergic pathway by ipratropium bromide inhaler to explore the role of vagal excitation and the lower airway passages.

Method: We report findings from the first 20 asthma patients in a larger study of emotion induction.

Patients were shown six films and six picture blocks, two in each of three categories: pleasant (amusing comedy), unpleasant (surgery scenes) and neutral on two separate occasions 3-8 days apart.

At the beginning of each session participants inhaled placebo or ipratropium (40 microgram), respectively, in a randomised, double-blind, double-dummy, cross-over design.

Before and during presentation we recorded respiratory resistance using impulse oscillometry (Jaeger/Toennies; impedance at 5 Hz).

After each presentation participants rated their physical symptoms and affective response. Before each session, the fraction of exhaled nitric oxide (FeNO) was measured as an indicator of airway inflammation.

Results: Changes in respiratory resistance during emotional stimulation varied significantly due to medication conditions (placebo vs. active medication), the type of stimuli (films vs. pictures), and the type of emotion (pleasant, unpleasant, neutral). In general, increases in resistance were stronger after placebo.

Airway responses were stronger in pleasant and unpleasant than in neutral stimulation. An interaction effect of Emotion by Type of stimulus suggested that these effects were stronger in films than in pictures. Also, effects of unpleasant stimuli were greater than those of pleasant stimuli, with surgery films showing the strongest effect.

Patients with higher FeNO had stronger airway responses to unpleasant stimuli.

Conclusion: Our results showed that reactions of the airway tract were generally attenuated due to active medication, suggesting that the lower airways show a general tendency to constrict through a cholinergic pathway in stimulation with pictures and films. This seems to be partly mediated by airway inflammation, as higher levels of FeNo can increase the impact of these stimuli.

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Stress increases airway hyperresponsiveness and allergic airway inflammation in mice via substance P

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Background: There is increasing evidence from studies in both animals and humans that stress results in concomitant activation of cells from the nervous, endocrine and immune systems and in the release of diverse biologically active mediators, including glucocorticoids, catecholamines, neuropeptides and cytokines. Despite the well documented clinical association of stress and bronchial asthma exacerbations, experimental data investigating the underlying mechanisms are still limited.

Tachykinins like substance P have been shown to play a critical role in the pathogenesis of bronchial asthma and furthermore to be released into tissues in response to stress.

To explore pathways linking stress and asthma we employed an animal model that combines an established protocol of allergic airway inflammation with stress exposure.

Method: BALB/c mice were systemically sensitized to the model allergen ovalbumin (OVA) on days 1, 14 and 21 and repeatedly challenged with OVA aerosol on days 26 and 27 to induce allergic airway inflammation.

Sound stress was applied to the animals for 24 h, starting with the first airway challenge.

To investigate the role of substance P in stress mediation, one group of stressed and one group of non-stressed mice received a highly specific neurokinin-1 receptor antagonist.

Bronchoalveolar lavage fluid was obtained and cell numbers and differentiation determined.

Airway hyperreactivity was measured by electrical field stimulation of tracheal smooth muscle elements.

Results: Application of stress in sensitized and challenged animals resulted in a significant increase in leukocyte number in the bronchoalveolar lavage fluid. Furthermore, stressed animals showed enhanced airway reactivity. The increase of inflammatory cells and airway reactivity was blocked by treatment of animals with the NK-1 receptor antagonist.

Conclusion: These data indicate that exogenously applied stress enhances allergen induced airway reactivity and airway inflammation via a neurokinin-1 receptor dependent pathway, which might be blocked by applying a specific NK-1 receptor antagonist.

Stressful life events and the course of asthma in children

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Background: While there is still an open verdict for the role of stress in the pathogenesis of childhood asthma, a growing body of research suggests that psychosocial stress is a likely factor contributing to the development of wheezing illnesses and asthma especially during early childhood. High levels of stress have also been shown to predict greater morbidity in children who already have asthma, and to correlate with poorer quality of life.

The aim of this study was to examine the role of psychosocial stress in new asthma exacerbations.

Method: 90 children, aged 6-13 years with chronic asthma were prospectively followed up for 18 months. Asthma was continuously monitored by use of daily peak-flows and symptom diaries. Acute life events, long-term psychosocial experiences and the child's personal characteristics were assessed by interviews.

Results: Severely negative life events significantly increased the risk of acute exacerbations of asthma immediately afterwards, and with a delay of a few weeks. Chronic background stress further magnified the risk caused by acute stressful events.

Positive life events protected against the increased risk precipitated by negative events.

