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Abstracts

Proceedings of the 20th annual meeting of the International Society for the Advancement of Respiratory Psychophysiology (ISARP) Leuven, Belgium, September 27–29, 2013☆

Elke Vlemincx

University of Leuven, Leuven, Belgium

The 20th annual meeting of the International Society for the Advancement of Respiratory Psychophysiology took place on September 27–29, 2013 in Leuven, Belgium. In the footsteps of ISARP's history, the meeting's attendees represented a variety of disciplines (psychology, biology, physiology, medicine) sharing an interest in the physiological and psychological mechanisms of breathing, both from a fundamental and clinical perspective. Researchers and clinical practitioners, senior members, new members and students presented their work during oral presentations in one of the symposia or in interactive discussions during poster session.

The focus of the first symposium was the interaction between emotions and the dynamics of the respiratory and the cardiovascular system. P. Lehrer gave a theoretical overview of how system and control theory can improve our understanding of respiratory and cardiovascular (in)stability during emotions and stress, and in health and disease. C. Sevoz-Couche discussed the effects of respiratory loads on cardiovascular measures of stress. M. Grassmann presented data on respiratory measures during mental load in a specific sample of pilot candidates. J. van Dixhoorn talked about the relation between respiratory symptoms and general distress and upper thoracic breathing. E. Vlemincx presented results on the relief effects of sighs. J.-M. Ramirez introduced his work on the neurobiology of sighs, discussing the different cellular mechanism generating and modulating sighs in the pre-boetzinger complex.

During the second symposium, the neural processing of dyspnea was discussed in depth. K. Pattinson reviewed the advantages, the challenges and the pitfalls when using FMRI to investigate neural mechanisms of breathing and breathing symptoms. T. Similowski gave an overview of studies investigating the role of the supplementary motor area in respiration and respiratory symptoms using TMS, EEG and FMRI. M.C. Stoeckel presented a study investigating the brain regions involved in the anticipation of dyspnea using FMRI. A. von Leupoldt showed FMRI data of the influences of genetics and catastrophizing on the neural substrates of anticipation and perception of dyspnea. K.C. Evans presented an arterial spin labeled FMRI study showing differential effects of air hunger on insular activation in healthy persons and panic disorder patients. P.W. Davenport concluded the symposium presenting a respiratory afferent integration model of dyspnea.

The third symposium consisted of a profound discussion of potential treatments and treatment implications for asthma and COPD. A. Harver presented the outcomes of a pulmonary rehabilitation in COPD patients. S. Miller showed the importance of psychological comorbidities in female COPD patients, specifically, for practice. P. Lehrer discussed the preliminary results of a heart rate variability biofeedback trial in asthma patients. D. Koinis Mitchell explained the response behaviors in urban families with children with asthma, and how they relate to asthma symptoms.

In the fourth symposium, the importance of swallowing, cough and urge to cough for airway protection was discussed in various patient groups. E. Silverman presented data on the effects of expiratory muscle strength training in swallow-related quality of life in patients with multiple sclerosis. P. Davenport, K.W. Hegland and M. Troche discussed the reduced sensitivity to cough and urge to cough induced by capsaicin in various patient groups, such as sarcopenia and Parkinson's disease with or without dysphagia.

The fifth symposium consisted of the discussion of dyspnea and asthma perception in both healthy persons and asthma patients. K. Arcoleo described ethnic and sociodemographic differences in illness representations of parents of their children's asthma and how these relate to their asthma control. J. Feldman showed the effects of depression and anxiety of both children with asthma and caregivers on asthma perception and asthma control. S. Petersen discussed how social comparisons influence dyspnea perception. M. Walentynowicz presented data on dyspnea memory in high vs. low habitual symptom reporters.

During the invited addresses, K. Schruers introduced a trans-species experimental model of panic, supported by an overview of studies in panic patients, healthy persons and rodents. T. Troosters discussed the effectivity of physical activity in pulmonary rehabilitation programs.

☆ Abstracts are given in alphabetical order.

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Respiratory compensatory responses to hypercapnia following multiple over-pressurization blast injuries in rats

Sherry Adams[1], *Jillian A. Condrey*[1], *Hsiu-Wen Tsai*[1], *Victor Prima*[2], *Stanislav I. Svetlov*[2,3], *Paul W. Davenport*[1]

[1]*Department of Physiological Sciences, University of Florida, Gainesville, FL 32610, USA*[2]*Banyan Laboratories Inc., Alachua, FL, USA*[3]*Department of Physiology and Functional Genomics, University of Florida, Gainesville, FL, USA*

Background. An over-pressurization blast (OB) injury in rats replicates traumatic brain injury (TBI). Soldiers can sustain multiple TBIs from exposure to IEDs. The OB injury is a closed-head brain injury that is reproducible, repeatable and results in alterations in respiratory reflexes. The rat OB model was used to test the hypothesis that multiple OB exposures would result in changes in the response to hypercapneic challenge. **Methods.** The animals were anesthetized and instrumented with diaphragm EMG (dEMG) and then allowed to recover 3–7 days. The first OB injury was produced by a compressed air-driven shock tube directed at the dorsal surface of skull with an average peak overpressure of 80.08 ± 8.59. The animals were allowed to recover for 14 days. The second OB injury was produced with as above with an average peak overpressure of 80.53 ± 12.18. Hypercapneic trials with dEMG recordings were obtained 48 h pre-OB and 48 h post-OB1 and 48 h post-OB2. The hypercapneic trial started with 2.5 min of baseline recording with 100% O_2, then the animals were exposed to 4% CO_2 for 5 min followed by 2.5 min of post-hypercapnia baseline at 100% O_2. dEMG was recorded on PowerLab used to determine integrated dEMG amplitude, inspiratory time (T_i), expiratory time (T_e), total breath time (T_{tot}) and frequency. **Results.** For pre-OB, post-OB1 and post-OB2, 4% CO_2 significantly increased amplitude. Ti, Te and Ttot significantly decreased during hypercapnia. There were no significant differences between pre-OB, post-OB1 and post-OB2 during the mid-hypercapneic period in amplitude, Ti, Te, Ttot and frequency. There was a significant treatment effect pre-OB vs. post-OB for only Te during the end-hypercapneic period, Te was significantly longer in the post-OB trials. **Discussion.** These results suggest that OB injury modulated the hypercapneic ventilatory response. The second OB injury did not produce an additional effect on hypercapneic sensitivity.

Inhibition of the startle reflex during interoceptive threat: A shift in attentio?

Manuela G. Alius, *Christiane A. Pané-Farré*, *Andreas Löw, Alfons O. Hamm*

Department of Biological and Clinical Psychology, University of Greifswald, Germany

Background. Respiration is essential for life. Therefore, the restriction of breathing is a highly aversive state. Research showed that the startle reflex is potentiated during a complete breathing occlusion, which is in line with the typically potentiated startle reflex during aversive emotional states. However, studies also indicated that the startle amplitude to an acoustic probe is reduced when attention is allocated away from the auditory channel, as might be the case when subjects are confronted with an interoceptive threat like restricted breathing. **Method.** Therefore, we measured startle reflex, respiration and ERPs (probe-evoked P3) in 34 participants during phases wearing a "face mask with tubing" (four times), a "face mask without tubing" (once) or "no face mask" (four times) in a within-subject design. During each of these phases eight acoustic startle probes were presented. **Results.** Participants showed the typical pattern of loaded breathing, characterized by increased inspiratory flow rate, tidal volume and minute ventilation accompanied by slower breathing frequency during the "face mask with tubing" condition. Furthermore, they reported higher subjective unpleasantness and a higher degree of subjective breathing restriction. This pattern was not observed during phases "face mask without tubing" and "no face mask". Interestingly, the startle reflex was inhibited, when participants wore the face mask, either with or without tubing, compared to no face mask. Moreover, the amplitude of the probe P3 was reduced during phases with face mask compared to no face mask, indicating that attention was shifted away from the acoustic startle probes towards the possible interoceptive threat, and in turn, leading to a reduction of startle amplitude. **Discussion.** Study results indicated that startle responses are also modulated by attentional processes in cross-modal designs typically used when studying interoceptive threat.

Influence of parental asthma illness representations on children's controller medication use and asthma control

Kimberly Arcoleo[1], *Jonathan Feldman*[2]

[1]*The Ohio State University, College of Nursing, Columbus, OH, USA*[2]*Yeshiva University, Ferkauf Graduate School of Psychology, Bronx, NY, USA*

Background. Research examining parents' asthma illness representations (AIR) on compliance with their children's controller medication regimen and subsequent asthma control is in its infancy. Parental ethnicity, education, age, poverty status, depression, and acculturation may be a factor in AIRs aligned with the lay model of asthma management; which has been associated with inadequate medication regimens and increased number of acute visits. **Methods.** 1-year longitudinal study of 300 Mexican and Puerto Rican mothers and 300 children ages 5–12 w/asthma recruited from 2 school-based health centers and Breathmobile in Phoenix, AZ and 1 pediatric asthma and allergy clinic in Bronx, NY. Interviews and child PFTs at baseline and 3, 6, 9, and 12 months; medical record reviews at 12 months. Preliminary results from $N = 245$ baseline interviews. SEM examined direct and indirect effects of parent characteristics and AIRs on children's controller medication use and clinician rated asthma control. **Results.** The data fit the hypothesized model well (RMSEA = .04, CFI = .90, $X^2 = .19$). Parents reporting lower depressive symptoms, not living in poverty, higher education, and Mexican ethnicity had AIRs aligned with the professional model. No effects observed for acculturation. AIRs congruent with the professional model were associated with increased controller medication use and better asthma control. There was a significant indirect effect of parents' education through AIRS on controller medication use and a trend for ethnicity and poverty. There were no significant indirect effects of parent characteristics on AIRs, controller medication use and asthma control. **Discussion.** These preliminary findings reveal significant ethnic and sociodemographic differences in asthma illness representations which are directly related to children's controller medication use and asthma control. During clinical encounters with parents, we need to assess these illness beliefs in order to arrive at a shared asthma management plan which will result in optimal health outcomes for the child.

Perceived control increases effort in a breathing challenge despite increased perceived stimulus intensity

Jessica Baeske[1], *Sibylle Petersen*[2]

[1]*University of Dortmund, Department of Rehabilitation Sciences, Germany*[2]*KU Leuven, Research Group on Health Psychology, Belgium*

Background. In research on perceived control and perception of dyspnea we find a paradox: increased perceived control over respiratory stimuli can lead to increased ratings of stimulus intensity,

particularly in individuals high in negative affect. However, little is known on whether increased breathing effort under higher perceived control might mediate the relationship between dyspnea and perceived control. **Method.** We manipulated perceived control and self-efficacy in 50 healthy participants ($n = 24$, higher perceived control HPC/$n = 26$, lower perceived control LPC). All participants completed three breathing tasks with respiratory loads of 6, 9, and 16 cmH_2O (order randomized). We measured respiratory flow and pressure breath by breath and participants rated stimulus intensity. Furthermore, participants completed questions on state and trait negative affect, success in performing the breathing task, and trait locus of control. **Results.** In the HPC group, ratings of stimulus intensity and unpleasantness were significantly higher than in the LPC group. However, in the HPC group inspiratory pressure and flow were also higher indicating higher effort. Furthermore, perceived success in completing the task was higher in the HPC group despite higher dyspnea ratings. Locus of control had significant influence on respiratory effort, but only in the LPC group. Negative affect had no significant influence on results. **Discussion.** Results suggest that higher perceived control is related to higher effort invested in a breathing task despite increased perceived stimulus intensity. Results suggest that increasing perceived self-efficacy can substantially increase respiratory exercise performance.