Anxiety and low mood increased the child's vulnerability to the effects of stress, whereas minor rebelliousness was protective.

Self esteem related to the risk caused by negative events in a U-shaped fashion.

The Discussion: focuses on the possible mechanisms by which stress exerts both immediate and delayed effects, and on the implications of the interconnections between stress and the child's personality for the clinical management of asthma.

Preliminary results of an uncontrolled 10-week heart rate variability (HRV) biofeedback treatment of major depressive disorder (MDD)

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Autonomic nervous system (ANS) dysfunction is thought to play an important role in depression. HRV biofeedback training is a non-invasive tool that involves identifying and teaching participants to breathe at the rate (their "resonant frequency") where amplitude of HRV is maximized.

Nine participants met inclusion criteria (a primary diagnosis of MDD as assessed by the Structured Clinical Interview for DSM-IV-[SCID]) and completed the study.

Questionnaires consisted of interviewer and self-rated measures of depression, anxiety, health status, quality of life and mood states administered at Sessions 1, 4, 7 and 10.

Physiological measures consisted of ECG, EMG, thoracic and abdominal breathing (respiration rates) and finger temperature.

Preliminary data already suggest that HRV biofeedback may be an effective treatment for depression. By as early as session four, there was an attenuation in depressive symptomatology: (HAM-D) ($x1 = 19.89 \pm 3.18$) and ($x4 = 11 \pm 4.92$; $t = 6.310$, $P = 0.00$); (BDI-II) ($x1 = 26.11 \pm 7.94$) and ($x4 = 17\pm$; $t = 10.32$, $P = 0.01$) while, the physiological marker (SDNN) evidenced an increase: ($x1 = 39.43 \pm 25.47$) and ($x4 = 50.57$; $t = 26.318$, $P = .043$).

Although insignificant, there appeared to be an inverse relationship between SDNN and depression scores across the data collection points. LFN, HF and VLF were elevated by Session four (n.s.). Additional physiological markers (heart rate, PNN50, and respiration) were explored as secondary outcome measures.

This data shows that HRV biofeedback both improves depression and increases respiratory sinus arrhythmia, suggesting increases in vagal tone; increases total HRV, suggesting better physical and emotional adaptability; and increases vagal baroreflex gain which may affect depression via projections of the baroreflex system to the limbic system.

Further evaluation of this promising intervention is warranted in controlled studies particularly since marked improvements are achieved in four sessions, it is easily learned and has no known adverse side effects.

Heart rate resonance features do not depend on respiration

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Background: Slow breathing at a frequency around 0.1Hz causes high amplitude heart rate (HR) oscillations due to resonant properties of the HR control system.

Although respiration plays a part in HR regulation, we suggest that breathing at 0.1Hz only serves as a rhythmical stimulus to provoke resonance. Other external stimuli may substitute for respiration.

Study method: Rhythmical emotional stimulation was used to elicit HR resonance. We evaluated HR and respiration volume (RV) reactions to emotionally salient pictures in 36 healthy, young social drinkers (21-24 years old).

180 pictures were presented in 6 blocks (negative, positive, neutral, alcohol, marijuana, and ecstasy). Each block included 30 pictures (5s - picture on, 5s - picture off), corresponding to a presentation frequency of 0.1Hz.

HR and RV reactions to each block were evaluated as power of the RRI and RV spectra at 0.1Hz.

Results: Picture presentation elicited high amplitude HR oscillation at 0.1Hz. High peaks in RRI spectra at 0.1Hz were found for all stimulus blocks except the neutral. The power of RRI spectra for neutral stimuli and baseline at this frequency did not differ significantly.

There were individual differences in reactions to different kinds of stimuli. Effects of picture presentation on respiration were also seen. The power of RV spectra increased in the low frequency (0.02-0.2Hz) range, but clear high spectral peaks were found only in the usual (0.2-0.35Hz) range.

Discussion: HR resonance was triggered by external rhythmical stimulation without involving respiration. RV spectra for picture presentation reflected emotional loading, but did not show any specific effects of rhythmical stimulation.

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Heart rate variability biofeedback: effects of age on heart rate variability, baroreflex gain, and asthma

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Objectives: This paper presents additional analyses of data from a previously published study showing that biofeedback training to increase heart rate variability (HRV) can be an effective component in asthma treatment.

HRV and intervention-related changes in HRV are negatively correlated with age.

Here we assess the effects of age on biofeedback effects for asthma.

Design: Ten sessions of HRV biofeedback were given to 45 adults with asthma. Medication was prescribed by blinded physicians according to NHLBI criteria. Medication needs were reassessed biweekly.

Results: Decreases in need for controller medication were independent of age.

There were larger acute decreases in forced oscillation frequency dependence in the older group, but larger increases in HRV variables in the younger group. Differences between age groups were smaller among subjects trained in pursed lips abdominal breathing as well as biofeedback, than among those just given biofeedback.

Conclusions: Age-related attenuation of biofeedback effects on cardiovascular variability does not diminish the usefulness of the method for treating asthma among older patients. Additional training in pursed lips abdominal breathing obliterates the effects of age on heart rate variability changes during biofeedback.

Perception of resistive loads applied for multiple-breaths in males and females

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Resistive (R) load magnitude estimation (ME) was measured over multiple breaths in human subjects. It was hypothesized that multiple breaths against a small R load will result in a decreased ME as the number of inspiratory efforts increase.

It was further hypothesized that multiple breaths against large R loads will increase the ME with increased breath number.

Methods: The subjects respired through a non-rebreathing valve, the inspiratory port connected to the loading manifold. The subject was inspired to a peak airflow target for each breath. Each R load and no-loads were presented for 10 continuous breaths.

The load was estimated at breath 1, 5, and 10 using a modified Borg scale. Each R presentation was separated by a minimum of 15 unloaded breaths. Each R was presented in a randomized block 3 times each in a single experimental session.

Results: There was no significant combined group difference between the ME for breath 1 and 10 for small R loads or large R loads. The ME for males did not change between breath 1 and 10 for all R magnitudes. The ME for the 10 breath of the large R load was greater than the 1st breath for females. Males estimated the large R load on the 1st breath the same as females but the ME on the 10th breath was significantly less for males compared to females.

Conclusions: These results demonstrate that ME of R loads with a sustained 10-breath trial changes in females but not in males. The increase in ME may represent increased respiratory discomfort.

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Effects of an inter-active biofeedback game on anxiety and pain in children with cancer

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Background: Anxiety and pain symptoms remain a major concern for cancer patients throughout their medical treatment. The Journey of the Wild Divine biofeedback game is designed to teach patients to control physiological functions by increasing, decreasing or synchronizing body rhythms (heart rate, skin conductance, and respiration rate), through various levels of breathing retraining, relaxation, and meditation techniques.

This study investigates the effectiveness of a biofeedback game that focuses on autonomic balance in reducing anxiety and pain levels in children with cancer.

Method: Participants between the ages of 6-17 were recruited at Children's Hospital in San Diego and were randomly assigned to either the biofeedback group or the standard group.

The biofeedback group received six sessions, each 45 minutes in duration, of the Wild Divine biofeedback game. During the first session, participants were educated about the rational of biofeedback and received training in abdominal breathing. In addition, participants received a copy of the Wild Divine program to practice at home once a day for 15 minutes.

The standard control group will receive the regular treatments at the hospital.

Baseline assessment of anxiety levels was assessed with the Spielberger State-Trait Anxiety Inventory for children and pain levels were assessed with a Visual Analogue Scale.

Further, physiological data (heart rate variability, skin conductance and respiration rate) were assessed at baseline, mid-treatment, and post treatment.

Results: Study is still in progress. Five cases will demonstrate how six sessions of the Journey of Wild Divine biofeedback game effects anxiety and pain levels in children with cancer.

Discussion: As preliminary conclusion, a brief biofeedback intervention that includes respiratory training, relaxation and meditation techniques could be used to decrease levels of anxiety and pain in children with cancer. Advantages of this treatment are that it is inexpensive and has few if any negative side effects.

Heart rate variability biofeedback for recurrent abdominal pain: a multiple case history study

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Background: Recurrent Abdominal Pain (RAP) has been hypothesized to be associated with a deficit in autonomic nervous system recovery to stress and an enhanced subjective response to pain. This study investigates the efficacy of a treatment protocol for RAP that focuses on autonomic balance.

Methods: Patients diagnosed with RAP were referred for Heart Rate Variability (HRV) Biofeedback by a pediatric gastroenterologist at Kaiser Permanente in San Diego.

Autonomic regulation measures were collected in the form of peak-valley differences of Respiratory Sinus Arrhythmia (RSA). Pain severity was assessed with a visual analogue scale completed by the participants. RAP symptom frequency was measured by the number of episodes per week. Twenty patients were monitored with ambulatory physiological monitoring equipment (VivoMetrics LifeShirt) for six to twelve hours.