Modulation of chewing, swallow and respiration during the stimulation of two cortical masticatory areas in the rat brain

Jillian A. Condrey, Hsiu-Wen Tsai, Paul W. Davenport

Department of Physiological Sciences, University of Florida, Gainesville, FL, USA

Background. The oral phase of swallow is under cognitive control whereas the pharyngeal phase is under reflex and cortical control. There are distinct cortical masticatory areas, CMAs, which induce different patterns of jaw movements when stimulated: the *A*-area in the orofacial motor cortex and the *P*-area in the insular cortex. Swallowing is inhibited during *A*-area stimulation but not *P*-area stimulation. Chewing is not coordinated with respiration while swallowing is; pharyngeal phase swallow apnea protects the airway from aspiration. The neural integration of chewing, swallowing and breathing are poorly understood. We tested the hypothesis that stimulation of the *A*-area will not alter breathing but will inhibit swallowing, however, *P*-area stimulation will elicit swallows that cause a modulation in breathing. **Methods.** Animals were implanted with EMG electrodes unilaterally in the caudal digastricus, inferior pharyngeal constrictor, diaphragm and bilaterally in the masseter and cranial digastricus muscles. After 4–7 days recovery, the rats were anesthetized and placed in a stereotaxic apparatus. The CMAs were exposed. *A*-area and *P*-area were stimulated using a concentric electrode at 30 Hz, 0.02 ms pulse width with 1–10 s trains. Swallows were elicited by probing the oropharynx before, during and after cortical stimulation. **Results.** Swallows elicited before cortical stimulation increased T_e and T_{tot}. *A*-area stimulation elicited only chewing muscle activity with no significant effect on T_i, T_e or T_{tot}. *P*-area stimulation elicited swallow muscle activity and increased Te and Ttot with no chewing. Swallows occurred after the cessation of *P*-area stimulation. Increased stimulus magnitude in the *P*-area recruited chewing and increased breathing frequency. **Discussion.** These results suggest that *A*-area stimulation activates motor pathways that induce chewing but do not inhibit swallow or respiration. *P*-area stimulation activates pathways that elicit swallows and modulate breathing pattern. We suggest that these areas are involved in cognitive control of upper airway behavior.

Emotional influences on symptom reporting: The effects of emotion regulation

Elena Constantinou, Maaike Van den Houte, Katleen Bogaerts, Ilse Van Diest, Omer Van den Bergh

Health Psychology, University of Leuven, Belgium

Background. Concurrent processing of unpleasant stimuli induces elevated symptom reporting, especially in persons who are vulnerable towards symptom over-reporting. The present study examines whether applying an emotion regulation technique, i.e., affect labeling, can reverse these effects. **Method.** Students ($N = 61$, 7 males) completed six picture viewing trials, including either pleasant or unpleasant pictures (10 pictures × 6 s each per trial) under three conditions: merely viewing, emotional labeling or content (non-emotional) labeling. After each trial, valence and arousal ratings and a symptom checklist, which included two respiratory sensations, were completed. **Results.** Repeated Measures ANCOVAs with scores on habitual symptom reporting (HSR) as a continuous predictor indicated that unpleasant picture viewing led to an increase in symptom reports compared to the pleasant trials. Labeling (either emotionally or non-emotionally) the unpleasant pictures significantly reduced the reporting of both symptoms in general and respiratory specific ones compared to merely viewing. Furthermore, HSR scores predicted elevated symptom reports after unpleasant picture viewing, but both labeling conditions reduced this effect. **Discussion.** Applying an emotion regulation strategy, such as labeling emotional stimuli, can reduce the augmenting effects of unpleasant cues on the subjective experience and reporting of symptoms. These findings provide indications for the usefulness of emotion-regulation strategies for high habitual symptom reporters.

Bedside method to assess dyspnea-pain counter-irritation

L. Dangers, L. Laviolette, T. Similowski, C. Morelot-Panzini

Pneumologie et Réanimation Médicale, Groupe Hospitalier Pitié-Salpêtrière and ER10, Université Paris 6 Pierre et Marie Curie, Paris, France

Background. Counter-irritation is the attenuation of a painful sensation by a newly occurring heterotopic stimulus that must be noxious in nature. Dyspnea-pain counter-irritation has been described with experimental dyspnea of the work/effort type, with dyspnea inhibiting laser evoked cortical potentials and RIII flexion reflex. Pain pressure threshold (PPT) using algometry is an easy to use and reliable model to induce acute experimental pain. The effect of experimental work/effort dyspnea on PPT has not been studied. The objective of the study was to assess the effects of experimental work/effort dyspnea on PPT. **Methods.** Inspiratory threshold loading was used to induce experimental dyspnea (work/effort) in 22 young and healthy volunteers. PPT were obtained using a pressure algometer at baseline and at two different intensities of dyspnea; visual analogic scale (VAS) ratings > 6 and > 8 cm. Force was applied incrementally on non-dominant trapeze, biceps and deltoid muscles of the subjects during 3 conditions: baseline, VAS dyspnea > 6 and VAS dyspnea > 8. **Results.** PPT increased significantly with increasing dyspnea ratings; trapeze (29 N to 32 N to 35 N; $p = 0.001$), biceps (28 N to 30 N to 34 N; $p = 0.04$) and deltoid (38 N to 43 N to 47 N; $p = 0.007$) for baseline, VAS dyspnea > 6 and VAS dyspnea > 8, respectively. Dunn's multiple comparison test showed that VAS dyspnea > 6 significantly increased PPT for the deltoid and trapeze, while VAS dyspnea > 8 increased PPT for all 3 muscle sites. **Discussion.** Work/effort dyspnea significantly increases PPT, with an apparent dose–response relationship. PPT is an easy to use method

for assessing dyspnea-pain counter irritation that could be applied in patient populations.

Afferent integration of respiratory sensory information mediating dyspnea

Paul W. Davenport

Department of Physiological Sciences, University of Florida, USA

It has long been recognized that cognitive perceptions of respiratory sensations has multiple expressions. These expressions have divergent and convergent sensory elements. The integration of the multiple sensory systems affected by respiratory stimuli allows for a high level of specificity for discrimination of the origin and modality of the respiratory perturbation. A model is proposed (the respiratory afferent integrator) to provide a sensory neural processing framework for understanding how multiple afferent systems mediate unique respiratory sensory modalities. Afferents are the first order of input for sensory neural processing of respiratory stimuli. The afferents are modulated by ventilatory related changes in mechanics, blood, cerebrospinal fluid and environmental state. Multiple populations of afferents project to specific neurons within the central nervous system synapsing on second order afferent integrator neurons. The second order neurons receive convergent and divergent afferent inputs forming subpopulations of neurons that are activated by unique combinations of inputs from groupings of sensory afferents. The second order subpopulations have convergent and divergent projection combinations on higher order neural networks. In this initial iteration of the afferent integrator model of dyspnea, specific respiratory sensations are elicited as a result of higher brain network activation by multiple sensory system transduction of respiratory related stimuli forming modality specific afferent convergences on second order afferent integrator neurons that form subpopulation projections to higher brain center neural networks.

Interoceptive fear conditioning and panic disorder: A differential design using inspiratory resistive loads and 35% CO_2

Klara De Cort[1*], *Ilse Van Diest*[2], *Anouk Janssen*[1], *Meike Pappens*[2], *Omer Van den Bergh*[2], *Lies Goossens*[1], *Eric Griez*[1], *Koen Schruers*[1,3]

[1]*Maastricht University, Institute for Mental Health and Neuroscience, The Netherlands*[2]*University of Leuven, Research Group Health Psychology, Belgium*[3]*University of Leuven, Center for Learning and Experimental Psychopathology, Belgium*

Background. Interoceptive fear conditioning has been proposed to explain why only a minority of the persons who ever experienced a panic attack develop panic disorder. **Method.** In this study, interoceptive fear learning was investigated with panic-relevant inspiratory resistive loads as conditioned stimuli and a single inhalation of 35% CO_2 as the unconditioned stimulus. High and low anxiety sensitivity healthy participants ($N = 66$) received either a moderate intensity load followed by the UCS (CS+) and a light load followed by room air breathing (CS−) or the reversed combination. Three CS+ and 3 CS− acquisition trials were followed by the same number of test trials in which no UCS were administered. **Results.** Self-reported anxiety, breathing behavior and skin conductance during the CSs in the acquisition phase was dominated by mere responding to the differences in loads, especially in participants scoring low on anxiety sensitivity. Despite these load effects in acquisition, learning-related differences in the test phase could be demonstrated in all measurements. With regard to breathing behavior significant different responding showed up to the light load as CS+ compared to as CS−. Whereas for self-reported anxiety a conditioning effect was shown towards the moderate load. Furthermore, a significant conditioning effect emerged for skin conductance responses. Interestingly, although discriminative learning seems irrespective of anxiety sensitivity, participants scoring high on anxiety sensitivity stayed aroused during the test phase. **Discussion.** The present study gives indications that slight feelings of dyspnea can become a predictor of panic attacks after conditioning. Moreover, participants scoring high on anxiety sensitivity appear to maintain a higher level of anxiety and arousal across the test trials indicating reduced extinction. This seems in line with the clinical feature of persistent anticipatory anxiety in PD patients, even in the absence of a panic attack.

Correlates of symptom confusion in Latinos with asthma and panic disorder

Nina Eisenberg[1], *Jonathan Feldman*[1,2]

[1]*Ferkauf Graduate School of Psychology, Yeshiva University, USA*[2]*Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Yeshiva University, USA*

Background. Panic disorder is more common in adults with asthma than the general population. Confusion between asthma and panic symptoms is common and can interfere with both asthma and anxiety management. The aim of this study was to identify correlates of symptom confusion in Latino adults with comorbid asthma and panic disorder. **Methods.** Data for these analyses ($N = 55$) were taken from baseline assessments as part of a larger randomized-controlled treatment study for Latinos with comorbid asthma and panic disorder. Interviewers assessed all DSM-IV-TR panic attack symptoms and rated the participant's ability to distinguish between panic and asthma symptoms using a 5-point scale. Assessment also included physician-classified asthma severity, control, and the Panic Disorder Severity Scale (PDSS). Pearson correlations and one-way analysis of variance were used to explore associations and between-group differences. **Results.** Symptom confusion was significantly associated with number of reported cardio-respiratory panic symptoms ($r = .31$, $p = .02$) but not somatic ($r = .12$, $p = .40$) or cognitive symptoms ($r = .03$, $p = .83$). There were no significant differences between asthma severity categories on ability to distinguish between panic and asthma symptoms ($F[2,48] = 1.07$, $p = .35$), and no significant association between ability to distinguish symptoms and panic disorder severity ($r = .07$, $p = .64$). Differences between asthma control categories approached significance for ability to distinguish between panic and asthma symptoms ($F[2,48] = 2.75$, $p = .07$). One item included in assessment of asthma control, a rating of subjective interference due to asthma, was associated with symptom confusion ($r = .32$, $p = .03$). **Discussion.** Ability to distinguish between panic and asthma symptoms was not associated with asthma severity or panic severity in this population. However, symptom confusion was associated with a cardio-respiratory panic symptom constellation and greater subjective impairment due to asthma.