Results: Of forty-three patients referred to for biofeedback, thirty- six were treated (age range of 7 to 18 years). A paired t-test analysis revealed a significant difference between pre and post pain intensity ($t(8) = 4.494$, $P < 0.001$, $?2 = 0.49$) and frequency ($t(14) = 4.498$, $P = 0.002$, , $?2 = 0.38$). Pre and post peak-valley differences of respiratory sinus arrhythmia (RSA) were also found to be significant ($t(6) = -3.20$, $P = 0.019$, $?2 = 0.36$).

Follow-up data were collected on 16 patients from a range of a one month to 2 years after treatment. Follow-up pain intensity and frequency were both significant compared to pre measures ($t = 3.810$, $P = 0.019$; $t = 3.627$, $P = 0.007$, respectively). Fifty-six percent of contacted patients were pain-free at follow-up interview. Examination of ambulatory data reveals hyperventilation patterns throughout normal activities in RAP children.

Discussion: Subjects with RAP were able to significantly lower their ratings of pain intensity and frequency within an average of six sessions of HRV Biofeedback administered by interns in a pediatric medical setting. This treatment method offers positive results and can be utilized to reduce treatment costs as well as to avoid distressing/painful diagnostic tests.

Experimental manipulation of intercostal muscle activity: development of an electromyographic feedback procedure and effects on heart rate and dyspnea

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Increased activity of intercostal muscles is a known input mechanism contributing to feelings of dyspnea. Patients suffering from respiratory diseases or anxiety frequently complain about dyspnea, which may in part be related to chronic tension of intercostal muscles and/or dynamic hyperinflation of the lungs.

In two studies we therefore tested a biofeedback procedure with the intercostal muscle tension as target. Electromyographic (EMG) activity was recorded from a bipolar electrode placement over the right external intercostal muscles of the second and third intercostal space. The signal was fed back visually on a screen.

Healthy students were tested in their ability to alter the signal during the alternating tension and baseline tasks of one minute duration each.

Heart rate was measured continuously throughout all training trails. After each trial volunteers rated the experienced dyspnea on a modified Borg scale.

The results showed that participants were able to increase the EMG activity considerably during four to six tension trials. Heart rate was increased during tension tasks, and the level of experienced dyspnea increased substantially. The changes in the EMG activity were achieved by most participants by manipulating their accessory muscle tension and/or altering their breathing pattern.

It is concluded that the EMG feedback technique is capable of altering intercostal muscle tension and associated levels of dyspnea. Further clinical studies may test the procedure as a relaxation technique in patients with respiratory disease or anxiety.

**Awareness of breathing:
German language descriptors of respiratory sensations
and their relationship with ventilatory adaptation
to respiratory challenge**

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Dyspnea is not a single sensation, but a multidimensional construct with distinct descriptors for separable types of sensations. We sought to explore the structure of dyspnea sensations using a German language list of 20 respiratory symptom descriptors adapted from Simon et al. (Am Rev Respir Dis 1998; 140:1021-1027).

In addition we studied the association of symptom clusters with ventilatory adaptation to respiratory challenge.

Fourteen healthy individuals participated in a protocol of seven conditions: Quiet breathing, climbing stairs, voluntary hyperinflation, breathing through an added resistive load, voluntary hyperventilation, breath holding and paced breathing at three different speeds (8-18 breath/min).

After each condition the participants judged their sensations of dyspnea during or following the task using the list of symptom descriptors.

Throughout the protocol respiration was recorded using ambulatory inductance plethysmography (LifeShirt, Vivometrics).

Within-individual cluster analysis identified four clusters from items with an acceptable interrater-reliability (ICC < 0.75): feelings of suffocation, air hunger, effort, and breathing obstruction.

Multidimensional scaling suggested an additional type of less unpleasant breathlessness that included items such as “I’m out of breath” or “my breathing is fast”.

The association of the clusters with respiratory parameters was studied using the two tasks with the greatest overall intensity of dyspnea ratings, climbing stairs and voluntary hyperinflation. As expected, inspiratory flow during stair climbing was associated with ratings of air hunger, but also suffocation.

No significant association between percent reduction in inspiratory volume during voluntary hyperinflation and sensations of effort or obstruction were found.

Thus, separable clusters of respiratory sensations can be found in German language descriptors of dyspnea, which resemble previously described clusters in other languages and are partly related to ventilatory adaptation to respiratory challenge.

Airway inflammation assessment by exhaled nitric oxide: Reproducibility and association with lung function, airway hyperresponsiveness, and negative affect

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The fraction of exhaled nitric oxide (FeNO) has been used as a noninvasive measure of airway inflammation in respiratory disease. It is known that FeNO is a very sensitive measure of asthmatic airway inflammation. As a non-invasive measure it correlates with other more common measures of asthma control, and is a sensitive marker of deterioration of asthma control.

However, an evaluation of spontaneous variability or temporal stability of values is critical if short- or long-term psychosocial influences on the inflammatory status of the airways are to be explored. In this context, the sensitivity of FeNO measurements to patients’ mood should also be investigated.

We measured exhaled FeNO in 40 asthma patients (mostly mild to moderate asthma) and 22 healthy controls in three separate sessions 5 to 18 days apart with a chemiluminescence gas analyzer (NIOX, Aerocrine, Sweden). FeNO was determined from nine separate breaths with an expiratory flow rate of 50 mL/sec in each session.

Lung function was measured by spirometry (forced expiratory volume in the 1st s, FEV1) and airway hyperreactivity was determined by methacholine provocation.

State negative affect was assessed at the beginning of each session using the Positive AND Negative Affect Scale (PANAS).

FeNO levels varied considerably between individuals, with higher mean levels in asthma than in controls.

Reproducibility was excellent (rtt = 0.98-0.99) within sessions and good to excellent between sessions (rtt = 0.85-0.94), with lower indices for asthma patients. However, even for a single breath reproducibility was still acceptable (rtt > 0.75) in patients across 18 days.

For patients, higher FeNO values were marginally associated with lower FEV1 and/or higher airway hyperresponsiveness. In addition, female asthma patients showed a significant association between higher negative affect and lower FeNO values in the first session.

Thus, individual differences in FeNO are stable and not substantially reflected in other indices of airway status. The correlation with negative affect should be interpreted with caution and requires replication in a larger patient sample.

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Psychophysiological treatment for stress-related somatic-complaints: a randomized waitlist-controlled study with 6 and 12 months follow-ups

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Brief background: Stress-related complaints are a major health problem for the Western world and cause substantial costs for the health care systems. Evidence-based treatments for these problems are lacking.

This randomized study investigated the effects of a psychophysiologically oriented intervention that spanned over three months.

Study method: Subjects were 26 women, 16 of whom were on full time sick-leave, with stress-related somatic complaints diagnosed by their physician and referred by the same physician to a behavior medicine treatment. After assessment and a randomization procedure 13 women began treatment and 13 were put on a waitlist as controls.

The treatment package included standard stress management and individualized biofeedback training focused on relaxation and breathing (e.g. skin temperature, ETCO2 and RSA). The treatment started with four group sessions and then continued individually.

Follow-up measures were collected 6 and 12 months after treatment with the two groups merged so that the control group got treatment after three months.

Results: Compared to the control group, the treatment group lowered their ratings for symptom level and on negative affect measured on Beck Depression Index. Sick-leave showed a tendency to be lowered.

There was however no effects on everyday functioning.

At the pre- post and pre- follow-up comparison, all measures were significantly improved, symptoms as well as everyday functioning. Sick-listing was significantly lower at follow-up compared with pre.

Discussion: Psychophysiologically oriented treatments are a promising contribution for stress-related somatic complaints.

* E. Olsson is part time employee of PBM Stress Medicine Systems. The company is selling psychophysiological equipment used in the research being presented.

Role of US-expectancy for symptom learning in an odor-CO2 conditioning paradigm with 20% CO2 as unconditioned stimulus

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Aim: To investigate the effect of more intense symptom episodes and the role of contingency awareness in an odor-CO2 symptom learning paradigm.

Method: Student participants (N=58) inhaled diluted ammonia or butyric acid (conditioned stimuli, CSs) mixed with 20% CO2 enriched air as an unconditioned stimulus (US).

One odor was presented with the US (CS+ trial), the other odor with room air (CS- trial).

Half of the participants received butyric acid as CS+ and ammonia as CS-, the other half received the reversed combination.

An acquisition phase with 3 CS+ and 3 CS- trials was followed by an extinction phase (3 CS+ without CO2 and 3 CS- trials).

Online US-expectancy measurements during acquisition were used to divide participants into good and poor predictors.

Somatic complaints, online anxiety and respiratory behavior (not reported here) served as dependent variables.

Results: Complaints were learned in response to the CS+, but only by good predictors receiving butyric acid as CS+. Learned complaints did not extinguish.

The findings further suggested that poor predictors remained anxious across all trials, whereas good predictors reported more fear to the CS+ compared to the CS- during acquisition and a tendency to reduced fear on the CS+ during extinction.