Air hunger evokes greater anxiety and insular cortical activity in panic disorder than in healthy individuals: An arterial spin labeled fMRI study

Karleyton C. Evans[1,2], *Tian-Yue Song*[1], *Jared P. Zimmerman*[1], *Michael J. Gustin*[1], *Donald G. McLaren*[2,3]

[1]*Department of Psychiatry, Massachusetts General Hospital, Boston, MA, USA*[2]*Harvard Medical School, Boston, MA, USA*[3]*Department of Neurology, Massachusetts General Hospital, Boston, MA, USA*

Background. Dyspnea (principally air hunger) has been hypothesized as a major interoceptive trigger in panic disorder (PD), yet the neural mechanisms of air hunger mediated anxiety are unknown.

This pulsed arterial spin-labeled functional magnetic resonance imaging (pASL-fMRI) study tested for differential limbic regional cerebral blood flow (rCBF) in PD patients compared to healthy controls (HCs) during air hunger stimuli. **Method.** Thirty-seven subjects (19-PD/18-HC) were first diagnostically screened and then trained to receive mechanical ventilation via mouthpiece during two mock scan sessions. Subjects subsequently underwent a 16-min pASL-fMRI scan (3-T; TR/TE/TI1/TI2 = 3000/15/600/1600 ms) on mechanical ventilation. Air hunger was provoked during 80-s periods of low tidal volume (V_t; mean = 0.67 L), alternating with relief periods of high V_t (mean = 1.08 L) at constant respiratory rate (12 bpm) and constant elevated end-tidal carbon dioxide (4.1 mmHg above resting level). Anxiety ratings were assessed during and immediately after the scan. Between-group rCBF effects of air hunger were tested via a priori small volume corrected analyses (amygdala, insular and anterior cingulate cortices) performed within SPM8. **Results.** Periods of low V_t evoked significantly greater air hunger sensation (7.6 ± 1.8 vs. 4.3 ± 1.8) and anxiety (7.5 ± 1.7 vs. 1.8 ± 1.9) in the PD group compared to the HC group (0–10 scales) and were also associated with significantly greater rCBF in the right insula in the PD group. The magnitudes of air hunger sensation and anxiety were correlated with the magnitude of change in insular rCBF from high to low V_t periods. **Conclusion.** This is the first neuroimaging study to demonstrate greater insular rCBF in anxious patients during air hunger stimuli. The findings provide further evidence for the insula's critical role in dyspnea perception. Given hypotheses related to aberrant interoceptive processing in PD, the findings suggest that this interoceptive dysfunction may be mediated by the insula.

Perception of pulmonary function and asthma control: The differential role of child vs. caregiver anxiety and depression

Jonathan M. Feldman[1,2], *Dara Steinberg*[1], *Haley Kutner*[1], *Nina Eisenberg*[1], *Kate Hottinger*[1], *Kimberly Sidora-Arcoleo*[3], *Karen Warman*[4], *Denise Serebrisky*[5]

[1]*Ferkauf Graduate School of Psychology, Yeshiva University, USA*[2]*Department of Epidemiology and Population Health, Albert Einstein College of Medicine, USA*[3]*Ohio State University College of Nursing, USA*[4]*Department of Pediatrics, Children's Hospital at Montefiore, Albert Einstein College of Medicine, USA*[5]*Department of Pediatrics, Jacobi Medical Center, USA*

Background. The objective of this study was to examine child and caregiver anxiety and depression as predictors of children's perception of pulmonary function, quick relief medication use, and pulmonary function. Prior research has shown relationships between anxiety and depression and different aspects of asthma control and well-being. Asthma and anxiety share strikingly similar symptoms, such as dyspnea, dizziness, chest tightness, choking and sensations of smothering. The overlap in symptoms may lead individuals to mistake anxiety as an asthma attack. Caregiver depressive and anxiety symptoms are risk factors for higher levels of asthma morbidity in children, although most prior studies have not included measures of children's pulmonary function. **Methods.** 97 children with asthma, ages 7–11 years old, reported their anxiety and depressive symptoms and completed spirometry. Caregivers completed a psychiatric interview. Children's predictions of their peak expiratory flow were compared with actual values across six weeks. Quick relief medication use was assessed by Dosers. **Results.** Children's anxiety symptoms were associated with over-perception of respiratory compromise and greater quick relief medication use. Children's depressive symptoms were associated with greater quick relief medication use, but not perception of pulmonary function. Children of caregivers with an anxiety or depressive disorder had lower pulmonary function than children of caregivers without anxiety or depression. **Discussion.** Children's anxiety and depression are related to asthma management via a different mechanism than caregiver anxiety and depression. Child anxiety was associated with a subjective pattern of over-perception. Caregiver anxiety and depression were risk factors for poor asthma control assessed with objective measures. Interventions focused on improving children's perception of pulmonary function and treating caregiver psychiatric disorders might be effective mechanisms for reducing pediatric asthma morbidity.

Assessing mental load in pilot selection: Taking a closer look at respiration

Mariel Grassmann[1], *Elke Vlemincx*[2], *Dirk Stelling*[1], *Andreas von Leupoldt*[2], *Omer Van den Bergh*[2]

[1]*Department of Aviation and Space Psychology, German Aerospace Center DLR, Hamburg, Germany*[2]*Department of Psychology, University of Leuven, Leuven, Belgium*

Background. Mental load has been shown to affect respiratory parameters, potentially impairing information processing and cognitive performance. In the present study we investigated basic and variability measures of respiration under mental load in order to evaluate their sensitivity as workload measures and analyse whether they are related to cognitive performance in the context of pilot selection. **Method.** A group of 61 pilot candidates performed a demanding multiple task and watched a relaxing movie subsequently. Respiration rate and end-tidal carbon dioxide ($etCO_2$) were measured continuously during baseline, task, and recovery period – each lasting for 6 min. As measures of respiratory variability, the coefficient of variation (CV) and autocorrelation (AR) at a lag of one breath were computed on the basis of a 5-min window. Aptitude of the pilot candidates was analysed using their total performance in the multiple task and their qualification as an airline pilot (i.e., whether they successfully completed the selection process). **Results.** Performing the multiple task caused an increase in respiration rate and a decrease in $etCO_2$. Respiration rate recovered whereas $etCO_2$ did not. Both CV and AR of respiration rate decreased from baseline to task and fully recovered after the task. The variability measures of $etCO_2$ did not show any significant change. Cognitive performance as well as pilot qualification was associated with a lower respiration rate at rest and a stronger increase in respiration rate during task performance. A positive relationship was found between task performance and AR of respiration rate at rest. **Discussion.** Our results confirm previous findings on the usefulness of respiration to monitor mental load. In addition, our findings indicate that respiratory measures are related to performance and success in the aptitude testing for airline pilots.

Pulmonary rehabilitation in COPD: Health-related expectations and outcomes

S. Shafer[1], *A. Harver*[2]

[1]*School of Nursing, The University of North Carolina at Charlotte, USA*[2]*Department of Public Health Sciences, The University of North Carolina at Charlotte, USA*

Background. In patients with chronic obstructive pulmonary disease (COPD), comprehensive pulmonary rehabilitation results in improved exercise capacity and health-related quality of life. In this retrospective analysis, we examined effects of health-related expectations on pulmonary rehabilitation outcomes in patients with moderate to severe lung disease. **Method.** 114 patients (M = 68 years of age) with a diagnosis of COPD and/or who met the Global Initiative for Chronic Obstructive Lung Disease criteria

were studied. The sample included females (61%) and males (39%); most participants were white (53%), married (65%), and demonstrated multiple co-morbidities including hypertension (54%) and osteoarthritis (45%). Participants attended an average of 15 rehabilitation sessions that consisted of both education and physical conditioning; and completed the six-minute walk test (6MWT), the SF-36, and St. George's Respiratory Questionnaire (SGRQ) before and after rehabilitation. **Results.** Participants demonstrated reliable improvements in exercise capacity as a function of pulmonary rehabilitation; the 6MWT increased significantly from 1.078 ft to 1.256 ft ($t = -12.9$, $p < 0.000$). Significant improvements occurred in general health status as measured by both the SF-36 ($t = 3.46$, $p < 0.001$) and the SGRQ ($t = -2.86$, $p < 0.006$). The benefits of rehabilitation were noted in all areas of the SF-36 including vitality ($t = -6.86$, $p < 0.000$), emotional functioning ($t = -3.35$, $p < 0.001$), social functioning ($t = -4.27$, $p < 0.000$), and mental health ($t = -4.83$, $p < 0.000$). Perceived physical functioning, lung function, age, gender, and expectations of worsening health pre-rehabilitation were reliable predictors of post-rehabilitation distance walked ($R^2 = 0.50$). **Discussion.** Participation in pulmonary rehabilitation is associated with improvements in physical functioning and quality of life. More importantly, health-related expectations – in addition to physical functioning, lung function, age, and gender – predict improvements in exercise capacity that follow comprehensive pulmonary rehabilitation.

Development of a reliable dyspnoea model for use with functional magnetic resonance imaging

Anja Hayen, *Mari Herigstad*, *Katja Wiech*, *Kyle T.S. Pattinson*

Nuffield Department of Clinical Neurosciences, University of Oxford, JR Hospital, England

Background. Functional magnetic resonance imaging (FMRI) allows the study of neural mechanisms of dyspnoea. Resistive respiratory loading (to induce dyspnoea) induces changes in end-tidal CO_2 ($PETCO_2$) that confounds interpretation of FMRI. Isocapnia (keeping $PETCO_2$ constant) avoids these confounds, but necessitates a continuous baseline of mild hypercapnia. We hypothesised that mild hypercapnia would have little subjective effect during unloaded breathing, but would make resistive loading more unpleasant (thus smaller resistive loads required to achieve same dyspnea rating). As intervention studies often require multiple sessions, we examined whether habituation or sensitization occurred. **Method.** Ten healthy non-smokers (23 ± 6 years, 4 females) participated in one training and four experimental sessions: poikilocapnia (freely varying $PETCO_2$), isocapnia at 0.4 kPa, 0.6 kPa, 0.8 kPa above baseline (counterbalanced) on five consecutive days. At the beginning of each experimental session, we determined the load needed to evoke 50% on a visual analogue scale (VAS) rating unpleasantness. This load was then applied for two 4-min blocks with 3 min unloaded breathing in between (VAS ratings every 15 s). Participants completed the multidimensional dyspnoea profile (MDP) after each session. **Results.** During poikilocapnia, mean $PETCO_2$ did not change (4.9 ± 0.4 kPa) from baseline during loading, but varied by more than 0.2 kPa in 4/10 participants. $PETCO_2$ remained within 0.2 kPa of baseline for 28/30 isocapnic sessions. Hypercapnia increased baseline unpleasantness (12–23%VAS, $p = .010$), but did not significantly decrease the load necessary to induce 50% VAS dyspnoea ($p = .486$). Participants perceived more chest tightness (10–37%VAS; $p = .028$ uncorrected) and increased mental effort (37–56%VAS, $p = .017$ uncorrected) during resistive loading during isocapnia compared with poikilocapnia. Loads required to induce 50%VAS dyspnea unpleasantness remained stable over all experimental sessions. **Discussion.** No habituation or sensitization occurred. Hypercapnia did not amplify the response to loading, but increased unpleasantness during unloaded breathing. Despite potential FMRI advantages, the hypercapnia necessary for isocapnia may have deleterious effects on the experimental model.