Conclusion: Compared to previous studies with lower CO2 concentrations, a strong US reduced the likelihood of learned symptoms to extinguish. For good predictors, the CS- became a safety signal during acquisition rather than that the CS+ became a cue for the aversive US.

Catastrophic thinking in asthma: validation of a questionnaire

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Aim: To design and validate a questionnaire to measure catastrophic thinking about asthma in order to elucidate the link between negative affectivity and symptom reporting in asthma.

Methods: We adapted the Pain Catastrophizing Scale (PCS; Sullivan, Bishop & Pivik, 1995) for asthma.

The Catastrophizing about Asthma Scale (CAS) was administered to asthma patients (N=94).

The structure of the CAS was explored by principal component analysis; internal consistency (Cronbach's alpha), test-retest reliability, and validity of the CAS were investigated.

Results: The CAS showed high internal consistency (Cronbach's alpha = 0.93), excellent test-retest reliability (r = 0.94), and good construct validity.

Conclusions: The CAS is a valuable tool to measure catastrophic thinking about asthma. Within the field of pain - especially chronic pain - the influence of catastrophic thinking on vigilance, fear/avoidance and the long-term evolution of the clinical state has been identified. Catastrophic thinking may appear to be of similar influence within the field of asthma.

Effects of feedback on the ability of children with asthma to detect inspiratory resistive loads

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Background: The purpose of the present study was to replicate in children with asthma, 9-12 years of age, previous findings that young adults improve in their ability to discriminate between the presence or absence of levels of inspiratory resistance with training.

Method: We compared the differential effects of two approaches to discrimination training in children with moderate-to-severe persistent asthma: no training (resistance breathing only) and discrimination training with immediate performance feedback.

In an initial session, subjects breathed on a mouthpiece and one of 10 loads was added to inspiration (range: 0.20-7.58 cmH2O/l/sec), once every 3 to 6 breaths. Each load was presented 10 times for a total of 100 load presentations.

Following this, subjects were assigned randomly to one of two conditions {no training (n = 10) or training with feedback (n = 12)} and participated in three subsequent experimental sessions. Children assigned to the no training condition repeated the threshold detection task; children assigned to the training condition participated in a signal detection (SD) task and were provided feedback about the accuracy of their responses on each trial.

Results: Sensitivity to inspiratory resistance was equivalent between groups in the initial session ($p = 0.73$) but in subsequent sessions sensitivity to added loads was significantly greater in the training group compared to the no feedback group [$F(1,20) = 5.57$, $p < .05$]; response bias was equivalent between groups.

Discussion: Discrimination training with immediate performance feedback results in improved sensitivity to increases in airflow obstruction in children with moderate-to-severe persistent asthma.

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Correlation of breath holding time and other measures of dysfunctional breathing to end-tidal CO2

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Shortened breath holding time (BHT) has been observed in persons with dysfunctional breathing patterns by a number of investigators. However measurement of BHT appears to not have been standardized as a clinical tool.

It has been proposed that the physiological rather than psychological breaking point of breath holding occurs when a person experiences the first involuntary motion of the diaphragm.

This way of measuring the breaking point of breath holding has also been utilized as way of determining hidden chronic hyperventilation by the Russian physician Dr. K.P. Butyeko. He claimed that breath holding performed to expiratory reserve volume and held to first involuntary diaphragmatic impulse was found to be correlated to end-tidal CO2 according to a specific mathematical formula. This formula was patented in the former Soviet Union (Buteyko, 1986).

Method: Capnometry and several other breathing tests including spirometry, manual assessment of respiratory motion, Nijmegen questionnaire, and self evaluation of breathing symptom questionnaires was administered to a group of 60 adults (of a future total of 120).

BHT according to various protocols was measured. BHT was used to predict PaCO2 according to Dr. Buteyko's formula.

Results: Dr. Buteyko's formula was able to predict ETCO2 levels within 0.2% of predicted CO2% in alveolar air in 27% of cases and within 0.5% in 40% of cases. However, the correlation was not significant, r= -0.112.

None of the other measures of dysfunctional breathing used showed a correlation with ETCO2.

Discussion: Results were not unexpected as it has been shown that factors other than central chemoreceptor sensitivity to carbon dioxide affect breath holding time and respiratory drive. Evaluation of dysfunctional breathing requires measurement tools in addition to CO2 measurement. Some of these are being evaluated in later stages of this research project.

Buteyko, K.P. (1986). Method of defining CO2 content in alveolar air. Soviet Union.