Respiratory modification of the PR-RR interval – Implications for psychophysiolog?y

James A.J. Heathers

University of Sydney, Sydney, Australia

Background. Electrocardiogram (ECG) traces are commonly divided into cardiac cycles between phases, overwhelmingly between R-waves. These are analysed in the time and frequency domains, and the information of the variability of these cycles is used to assess autonomic state. However, little attention is paid to the manner in which these cycles are defined. This is problematic, as cycles between different peaks in ECG phases may result in different spectral information if those peaks are not consistently related. This has recently been observed during exercise, but not at rest. **Method.** $N = 14$ participants undergo novel ECG testing where separate lead configurations are used to identify the P-wave (Lewis Lead) and R-wave (modified Lead II), and the timings are compared by either template matching or by identifying local threshold. These participants performed several breathing protocols; free breathing, 10 s I/E cycles at a 1:2 through 2:1 ratio, brief static apnoea during inspiration and expiration, etc. at both rest and during exercise. **Results.** Decoupling between the P and R waves of the electrocardiogram occurs at slower rates than the intrinsic heartbeat (approx 90 bpm). During maximum inhalation in particular (i.e., breathing with a 2:1 I/E cycle), transient tachycardias are reliably provoked in normal subjects (i.e., $n = 10/14$) at physiological heart rates. During these periods, the linear PR to RP interval is uncoupled and reversed. Normal laboratory stress contributes only equivocally to this process. **Discussion.** While two primary respiratory variables are not controlled (tidal volume and the lung volume vis. the Hering–Breuer reflex), it seems that deep breathing (especially when at maximal inspiration) is capable of modifying the proportional cycle length of individual phases of the ECG on a beat-to-beat basis. The immediate problem this presents is that it challenges the basis of how HRV calculations are performed, as the 'recovery' inverse relationship between PR and RP intervals clearly violates the assumption on which HRV is calculated from RR intervals.

Differences in urge to cough and total coughs produced in Parkinson's disease vs. healthy adults

Karen W. Hegland[1], *Michelle S. Troche*[1], *Michael Okun*[2], *Paul W. Davenport*[3]

[1]*Department of Speech, Language, and Hearing Sciences, USA*[2]*Department of Neurology and Neurosurgery, University of Florida, USA*[3]*Department of Physiological Sciences, University of Florida, USA*

Background. The urge-to-cough (UtC) provides a measure of respiratory sensation related specifically to an irritating airway stimulus. There is evidence to suggest that blunted UtC ratings may relate to development of aspiration pneumonia; a leading cause of death in Parkinson's disease (PD). The goal of this study was to determine the UtC as it relates to the total reflex cough response in participants with PD compared to healthy control participants. **Method.** Twenty participants with mild to moderate PD, and 24 healthy participants with no history of PD or any other neurologic or neurodegenerative disease were recruited for this study. Participants completed a capsaicin challenge with three trials of 200 μM capsaicin. Following each presentation,

participants rated their UtC on a modified Borg scale. The total number of coughs produced (CrTot) for each of the three trials was recorded. An independent samples Mann Whitney U test was used to determine whether there were significant differences for UtC and CrTot between the 2 participants groups (PD and healthy). **Results.** There were significant differences between PD and healthy participants for UtC, and marginally significant differences for CrTot. These results show that for PD participants, there are fewer total coughs produced, and a reduced or blunted UtC compared to those responses for healthy participants when tested at the same concentration of the capsaicin stimulus. **Discussion.** Our understanding of airway protection deficits in Parkinson's disease (PD) continues to expand, including now reflex and perceptual measures of cough. These measures of sensation and perception may be important as we move towards determining the factors that significantly contribute to the increased morbidity and mortality related to airway protection deficits in people with PD. Specifically, we aim to develop a better understanding of what affective dimensions may contribute to the UtC sensation, and how those are impacted by PD.

Respiratory hypoalgesia: Exploring the effect of respiratory phase and breath holding on the nociception flexion reflex and subjective pain

Hassan Jafari, Johan Vlaeyen, Omer Van den Bergh, Ilse Van Diest

University of Leuven, Belgium

Background. Several observations suggest a respiratory modulation of pain sensitivity. First, slow and deep breathing is often applied as a strategy to control pain. Second, acute pain typically triggers an inspiratory gasp that is followed by a post-inspiratory breath-hold. Given this, the present study hypothesized that respiratory phase and depth of breathing modulate pain sensitivity. To test this, we studied the influence of respiratory phase during spontaneous breathing (inhalation vs. exhalation), and of instructed breath-holding on pain sensitivity. **Method.** Thirty-two healthy individuals received suprathreshold electrocutaneous stimulations applied on the sural nerve to elicit both Nociception Flexion Reflex (NFR) and pain. Participants rated their perception of pain intensity and unpleasantness, while a pneumograph chest belt was measuring respiratory cycles. Pain measures were recorded during 20 counterbalanced spontaneous inhalations and exhalations, and also during 3 types of instructed breath-holds: following exhalation, at 50%, or at 80% of maximal inspiratory capacity. **Results.** During spontaneous breathing between inhalation and exhalation no significant difference was found for NFR, self-reported pain and unpleasantness. Nonetheless the NFR, but not self-reported pain and unpleasantness were reduced during breath-holds following exhalation and at 80% of one's inspiratory capacity compared to breath-holds at 50% of inspiratory capacity. **Discussion.** In conclusion, respiratory breath-holding modulate spinal nociception sensitivity, but the modulation might be too weak to influence the subjective pain perception.

Load compensation and magnitude estimation of inspiratory resistive loads in an individual with SCI-case study

Poonam B. Jaiswal[1], *Nicole J. Tester*[2,3], *Paul W. Davenport*[1]

[1]*Department of Physiological Science, University of Florida, Gainesville, FL, USA*[2]*Department of Physical Therapy, University of Florida, Gainesville, FL, USA*[3]*Brain Rehabilitation Research Center, Malcom Randall Veterans Affairs Medical Center, Gainesville, FL USA*

Background. Acute intermittent hypoxia (AIH) treatment improves ventilation in animals with spinal cord injury (SCI) and may enhance ventilation in individuals with SCI. We postulated that ten days of AIH would improve load compensation and decrease perceptual sensitivity to inspiratory resistive loads (IRL), in a SCI individual. We evaluated the changes in ventilation and magnitude estimation (ME) to IRL, before and after AIH, in an individual with SCI. **Method.** The subject was a 55-year-old female with chronic, incomplete C4–C5 injury. The subject reclined on a flat bench and respired through a mouthpiece which was connected to a resistive loading manifold via a non-rebreathing valve and a tube. A light cued the subject when an IRL (0, 5, 15, 30 and 50 $cmH_2O/L/s$) was applied for a single inspiration. Each IRL was presented five times in a randomized block. The subject estimated the magnitude of the IRL using a modified Borg Scale. There were four IRL trials: Baseline, Post Sham, AIH Days 1 and 10. Pressure (P), airflow (AF) and ME were analyzed using one way RMANOVA. **Results.** The subject had a significantly greater P at IRL 30 on AIH Day 1 vs. Baseline ($p \leq 0.01$). The slope of P vs. IRL was significantly decreased on AIH Day 10 vs. baseline ($p \leq 0.01$). AF was significantly increased for IRLs 15, 30 and 50 on AIH days 1 and 10 ($p \leq 0.05$). The slope of AF vs. IRL was significantly increased on AIH Day 10 vs. Baseline ($p \leq 0.05$). The slope of Log ME vs. Log P did not change across conditions. **Discussion.** The decrease in slope of P vs. IRL and a corresponding increase in slope of AF vs. IRL suggest an improved ability to load compensate to repeated IRL after AIH. This paradigm showed improved load compensation without altering the IRL perceptual sensitivity.

Generalization of respiratory symptom triggers

Thomas Janssens, Farah Martens, Nathalie Storms, Meike Pappens, Ilse Van Diest, Omer Van den Bergh

Health Psychology, University of Leuven, Belgium

Background. Behavioral management of asthma requires accurate identification of asthma triggers. However, identification of asthma triggers is prone to inaccuracies. Generalization, the tendency to exhibit a conditioned response to a stimulus that resembles a conditioned stimulus, may help explain the development of inaccurate trigger identification. Generalization can occur along perceptual dimensions, but also along other dimensions of similarity, such as conceptual similarity or category membership. In this experiment, we studied the generalization of asthma trigger learning and explored individual differences in the acquisition of trigger-symptom contingencies and their generalization to conceptually similar trigger categories. **Method.** 48 individuals without any history of asthma or allergies performed 20 breathing trials. Participants rated their symptom expectancy for 10 CS+ (e.g., bird) and 10 CS− (e.g., flower) pictures, which were followed by a 60 s inhalation of a 7.5% CO_2 air mixture (half of the CS+ trials) or room air (other trials). Finally, they rated symptom intensity and unpleasantness. Either 24 h or 1 week after session 1, participants filled out a measure of suffocation fear (SF), and completed symptom expectancy ratings and recognition ratings for old and novel CS+/CS− exemplars, as well as generalization stimuli (e.g., G+, mammals; G−, molds). **Results.** Participants showed increased expectancies for the CS+ compared to CS− exemplars, which developed across trials. During the recognition task, symptom expectancies generalized to CS+ stimuli that had not been previously paired with CO_2. High SF individuals showed increased symptom expectancies. For G+ stimuli, the differences in symptom expectancy for low and high SF individuals were smaller. High SF individuals furthermore had higher false CS+ false alarm rates when tested 24 h later. **Discussion.** Participants generalize trigger-symptom experiences to novel exemplars of the same or similar categories. High SF individuals may be especially prone to overgeneralization.

Electrophysiological correlates of emotion processing in dyspnea

Georgiana Juravle[1], *Cornelia Stoeckel*[1], *Michael Rose*[1], *Matthias Gamer*[1], *Christian Büchel*[1], *Matthias Wieser*[2], *Andreas von Leupoldt*[1,3]

[1]*University Medical Center Hamburg-Eppendorf, Hamburg, Germany*[2]*University of Würzburg, Würzburg, Germany*[3]*University of Leuven, Leuven, Belgium*

Background. Dyspnea is recognized as a threatening bodily sensation and a key symptom in respiratory and psychological disorders. It has been demonstrated that emotional contexts can substantially influence its perception and neural processing. Nevertheless, little is known about the reverse influence that dyspnea could have on the neural processing of emotion. In the present study we examined the influence of dyspnea on emotional picture processing. **Methods.** The continuous electroencephalogram (EEG) was recorded while 20 healthy participants viewed positive, neutral, and negative picture series under conditions of resistive-load-induced dyspnea, auditory noise of matched intensity, as well as an unloaded baseline. **Results.** Results indicated attenuated visual processing during dyspnea, as indexed by reduced event-related potential (ERP) amplitudes of the P1 and the early posterior negativity (EPN) deflections, irrespective of picture valence. Furthermore, both the EPN and the late positive potential (LPP) ERPs exhibited the commonly observed emotional modulation: That is, larger mean ERP amplitudes were found for positive and negative picture viewing, as compared to neutral picture viewing, without differences between conditions of dyspnea, noise, and baseline. **Discussion.** These findings replicate previous ERPs results on affective picture processing and suggest that dyspnea impacts on the early attention-related neural processing of emotional pictures, but leaves the emotional discrimination between these stimuli intact.