Anxiety Sensitivity, subjective air hunger and ventilatory behavior during repeated hypercapnic stimulation

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As a subjective response, the perception of air hunger may be influenced by several variables such as trait anxiety, anxiety sensitivity, repeated experiences, and so on. In this study we investigated how these variables shaped the intensity of air hunger ratings during gradually increasing levels of CO2.

Normal high and low anxiety sensitivity (AS) participants (N=31) went through three subsequent trials with the rebreathing test while rating air hunger at any time when they experienced a change in their air hunger.

After each trial participants rated the maximal intensity of state anxiety and fatigue they had felt during the trial.

Repeated measures ANOVA (Statistica 6.0) was performed on the calculated changes for each variable using 2 between-groups design.

The within factor was trial.

The threshold was lower for the subjective rating than for the ventilatory response during the first exposure to hypercapnia but across trials both of them synchronized.

Habituations across trials for both the ventilatory response and the air hunger rating were observed in low AS groups and illustrate that anxiety sensitivity could influence the air hunger perception and respiratory behaviors.

Respiration and panic: looking at the future

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Several experimental evidences support the existence of a panic respiration connection, however only recent studies, investigating the complexity of respiratory physiology, showed significant irregularities in respiratory pattern. The source of this high irregularity and the unpleasant respiratory sensations in patients with PD has not been fully understood.

This abnormality might be the effect of compensatory responses to abnormal respiratory inputs or to an intrinsic deranged activity in the brainstem network modulating the respiratory rhythm. Since basic physiological functions in the organism are strictly interrelated with complex reciprocal influences and patients with panic disorder show also abnormalities in the cardiac and the balance system functions.

Cardiovascular and respiratory functions are highly interconnected with reciprocal influences, and fluctuations in cardiac function or in cerebral blood flow could affect the entity and the time-course of the respiratory control mechanisms by inducing variations in gas exchanges and in circulatory function.

Patients with PD show a decreased global heart rate variability and since the cardiac function is regulated by connections between respiratory and sympathetic/vagal cardiac centres within the brainstem, an abnormal function of the respiratory network could influence the autonomic regulation of the cardiac activity.

The brainstem respiratory network is also highly connected with the brainstem vestibular nuclei to maintain blood gas homeostasis during movement and changes in posture and we have recently found that many patients with PD have subclinical abnormalities in their balance system function also linked to CO2 reactivity.

Given these considerations, the respiratory irregularities found might arise from perturbations of these other basic physiologic systems or from a more general abnormal function of the homeostatic brain.

Phylogenetically ancient brain circuits process physiological perceptions/sensations linked to homeostatic functions, such as the respiration, and parabrachial nucleus might filter and integrate interoceptive information from the basic homeostatic functions. These processes take place continuously beyond the consciousness and only rarely they pervade the conscious awareness as “primal emotions”.

Panic attacks could be the expression of primal emotion arising from an abnormal modulation of the respiratory/homeostatic functions.

Measuring respiration in panic disorder

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Respiration is one of the main functions involved in the pathophysiology of Panic Disorder (PD) (Griez & Perna, 2003). Experimental evidence support the existence of a panic-respiration connection: (a) the association between PD and both hyperventilation and respiratory diseases, (b) the hyperreactivity to hypercapnia in PD.

However, the lack of clear evidence of abnormalities in chemosensitivity and in the mean baseline respiratory measures in patients with PD have led to criticism. Thus, we focused on the experimental study of the respiratory function in patients with PD.

Respiratory signals usually represent the output of complex mechanisms, including multiple feedback/coupling interactions and inputs from internal and external sources. Thus, the best way to determine respiratory

abnormalities is an analysis of the complexity of the respiratory tracing over time, by employing non-linear statistic methods, considered the gold standard for the study of physiological functions.

Using this approach, we found that patients with PD have higher entropy in respiratory baseline patterns than healthy controls, indicating higher levels of irregularity and complexity in their respiratory function.

Entropy describes the amount of disorder in processes and systems. The higher respiratory entropy might indicate an instability in their respiratory homeostasis on which different inputs could act as “disruptive” factors leading to panic attacks.

According to this idea, we found that the baseline respiratory instability may underlie the hyperreactivity to hypercapnia in patients with PD and that smoking might act on the baseline respiratory instability, possibly influencing the onset and/or the maintenance of the disorder.

Overall, our findings support the idea that panic attacks might be linked to a malfunction of the respiratory system rather than being simply equivalent to fear/stress reactions.