Urban families' responses to their children's asthma: What families do when faced with symptoms

D. Koinis Mitchell, *C. Esteban*, *S.J. Kopel*, *E.L. McQuaid*, *B. Jandasek*, *R. Seifer*, *G. Fritz*, *R.B. Klein*

Brown Medical School/Bradley Hasbro Research Center, Providence, RI, USA

Background. The current study examines the step-by-step decision making and rescue response behaviors that a sample of urban families implement when their children have asthma symptoms. We applied a coding system based on clinical guidelines (NHLBI, 2007) to categorize rescue response behaviors into appropriate and inappropriate categories. We examined the association between asthma response behaviors, asthma activity, and clinically significant events (e.g., ED use). We assessed asthma response behaviors in the context of upper airway function. **Method.** Data were examined from 200 urban children (aged 7–9) with persistent asthma and their families enrolled in Project NAPS. One question from the subscale of The Family Asthma Management System Scale, developed by our group, involved asking families a series of questions that elicit the response steps taken when their children experience asthma. Lung function was assessed (FEV1 percent predicted) via the AM2. Children and caregivers recorded the days when asthma and rhinitis symptoms were present. Peak nasal inspiratory flow data and rhinitis control was also assessed. **Results.** For children with at least 1 ED visit, the asthma response plans were poorer ($M_n = 4.6$) than for children who had not been to the ED ($M_n = 5.5$). The majority of the families (75%) had inappropriate rescue plans. Children of families with inappropriate plans reported more rhinitis symptoms compared to children of families with appropriate plans ($M_n = 40\%$ of monitored days vs. 11%). Many families with inappropriate plans reported going to the ED after only 1 albuterol dose. Fewer rhinitis symptoms were reported among children in families with an appropriate plan vs. those with an inappropriate plan (7% v. 30% rhinitis symptom days, $F(1,21) = 3.9$, $p = .05$. **Discussion.** Many urban families in this sample implement inappropriate asthma rescue response behaviors, which appear to be linked with more clinically significant events for asthma and more rhinitis symptoms.

An interim report on a two-center trial of heart rate variability biofeedback for asthma

Paul Lehrer[1], *Frederick Wamboldt*[2]

[1]*Rutgers Robert Wood Johnson Medical School, Piscataway, NJ, USA*[2]*National Jewish Health, Denver, CO, USA*

Background. This report is based on data from 36 participants. It is an interim analysis of data from an ongoing study. **Method.** We compared training in heart rate variability biofeedback with a complex control condition that included 1) training in breathing at normal relaxed respiratory rate (approx 15/min), 2) EEG biofeedback to increase and decrease alpha from the Oz to pFz sites, 3) listening to relaxing music. This is a two-center trial, performed on patients with mild or moderate symptomatic asthma, who are not taking inhaled steroids or other anti-inflammatory drugs. **Results.** Thus far we have found that both conditions produced significant improvements in measures of pulmonary function, airway inflammation, quality of life, and general asthma symptomatology, with a small advantage to HRV biofeedback. Symptoms continued to improve after administration of an inhaled steroid for one month. **Discussion.** Thus far, it appears that heart rate variability biofeedback does not substitute for inhaled steroids. Some elements of the control condition may have effects that are almost as powerful as biofeedback effects. However the study was not powered for such a small sample. Research is continuing.

An update on systems theory for psychophysiology

Paul Lehrer, *David Eddie*

Rutgers, The State University of New Jersey, USA

Systems theory has long been used in psychology, biology, and sociology. This paper applies newer methods of control systems modeling for assessing system stability in health and disease. Control systems can be characterized as open or closed systems with feedback loops. Feedback produces oscillatory activity, and the complexity of naturally occurring oscillatory patterns reflects the multiplicity of feedback mechanisms, such that many mechanisms operate simultaneously to control the system. Unstable systems, often associated with poor health, are characterized by absence of oscillation, random noise, or a very simple pattern of oscillation. This modeling approach can be applied to a diverse range of phenomena, including cardiovascular and brain activity, mood and thermal regulation, and social system stability. External system stressors such as disease, psychological stress, injury, or interpersonal conflict may perturb a system, yet simultaneously stimulate oscillatory processes and exercise control mechanisms. Resonance can occur in systems with negative feedback loops, causing high-amplitude oscillations at a single frequency. Resonance effects can be used to strengthen modulatory oscillations, but may obscure other information and control mechanisms, and weaken system stability. Positive as well as negative feedback loops are important for system function and stability. Examples are presented of oscillatory processes in heart rate variability, and regulation of autonomic, thermal, pancreatic and central nervous system processes, as well as in social/organizational systems such as marriages and business organizations. Resonance in negative

feedback loops can help stimulate oscillations and exercise control reflexes, but also can deprive the system of important information. Empirical hypotheses derived from this approach are presented, including that moderate stress may enhance health and functioning.

Psychological comorbidities in the female COPD patient: Implications for practice

Sarah Miller[1], *Emily Plowman*[2]

[1] *University of Memphis Loewenberg School of Nursing, USA* [2] *University of South Florida, USA*

Background. To provide advance practice nurses (APNs) an overview of the need for assessment of psychological comorbidities in the female patient with chronic obstructive pulmonary disease (COPD) to better manage patient outcomes and improve quality of life. Women with COPD report lower health-related quality of life (HRQOL) indices and suffer from nearly double the prevalence of anxiety and depressive comorbidities than men. Heightened emotional burden of respiratory disease can be partially attributed to an increase in sensitivity (hyperperception) of respiratory related symptoms leading to inaccurate symptom reporting, and contributing to a subjective sense of poor disease control. This varied affective and sensory dimension of respiration needs to be considered by APNs and integrated into standardized assessment in the clinical setting to optimize individual care and evaluate specific therapeutic interventions. **Method.** An evidence-based approach to nursing care is incorporated into clinical practice settings to improve patient outcomes. To more completely understand the interactions of respiratory hyperperception, psychological comorbidities and COPD in women; an extensive literature search across multiple databases (PubMed, CINAHL, Medline Plus with full text, PsychINFO and Health Source: Nursing/Academic Edition) was performed by a single rater. **Results.** The link between symptoms of anxiety and depression in patients with COPD is well documented with the most significant emerging associative factors identified being: gender, race and age, with female gender being the most significant. The literature highlights the need for additional studies to better facilitate our understanding of the relationship between enhanced respiratory symptom perception and psychological comorbidities. **Discussion.** Larger and more rigorous studies are needed to facilitate APN's ability to recognize and appropriately care for psychological comorbidities in the female COPD patient. Training to increase screening skills and awareness needs to be targeted to APNs to provide a clearer understanding of assessing and caring for this patient population.

The effect of interoceptive fear conditioning on breathing behavior and dyspnea intensity perception in asthma patients and healthy controls

Meike Pappens, *Laure Meulepas*, *Omer Van den Bergh*, *Ilse Van Diest*

University of Leuven, Leuven, Belgium

Background. The high comorbidity between asthma and anxiety disorders suggests that psychological factors might play a role in asthma. In this study we wanted to investigate the influence of fear conditioning mechanisms on breathing behavior and self-reported dyspnea intensity. **Method.** The conditioned stimulus (CS) was a small respiratory load (applied for 8 s); the unconditional stimulus (US) was a breathing occlusion (applied for 40% of the personal breath holding time). Half of the participants were asthma patients ($N = 26$), half were healthy controls ($N = 30$). The experimental groups (ASTHMA: $N = 13$; HEALTHY: $N = 15$) received 6 acquisition trials with paired CS–US presentations followed by an intertrial interval (ITI, 27–30 s). The control groups (ASTHMA: $N = 13$; HEALTHY: $N = 15$) received 6 trials of unpaired presentations of CS and US separated by an ITI. In the extinction phase, all groups were administered 6 CS-only trials. Three CS pre-exposure trials were given before acquisition. After each trial participants rated their dyspnea intensity during the CS. **Results.** In the acquisition phase, Tidal volume (V_t) significantly decreased during the CS in the control but not in the experimental groups compared with pre-exposure. Respiratory rate also decreased during acquisition in the experimental groups but not in the control groups. Results show that all groups reported more dyspnea at the end of acquisition compared to CS pre-exposure. At the end of extinction the two groups in the experimental condition and the healthy group in the control condition reported significantly less dyspnea than during CS pre-exposure. Remarkably, this was not the case for the asthma group in the control condition, who displayed the same level of dyspnea at the end of extinction as during CS pre-exposure. **Discussion.** Our findings shed an important light on the role of safety learning/unpredictability in dyspnea severity perception and on the influence of breathing behavior on this perception.

The effect of interoceptive fear conditioning on breathing behavior

Meike Pappens, *Omer Van den Bergh*, *Ilse Van Diest*

University of Leuven, Leuven, Belgium

Background. It has been demonstrated that fear can be learned to mild, innocent dyspnea by pairing it with an aversive event. Traditionally in fear conditioning research, fear measures include startle blink EMG, skin conductance responses and self-reported fear. Breathing behavior has hardly been investigated despite its possible role in the extension and aggravation of fear. The aim of the present study was to monitor respiratory responses in an interoceptive fear conditioning paradigm. **Method.** Fifty-six healthy participants received a mild respiratory load (10 $cmH_2O/l/s$ for 8 s) as CS and a severe respiratory load (40 $cmH_2O/l/s$ for 30 s) as US. 3 CS pre-exposure trials were administered before acquisition, in which the experimental group (N) received 6 explicitly paired CS–US presentations and the control group (N) 6 explicitly unpaired CS–US presentations. In the extinction phase, both groups were exposed to 6 CS-only presentations. Respiratory measures included respiratory rate (RR) and Tidal volume (V_t). **Results.** RR in response to the CS-load decreased but to a lesser extent in the experimental group than in the control group. The same pattern was visible in V_t: while during the CS the control group significantly reduced its V_t over acquisition, the experimental group did not. **Discussion.** Our data show that fear conditioning to a respiratory stimulus induces maladaptive respiratory behavior in healthy individuals. These findings highlight the importance of studying respiratory behavior in the context of fear conditioning.

FMRI and respiratory control

Kyle Pattinson

University of Oxford, John Radcliffe Hospital Oxford, United Kingdom

Functional magnetic resonance imaging (FMRI) allows the identification of location, pattern, and time course of brain activity, in vivo, without the need for administration of exogenous contrast or radioactive tracers. Although FMRI has become a standard tool in psychology research, when used to investigate neural control of breathing, alterations in systemic cardiorespiratory physiology have the potential to confound its interpretation.In this lecture I will explain the basis of FMRI responses, and the challenges faced

when trying to understand the neural control of breathing and breathlessness. I will explain some of the strategies my group has used to help overcome these issues and how these have helped us to better understand the effects of opioid pain killers on the neural control of breathing.