Griez, E. & Perna, G. (2003). Anxiety and Respiration. In: J.R. Davidson & D. Nutt (eds), Anxiety Disorders. Blackwell.

Interoceptive fearconditioning to an inspiratory load using 20% CO2 inhalation as an unconditioned stimulus

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Background: Previous research showed that inhalations of 20% CO2 enriched air can be used to establish fearconditioning to exteroceptive stimuli. The present study explored whether the same stimulus can establish interoceptive conditioning in healthy subjects.

Method: Participants (N = 28) were tested in a differential conditioning paradigm. An inspiratory resistive load (15 cmH20) and an increased pressure on the upper arm (40 mmHg) served as conditional stimuli (CSs); a 20 s inhalation of 20% CO2 enriched air served as unconditional stimulus (US).

Half of the subjects received the resistive load as CS+ and the arm pressure as CS-; this was reversed for the other half.

Both the training and the extinction phase consisted of 3 CS+ and 3 CS- presentations (semi-randomized). SCR, EEG, pulse rate, FETCO2, mouth pressure, airflow and tidal volume were recorded during stimulus presentations.

Following each trial, participants rated the trial on 3 emotional dimensions of pleasantness, arousal and dominance. Subjects also rated fear, breathlessness and other panic symptoms experienced after each stimulus presentation.

Results: The subjective rating results indicate that the inspiratory resistive load and CO2 inhalation were equally aversive and were not additive. The inspiratory load elicited greater breathlessness than CO2 inhalation. Both load and CO2 independently elicited panic symptoms.

Discussion: These results suggest that both CO2 inhalation and inspiratory loads elicit aversive subjective sensations. These results further suggest that loads can be used to investigate panic symptoms.

Clinical anxiety and respiration: Palo Alto studies in progress

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We have begun comprehensive psychophysiological testing of three clinical groups: patients with Panic Disorder (PD), Generalized Anxiety Disorder (GAD), and a more broadly defined group who reports experiencing unpleasant tension on more than half the days in the previous 6 weeks.

Each group is offered therapy: the PD group breathing training, the GAD group, muscle relaxation, and the tension group a 2-hour seminar in managing tension. Each group and matched controls undergo testing in the laboratory and ambulatorily.

Our breathing training therapy for PD is unique in that half of the participants receive feedback training in raising CO2 and half in lowering CO2.

Our laboratory tests include reactions to voluntary relaxation, to voluntary hyperventilation, and to a series of breathing instructions that will be reported separately at this meeting.

Our ambulatory protocol is limited to 24-hour recording of skin conductance, temperature, and activity.

Subjects carry on their normal activities except for performing a relaxation test following taped instructions several times while being monitored.

Preliminary results suggest that learning to lower CO2 can produce considerable improvement in PD, contrary to the beliefs of many therapists. It looks as if previous findings of slow recovery to voluntary hyperventilation in PD may be replicated, although this finding may also be present in tense patients who have not had panic attacks.

We are also trying to replicate previous findings of slower voluntary relaxation in PD and of greater muscle tension in GAD patients. Several physiological measures (heart rate, skin conductance (SC), end-tidal pCO2, 2 EMG channels) indicate higher activation and less ability to relax in GAD patients than in controls.

Our tense group appears to have chronically elevated sympathetic tone as indicated by higher SC levels both during laboratory testing and ambulatorily while awake.

Presidents Address

Subjective health complaints and respiratory behavior: The role of anticipation.

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Anticipation is a pervasive functional characteristic of most, if not all, living organisms. It is based on detecting regularities in the relationship between stimuli in the environment. As a result, the functional repertoire of the organism will be expanded as it allows for adaptive responding to changes and challenges in the (internal and external) environment before they actually occur. Likely, however, under certain circumstances anticipation may also lead to maladaptive responses.

Most functional systems in the body are affected by anticipation. In a review of studies, we show that anticipation of respiratory challenges causing subjective symptoms will affect perceptual-cognitive and motivational-emotional processes producing subjective symptoms unrelated to the physiological disturbances that originally caused the symptoms.

At the level of respiratory behavior, anticipation may allow for feed-forward regulation of blood gas levels, that is, error correction before actual errors occur. The evidence for feed-forward regulation of breathing and the processes and systems underlying it are less clear, despite its potential to explain as of now poorly understood phenomena, such as exercise hyperpnea, psychogenic hyperventilation and medically unexplained dyspnea. A claim is made that research focusing on feed-forward regulatory mechanisms in respiration may potentially lead to important new insights into these issues.