Relative breathless: Comparison with others can affect feelings of breathlessness

Sibylle Petersen, Omer Van den Bergh

University of Leuven, Leuven, Belgium

Background. Social comparison has a longstanding research tradition, showing that we cannot construct our self-concept in terms of skills, attractiveness, personality, or mood independent of comparison with others. However this perspective has rarely been applied to perception of bodily sensations and symptoms. Furthermore, little is known on differential effects of social comparison on self-report and exercise behavior. **Methods.** In four studies with healthy individuals and individuals with asthma and Chronic Obstructive Pulmonary Disease we tested the hypothesis that social comparison affects perception of breathlessness and breathing-related behavior. In all studies, participants received information about others less or more likely to experience breathlessness during physical activity (upward and downward comparison standards). In all studies, participants completed breathing Tasks with external respiratory loads of low to moderate magnitude (6–20 cmH_2O) or standardized exercise tests (six-minute walking test, 6MWT) and gave self-report of breathlessness. In two studies, we measured inspiratory pressure and flow. **Results.** In all studies, social comparison had a significant effect on self-report of dyspnea. Furthermore, we found effects of social comparison on inspiratory pressure and flow and on performance in exercise tests. However, effects were strongest in loads of low to medium magnitude (6–9 cmH_2O). **Discussion.** Social comparison can bias the perception of dyspnea and can change breathing behavior and exercise performance in healthy individuals and individuals with respiratory disease. Social cognitive processes may be an important source of bias in symptom perception and report and exercise behavior.

The relationship between voluntary cough production and swallow safety in individuals with amyotrophic lateral sclerosis

E.K. Plowman, S.A. Watts, A. Domer, J. Gaziano, S. Miller, T.E. Pitts, D. Estores, J. Richter, K. Donoghue, C. Gooch, T. Vu

University of South Florida, Departments of Communication Sciences and Disorders and Neurology, USA

Background. Cough is an essential airway protective mechanism and is particularly important for those with disordered swallowing. With the necessity for fine-tuned laryngeal and respiratory coordination for both cough and swallow, we hypothesize that dystussia (disorder of cough) may be predictive of swallowing dysfunction. The aim of this study was to examine the relationship between voluntary cough production and swallow safety in persons with Amyotrophic Lateral Sclerosis (ALS). **Method.** Physiologic measures of voluntary cough production from 10 individuals with ALS showing no videofluoroscopic evidence of penetration/aspiration were examined and compared to 10 ALS participants with evidence of penetration/aspiration. Group differences were assessed using a one-way ANOVA and a series of Spearman's Rho correlations performed to assess the degree of relationship between voluntary cough measures and airway safety during swallowing. **Results.** The penetrator/aspirator group presented with lower cough volume acceleration ($p < 0.05$) and longer compression phase duration ($p < 0.05$) voluntary cough waveforms when compared to the non-penetrator/aspirator group. A significant positive correlation was revealed between PAS score and cough compression phase duration ($r = 0.48$, $p < 0.05$) indicating that the longer the duration of glottic closure during voluntary cough, the higher the PAS score observed. **Discussion.** In this study, ALS patients who penetrated/aspirated demonstrated less effective voluntary cough with a slower compression phase. Compression phase duration (time of glottic closure during cough) was related to the degree of penetration/aspiration. Measures of voluntary cough may be useful predictors of penetration and aspiration in individuals with ALS.

The neurobiology of the sigh: From the respiratory network to arousal

Jan-Marino Ramirez[1,2], Tatiana Dashevskiy[1]

[1]Center for Integrative Brain Research, Seattle Children's Research Institute, Seattle, WA, USA[2]Department of Neurological Surgery, University of Washington, Seattle, WA, USA

Background. Here we describe the neurobiological basis of the sigh, a distinct breathing behavior that has been associated with three specific behavioral roles: (1) sighs monitor changes in brain states, (2) induce arousal and (3) play a role in resetting breathing variability. These three roles are adaptive and may help to homeostatically regulate breathing stability in normal life activities, but sighs can also be maladaptive: Hypo-arousal and failure to sigh have been associated with SIDS, while increased breathing irregularity may provoke excessive sighing and hyperarousal, a behavioral sequence that may play a role in panic disorders. **Methods.** All methods have previously been described in Weese-Mayer et al., 2006, and Lieske et al., 2000. **Results.** We demonstrate that sighs and breathing critically depend on the pre-Boetzinger complex (preBoetC), a network located within the ventrolateral medulla. Both respiratory patterns continue to be generated upon isolation in a transverse slice. Even in isolation, sighs reset ongoing respiratory activity and decrease the approximate entropy of respiratory activity. Mechanistically our data demonstrate that the *P*/*Q*-type calcium channel, persistent sodium current-dependent burst mechanisms, intrinsic oxygen sensitivity, as well as modulatory and synaptic interactions within this local network can explain many of the observed behavioral characteristics of the sigh. Moreover, our recent data suggest that glia play a critical role in the generation of the sigh, as lesioning glia specifically abolishes sighs. **Discussion.** Although breathing and sighs are generated within the same local network in the PreBoetC, these activities are characterized by distinct cellular mechanisms. Understanding the neuronal basis of the sigh and its interaction with ongoing respiratory activity is an important prerequisite to unravel how sighs interact and control higher brain functions.

Breath holding duration as a measure to assess distress tolerance: Does it relate to executive contro?l

Mathias Schroijen[1], Stefan Sütterlin[1,2], Elena Constantinou[1], Omer Van den Bergh[1], Ilse Van Diest[1]

[1]Research Group on Healthy Psychology, University of Leuven, Belgium[2]Research Unit INSIDE, University of Luxembourg, Luxembourg

Background. Distress (in)tolerance is put forward as a crucial concept in both the etiology and course of various forms of psychopathology (e.g., anxiety, depression, addiction and chronic pain). In this study we wanted to investigate whether the Breath Holding Task (BHT) can be used as a behavioral indicator for distress tolerance. We assessed its test–retest reliability and its

relationship with classical executive function tasks measuring trait-like inhibitory capacities. **Methods.** 113 students completed a collective BHT assessment. A subset ($N = 58$) also completed a series of executive function tasks: the Wisconsin Card Sorting Test measuring cognitive flexibility, the Parametric GO/No-GO measuring response inhibition and the N-back task measuring memory updating. Another subset of these students ($N = 34$) repeated the BHT one year later. **Results.** Test–retest reliability over a one-year period was high with ($r = .67$, $p < .001$). None of the executive functioning tasks was significantly associated with BHT. **Discussion.** The lack of associations with executive function tests challenge previous assumptions of active inhibitory control in the breath holding task. However, breath holding induced rather moderate levels of unpleasantness, suggesting that executive control resources were not sufficiently activated due to a low level of perceived distress. Exploratory findings further suggest that individual differences (e.g., in interoceptive or anxiety sensitivity) should be taken into account when examining the validity of BHT as a measure of distress tolerance.

A trans-species approach to panic

Koen Schruers

School for Mental Health and Neuroscience & Academic Anxiety Center, Maastricht University, The Netherlands

Panic is a common phenomenon of which the pathophysiology is not fully understood. A long tradition exists of experimental panic provocation in the lab by inhalation of increased concentrations of carbon dioxide. Originally, research focused on patients with panic disorder. Recent data show however that panic can be reliably provoked in healthy volunteers as well. This fits the hypothesis that panic is a fear response to bodily internal signals of danger and that every person is equipped with a system to detect such signals. Methods to investigate the underlying mechanisms include pharmacological challenges, gene–environment interaction studies and functional neuroimaging studies. To study some of the cellular and molecular aspects, the use of animal models is required. This lecture will give an overview of experimental studies into the pathophysiology of panic, starting in patients and then moving into healthy volunteers and ultimately also in rodents, introducing the first trans-species experimental model of panic.

Dysautnomia induced by inspiratory threshold loading in healthy subjects

Caroline Sevoz-Couche[1], *Anna L. Hudson*[2,3], *Marie-Cécile Niérat*[2,4], *Thomas Similowski*[2,4], *Louis La Violette*[2,4]

[1]*CR-ICM, UPMC/INSERM, UMR-S 975, CNRS UMR 7225, Faculté de médecine UPMC, Paris, France*[2]*Université Paris 6, ER10UPMC, Paris, France*[3]*Neuroscience Research Australia and University of New South Wales, Sydney, Australia*[4]*Assistance Publique-Hôpitaux de Paris, Groupe Hospitalier Pitié-Salpêtrière, Service de Pneumologie et Réanimation Médicale, Paris, France*

Background. Dyspnea is a subjective experience of respiratory discomfort associated with negative affects. As such, it is bound to affect the autonomic balance, but these effects have scarcely been studied. **Method.** Eleven naive healthy subjects (9 women, age 29 ± 7 years, mean $\pm$ SD) were exposed in random order to 3 levels of inspiratory threshold loading (ITL, 5 min each) to induce experimental dyspnea of the "work/effort type" (intensity evaluated using a visual analogue scale). Powers of spectral density of R–R interval variability were calculated at baseline, during the inspiratory loading and recovery, within the frequency ranges of 0.04–0.15 Hz (low frequency, LF) and 0.15–0.4 Hz (high frequency). The LF-to-HF ratio (LF/HF), an index of sympathetic activity, was calculated. Temporal R–R interval variability was also calculated. **Results.** The peak inspiratory work/effort sensation intensity was 26 ± 26, 41 ± 26 and 62 ± 24% of full scale" for low, medium and high levels of ITL, respectively. During loading, heart rate and LF/HF increased, while HF and temporal R–R interval decreased compared to baseline spontaneous ventilation values. Maximal increases (+15% and +161%, respectively) and decreases (−35% and −20%, respectively) were found after the first ITL load, independently of its magnitude. Values returned to baseline during recovery. **Discussion.** An increase in sympathetic activity and a decrease in parasympathetic tone were induced by first exposure to ITL and did not depend of ITL level. Therefore, in young healthy subject, experimental inspiratory loading can induce autonomic imbalance. Inspiratory loading can be considered a stressful situation that could have important repercussions on whole-body stress responses.

Swallow-related quality of life changes before and after expiratory muscle strength training (EMST) in individuals with multiple sclerosis

Erin Silverman[1,5,6], *Paul W. Davenport*[1], *Nan Musson*[2], *Mary Edwards*[2,5], *Toni Chiara*[3,6], *Christine Sapienza*[4,5]

[1]*Department of Physiological Sciences, University of Florida, Gainesville, FL, USA*[2]*North Florida South Georgia Veteran's Health System, Malcom Randall VAMC, USA*[3]*North Florida South Georgia Veteran's Health System, Lake City VAMC, USA*[4]*Jacksonville University, Jacksonville, FL, USA*[5]*Brain Rehabilitation and Research Center – BRRC, Malcom Randall VAMC, Gainesville, FL, USA*[6]*Rehabilitation Outcomes Research Center – RORC, Malcom Randall VAMC, Gainesville, FL, USA*

Background. Multiple sclerosis (MS) is a progressive, inflammatory, demyelinating disease of the central nervous system. MS exerts deleterious effects on respiratory muscle strength. MS also affects laryngeal muscle strength and coordination. Swallow dysfunction, coupled with impaired respiratory muscle strength and impaired cough, places an individual with MS at high risk for penetration and aspiration and aspiration pneumonia. Expiratory muscle strength training (EMST) improved swallow function and swallowing-related quality of life (QOL) in individuals with Parkinson's disease. We hypothesized that respiratory and swallow related QOL will improve following EMST in individuals with MS. **Methods.** Swallow-related quality of life (SWAL-QOL) was measured in a 32 individuals with MS. All participants were diagnosed with relapsing–remitting MS. 19 participants were in the EMST group and 13 in the sham group. All participants completed the SWAL-QOL at baseline and following completion of 5 weeks of training. The EMST group received 5 weeks of EMST training set to 75% their average maximum expiratory pressure (MEP). EMST group subjects completed 5 sets of 5 repetitions (25 "blows") into the device per day, 5 days per week. The sham group was given a device identical in appearance and operation to the EMST device, the sham devices were non-functional by removal of the pressure release valve. The sham group training protocol was identical to the EMST group. This was a double-blind sham controlled experimental design. **Results.** The Sham group had no significant change in MEP from pre- to post-training. The EMST group had a significant increase in MEP post-training. Both groups significantly improved their self-perceived SWAL-QOL pre- to post-treatment with no significant difference in the change in SWAL-QOL between groups. **Discussion.** These results show a respiratory treatment effect for EMST in individuals with MS. The SWAL-QOL change may be related to interaction with the clinicians.

The supplementary motor area and human respiration from volitional breathing to the compensation of mechanical inspiratory loading: Neurophysiological substrates of "work/effort" dyspne?a

Thomas Similowski, Mathieu Raux, Anna L. Hudson, Marie-Cécile Nierat, Dan Adler, Cécile Chenivesse, Louis Laviolette, Capucine Morelot-Panzini

ER10upmc "Experimental and Clinical Respiratory Neurophysiology", Paris 6 University, Paris, France

Background. In vertebrates, breathing is the only vegetative function that depends on a motor command originating in the central nervous system (brainstem central pattern generators) rather than being intrinsic to the concerned organ system. This organization allows for the decoupling of respiratory muscle activity from homeostasis. Indeed, breathing can be altered through emotion-activated limbic networks or in response to volitional programs (voluntary breathing or speech). Respiratory-related volitional cortical networks involve respiratory representations within the primary motor cortex and premotor structures including the supplementary motor area (SMA). **Method.** This presentation reports investigations of the respiratory-related function of the SMA performed using repetitive transcranial magnetic stimulation (rTMS), electroencephalographic averaging techniques (EEG), and functional magnetic resonance imaging (fMRI). **Results.** Functional connectivity exists between the SMA and phrenic spinal motoneurones, with a tonic excitatory influence that can be modulated in either direction by rTMS. ITL activates cortical networks from the first breath on, with a conjunction of limbic and subcortical signals, default-mode deactivation, and SMA activation. This initial response contrasts with the response to sustained ITL that is focused on the SMA, which suggests cortical automatization as does the perennial nature of the respiratory-related EEG response to prolonged ITL (premotor potentials, PMPs). PMPs precede inspiration in normal subjects faced with ITL who report ITL-induced dyspnea, their amplitude seemingly depending on the magnitude of the load. In patients mechanically ventilated with signs of respiratory distress, adjusting ventilator settings alleviates dyspnea and can extinguish inspiratory PMPs. In patients suffering from amyotrophic lateral sclerosis (ALS) with respiratory insufficiency, PMPs are present during spontaneous breathing and disappear under non-invasive ventilation. **Discussion.** The cortical networks subserving volitional breathing are activated by inspiratory loads in humans. This probably accounts for the fact that such loads are compensated during wake but not during sleep. Because inspiratory loads also induce dyspnea, it is hypothesized that these networks play a role in its pathogenesis.

Activation of right insular cortex during the anticipation of dyspnea

M.C. Stoeckel[1], *R.W. Esser*[1], *M. Gamer*[1], *C. Büchel*[1], *A. von Leupoldt*[1,2]

[1]*Department of Systems Neuroscience, University Medical Center Hamburg-Eppendorf, Hamburg, Germany*[2]*Research Group Health Psychology, University of Leuven, Leuven, Belgium*

Background. Dyspnea is an aversive bodily sensation processed by a neuronal network of sensorimotor and emotion-related areas. Patients suffering from chronic diseases such as asthma and COPD with dyspnea as leading symptom might learn to anticipate dyspnea under circumstances such as physical exercise. However, little is known about the brain mechanisms underlying the anticipation of dyspnea. **Methods.** Inspiratory resistive load induced dyspnea was presented to 46 healthy subjects during parallel acquisition of fMRI-data. Blocks of severe dyspnea alternated with blocks of mild dyspnea, each lasting 24 s. Each block was visually cued for 6 s (anticipation periods). After each block subjects gave intensity and unpleasantness ratings of dyspnea. At the end of the experiment subjects further indicated their anticipatory fear during the two different cue periods (announcing mild and severe dyspnea, respectively). **Results.** Subjective reports on the perceived intensity of dyspnea confirmed the successful induction of severe and mild dyspnea. Subjects furthermore reported significantly more fear during the anticipation of severe vs. mild dyspnea. Dyspnea activated an extensive network of sensorimotor (SMC, SMA, SII) and limbic areas (bilateral insular cortex) as previously described. The right insular cortex showed an increase during the anticipation of severe as compared to mild dyspnea. This right insular area furthermore showed increased connectivity with periaqueductal grey (PAG) and bilateral amygdala when severe as compared to mild dyspnea was anticipated. **Discussion.** The anticipation of dyspnea involves the activation of an emotion-related area in the right insular cortex, most likely mirroring anticipated unpleasantness rather than preparatory motor activity. The increased connectivity to other emotion-related areas such as bilateral amygdala and PAG underlines the importance of dyspnea as bodily threat with the potential to evoke fear reactions.

Decreased sensitivity to cough stimulus in persons with Parkinson's disease and dysphagia

Michelle S. Troche[1], *Karen W. Hegland*[1], *Michael Okun*[2], *Paul W. Davenport*[3]

[1]*Department of Speech, Language, and Hearing Sciences, University of Florida, Gainesville, FL, USA*[2]*Department of Neurology and Neurosurgery, University of Florida, USA*[3]*Department of Physiological Sciences, University of Florida, USA*

Background. Pneumonia and lung infection are leading causes of death in persons with Idiopathic Parkinson's disease (PD). The pathogenesis of these infections is largely attributed to the presence of silent aspiration (or aspiration without cough response). There are no studies investigating reflex cough thresholds and urge to cough (UTC) in PD utilizing Capsaicin as the tussigenic agent. The goal of this study was to test reflex cough thresholds and associated UTC ratings in PD participants with and without dysphagia. **Method.** Twenty participants with mild to moderate PD were recruited for this study. Participants completed a capsaicin challenge with three randomized blocks of 0, 50, 100 and 200 μM capsaicin. Following each presentation, participants rated their UTC by modified Borg scale. The concentration of capsaicin that elicited the reliable 2-cough response (Cr2) served as our measure of cough reflex threshold. The sensitivity of the participant to the cough stimulus was measured as the slope of the line from the log–log relationship of capsaicin concentration and UTC. Participants were identified as 'dysphagic' or 'non-dysphagic' according to the penetration–aspiration scale. **Results.** Most participants did not have a reliable C2 cough response to 200 μM. When a cough was elicited at 200 μM Capsaicin, median UTC scores were five vs. median UTC of 2 where cough was not elicited. UTC ratings for dysphagic participants at 200 μM Capsaicin were significantly lower than those for non-dysphagic participants. Cough reflex thresholds were significantly higher and cough sensitivity significantly blunted in dysphagics. **Discussion.** UTC ratings may be important in understanding the mechanism underlying morbidity related to aspiration pneumonia in people with PD and dysphagia. Further understanding decreased UTC in people with PD and dysphagia will be essential for the development of strategies and treatments to address deficits of airway protection in this population.

Pulmonary rehabilitation where physiology meets behavioral science

Enhancing physical activity with pulmonary rehab: Changing the exercise training paradig?m

Thierry Troosters

Department of Rehabilitation Sciences, University of Leuven, Leuven, Belgium

Pulmonary rehabilitation is nowadays a recognized treatment option for patients with respiratory disease that remain symptomatic despite optimal pharmacotherapy. Most of the evidence for the efficacy of pulmonary rehabilitation is obtained in COPD, but also other patient groups may benefit from rehabilitation programs. Although programs are ideally set up as multidisciplinary programs, an exercise training program, ran by physiotherapists forms the core of the rehabilitation program. Over the past three decades the evidence base on the trainability of patients with ventilatory exercise limitation has built-up. When high intensity exercise training is used, adapted to the limitations of COPD patients is used these patients substantially improve their skeletal muscle function, exercise tolerance and health related quality of life. Symptoms associated with exercise decrease and patients report that coping with daily life is easier after rehabilitation. As an example, whole body exercise endurance nearly doubles following at least 8 weeks of exercise training. Despite the success of pulmonary rehabilitation and its incorporation in most major guidelines for the management of COPD there are two remaining challenges: (1) Effects of a rehabilitation program are only temporary. Most studies report that the effects of rehabilitation wear off after 6–12 months. (2) Patients improve their exercise physiology mainly through improved skeletal muscle function, but little effect is observed on physical activity. Low levels of physical activity form the basis of the non-respiratory consequences of COPD, such as skeletal muscle dysfunction. Since physical activity does not improve much with rehabilitation, it is no surprise that effects of a rehabilitation program wear off and long term benefits may be less than expected.Significant further improvement in the long term outcomes of rehabilitation can come from more intense collaboration between experts in physiology and experts in behavioral medicine. Efforts made so far are fragmented and lack a solid behavioral science basis. Nevertheless these seeds of collaboration have had a spin off in successful pilot studies. A third partner in this collaboration may be health technology experts who could help developing technical applications that are user friendly to patients and clinicians and allow monitoring and remote coaching of patients to enhance physical activity levels once patients have increased their exercise capacity to the maximal achievable exercise tolerance through exercise training. Only through such efforts, rehabilitation programs will be able to fulfill the expectations of the new and –in my opinion – challenging definition which is put forward this year by the American Thoracic Society and European Respiratory Society: Pulmonary Rehabilitation is designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviors. Currently the evidence for the last goal is largely absent. Through collaborative efforts, however breakthroughs may be looming on the horizon.

Capsaicin induced cough and Urge-to-Cough in elderly individuals with sarcopenia

Hsiu-Wen Tsai[1], *Kevin Fennelly*[2], *Karen Wheeler Hegland*[3], *Sherry Adams*[1], *Jillian Condrey*[1], *Jennifer L. Hosford*[2], *Paul W. Davenport*[1]

[1]*Department of Physiological Sciences, University of Florida, Gainesville, USA*[2]*Department of Medicine, University of Florida, Gainesville, USA*[3]*Department of Speech, Language, and Hearing Sciences, University of Florida, Gainesville, USA*

Background. Sarcopenia is defined as age-related loss of skeletal muscle mass and strength. Diminished muscle mass and strength is related to the risk of dysphagia which can lead to aspiration pneumonia in sarcopenic patients. Impaired Urge-to-Cough may increase the prevalence of aspiration pneumonia. In this study, we hypothesized that sarcopenic subjects have decreased cough sensitivity which mean higher threshold for inducing the Urge-to-Cough compared to subjects without sarcopenia (control subjects). We used capsaicin induced cough to determine their cough response. **Methods.** Seven female sarcopenic (age: 77.28 ± 6.42) and five control subjects (age: 76.60 ± 3.78) participated in the study. Four concentrations of capsaicin (50, 100, 200, 500 μM) plus placebo (0 μM capsaicin) were presented to the subject three times each in a blinded-randomized block order. Each capsaicin presentation was separated approximately 1 min. At the end of each capsaicin presentation, subjects were asked to rate their Urge-to-Cough using the modified Borg scale from 1 (no Urge-to-Cough) to 10 (maximum Urge-to-Cough). Cough response was defined as single or multiple coughs elicited by capsaicin inhalation. **Results.** There was no significant difference in cough response. Sarcopenic subjects showed lower Urge-to-Cough at the lowest capsaicin concentration compared to control subjects ($p < 0.05$). There were no significant differences in the Urge-to-Cough score between sarcopenic and control subjects when the capsaicin concentration was greater than 50 μM. **Discussion.** The result suggests that sarcopenic subjects have lower Urge-to-Cough sensitivity to low concentration capsaicin compared to control subjects. This result may explain why they do not cough as much with airway irritants when the stimulus is relatively small.

Stress reduction through heart rate variability biofeedback, mindfulness meditation, or physical activity

J.E. van der Zwan[1], *W. de Vente*[2], *E.I. de Bruin*[2], *S.M. Bögels*[2], *A.C. Huizink*[1]

[1]*Department of Developmental Psychology, VU University Amsterdam, The Netherlands*[2]*Research Institute of Child Development and Education, University of Amsterdam, The Netherlands*

Background. Many people experience higher levels of stress than what they believe is healthy; therefore, the need for stress-reducing methods is high. The purpose of this study was to compare the efficacy of three stress-reducing interventions – heart rate variability (HRV) biofeedback, mindfulness meditation, and physical activity – on stress and its related symptoms. **Method.** 76 participants (20 males; mean age 25.8, range 18–40) were randomly allocated to HRV biofeedback, mindfulness meditation, or physical activity. The three interventions consisted of five weeks of daily exercises at home increasing in duration over time: week 1: 10 min/day, week 2: 15 min/day, and weeks 3–5: 20 min/day. For the HRV biofeedback condition, exercises consisted of slow breathing (~6 breaths per minute) while using a HRV biofeedback device; the mindfulness meditation exercises consisted of several guided mindful meditations, including mindful breathing meditations, recorded on a CD; for the physical activity exercises participants were free to choose a vigorous intensity activity of their liking. Psychological wellbeing, stress, anxiety, depression, and sleep quality were assessed prior to and after the training (pre- and post-intervention), and 6 weeks later (follow up), using questionnaires. **Results.** Preliminary results indicate an overall beneficial effect consisting of improved sleep quality, improved psychological wellbeing and reduced stress. No significant effect

of intervention was found on any of the variables. **Discussion.** Preliminary results suggest that HRV biofeedback, mindfulness meditation, and physical activity all could play a role in the reduction of stress and the promotion of psychological wellbeing and sleep quality; results are inconclusive on which intervention is most beneficial.

Upper-thoracic (tense) breathing pattern: Relationship to respiration, tension/anxiety and general distress

Jan van Dixhoorn, Els Anthonissen

Centre for Breathing Therapy, Amersfoort, The Netherlands

Background. In a previous study it was shown that unexplained dyspnea in patients with stress related complaints was partly mediated by an upper thoracic (dysfunctional) breathing pattern. In this study one purpose was to replicate these findings on a larger population. Secondly, the presence of the breathing pattern in patients with different diagnostic labels was studied, as well as its relationship to general condition. **Methods.** A total of 208 patients referred to the breathing therapy practice of the second author were included. Their diagnostic labels included tension problems ($n = 69$), hyperventilation complaints ($n = 31$), anxiety ($n = 15$), sleeping problems ($n = 15$), headache ($n = 8$), burnout ($n = 8$), and a rest group ($n = 62$) of many small categories. Manual assessment respiratory movement (MARM) and questionnaire data, including Nijmegen Questionnaire (NQ), a NQ subset of four respiratory items (Dyspnea) and General Distress (GD), were obtained at the start and end of treatment. **Results.** The presence of upper thoracic breathing (MARM > 105) was significantly associated with higher values for NQ, in particular the dyspnea items, but was unrelated to GD. MARM, NQ and Dyspnea differed significantly between groups. They were highest for patients with hyperventilation complaints, followed by patients with tension, anxiety and burnout, and lowest for patients with headache and sleeping problems, with the rest group showing average values. There were no significant differences between the groups for GD. **Discussion.** Upper thoracic breathing seems in particular related to functional breathing problems and to tension/anxiety, but not to general distress. A possible mechanism for the specific breathing pattern and the concomitant form change of the thorax with breathing will be discussed.

Sigh as a trigger for the baroreflex protective mechanism

Evgeny G. Vaschillo, Bronya Vaschillo, Jennifer F. Buckman, Tam Nguyen, Alexander Puhalla, Richard Wille, Marsha E. Bates

Center of Alcohol Studies, Rutgers, The State University of New Jersey, USA

Background. The effects of sighing on the respiratory system have been well-described. A sigh has been shown to restore structured respiratory variability when it is disturbed by stress, emotions, sustained attention, or other events, and is defined as a resetter of the respiratory system. However, to date, no explanations regarding the mechanism of its action have been put forth. Based on evidence that the cardiovascular system (CVS) plays an active role in the regulation of emotions, cognition, behavior, and stress, we hypothesized that sighing strongly affects the CVS by modulating afferent firing from baroreceptors. This, in turn, is protective against stress because it increases neural inhibition. **Method.** We instructed 24 young participants (12 women) to sigh at paced intervals and examined CVS reaction. ECG, beat to beat blood pressure, and respiration were recorded at baseline and during an 8-min paced sighing task where normal breathing was interspersed with a sigh every 50 s. Current heart rate (HR), systolic (SAP), diastolic (DAP), mean (MAP), and pulse (PAP) arterial blood pressure, stroke volume (SV), and pulse transit time (PTT) were calculated. **Results.** Each sigh caused a strong positive shift of ~20 bpm in HR, ~30 mmHg in SAP, ~15 mmHg in DAP, ~15 mmHg in MAP, ~30 mmHg in PAP, ~10 ml in SV, and ~12 ms in PTT that gradually faded over ~30 s. **Discussion.** These results suggest a mechanism by which sighing functions to "reset" the respiratory system. Specifically, we propose that sighing affects the CVS by acting as a trigger of the baroreflex. Bidirectional communication between the brain and the CVS is accomplished through the baroreflex and the central autonomic network. Thus, sighing serves as a protective mechanism that reduces the negative effects of stress and strong emotions via enhanced inhibitory activity in the brain.

Transitioning between safety and danger: The relation between sighs and relief

Elke Vlemincx[1], *Nicholas Giardino*[2], *James L. Abelson*[2]

[1]*Research Group on Health Psychology, University of Leuven, Belgium*[2]*Trauma, Stress and Anxiety Research Group, University of Michigan, USA*

Background. Sighs have been proposed to be both physiological and psychological resetters. Psychologically, sighs occur more frequently during emotions, and are specifically related to relief. Relief is an emotion elicited by a transition to something less aversive that is certain to occur. The current experiment aimed to compare sigh rates during transitions to certain safety (eliciting relief) vs. transitions to certain danger. **Method.** The experiment consisted of a series of trials, each composed of a 2-s fixation phase, two 20-s cue phases (CuePh), a 5-s stimulus phase (StPh) and an 8-s intertrial interval. During CuePh1, one of three different cues was presented: (1) a certain danger cue (CDC) signaling a negative stimulus in the StPh, (2) a certain safety cue (CSC) signaling a positive stimulus in the StPh, (3) an uncertain cue. In CuePh2, the certain cues remained presented, whereas the uncertain cues were switched to CDCs and CSCs in CuePh2. This way, three different conditions were created: (1) transitions to certain danger (the transition from a fixation to a CDC in CuePh 1 and the transition from an uncertain cue in CuePh 1 to a CDC in CuePh 2), (2) transitions to certain safety (the transition from a fixation to a CSC in CuePh 1 and the transition from an uncertain cue in CuePh 1 to a CDC in CuePh 2), and (3) no transitions (the continued presentation of CDCs and CSCs from CuePh1 to CuePh2). **Results.** Transitions to certain safety elicited significantly more self-reported relief than transitions to certain danger and no transitions, and additionally showed significantly higher sigh rates. In addition, sigh occurrence could be predicted by increases in self-reported relief. **Discussion.** These results confirm the close link between sighs and relief, and support the idea that sighs function as emotional resetters inducing relief to cope with emotions.

Differential influence of serotonin transporter gene polymorphism and catastrophizing on the neural processing of dyspnea

A. von Leupoldt[1,2], *M.C. Stoeckel*[1], *R.W. Esser*[1], *M. Gamer*[1], *C. Büchel*[1]

[1]*Department of Systems Neuroscience, University Medical Center Hamburg-Eppendorf, Hamburg, Germany*[2]*Research Group Health Psychology, University of Leuven, Leuven, Belgium*

Background. The anticipation and perception of dyspnea varies largely between individuals. Negative affective personality traits such as dyspnea catastrophizing were suggested as underlying causes. In addition, genetic factors related to negative affect such as the polymorphism in the promotor region of the serotonin transporter gene (5-HTTLPR) might be influential, but have rarely been examined. We studied the impact of both potential mechanisms

on the neural processing of dyspnea to investigate overlapping vs. differential effects. **Methods.** We investigated healthy subjects, stratified for their 5-HTTLPR-genotype, using resistive load induced dyspnea with parallel acquisition of fMRI-data. Alternating blocks of severe and mild dyspnea were differentially cued for 6 s (anticipation periods) and followed by intensity and unpleasantness ratings. After the experiment subjects indicated their anticipatory fear during the two anticipation periods. Subjects also answered the Dyspnea Catastrophizing Scale (DCS). In separate analyses subjects were split into low vs. high catastrophizers based on DCS scores and assigned to low vs. high risk 5-HTTLPR-genotype groups. **Results.** High catastrophizers contained a higher percentage of high risk allele-carriers. Conversely, when subjects were grouped according to 5-HTTLPR-polymorphism, the high risk group showed stronger dyspnea catastrophizing. Neither classification showed significant between-group differences concerning perceived dyspnea intensity and unpleasantness ratings or brain activation when contrasting severe vs. mild dyspnea. However, high compared to low catastrophizers reported more anticipatory fear and stronger activation of the right insular cortex during the anticipation of severe vs. mild dyspnea. In high risk allele-carriers higher anticipatory fear of severe dyspnea was paralleled by stronger amygdala activation. **Discussion.** We conclude that in healthy young subjects catastrophizing and 5-HTTLPR-genotype shape predominantly the anticipation of dyspnea with increased anticipatory fear and stronger activation of emotion-related brain areas. Although 5-HTTLPR-genotype and catastrophizing were clearly linked, they had a differential effect on anticipatory activation in limbic areas.

I felt SO breathless: Retrospective inaccuracy and overestimation of respiratory sensations

Marta Walentynowicz[1], *Katleen Bogaerts*[1], *Filip Raes*[2], *Ilse Van Diest*[1], *Omer Van den Bergh*[1]

[1]*Health Psychology, University of Leuven, Leuven, Belgium*[2]*Learning and Experimental Psychopathology, University of Leuven, Leuven, Belgium*

Background. Retrospective evaluation of bodily sensations is susceptible to various distortions leading to inaccurate symptom memory. Overestimation of recalled daily symptoms was found to increase over time in high habitual symptom reporters. The present study examines memory accuracy of experimentally induced dyspneic sensations in high (HSR) and low habitual symptom reporters (LSR). **Methods.** Healthy female students ($N = 43$; 19 HSR/24 LSR) participated in a rebreathing task. Two subsequent trials consisted of baseline (60 s room air) and rebreathing phase (150 s) leading to a gradual increase in PCO_2, ventilation and breathlessness. The short trial ended at peak breathlessness, the long trial continued with an additional recovery phase (150 s room air). The order of trials was counterbalanced across participants and groups. Breathlessness was measured with use of visual analogue scale at four moments: (1) every 10 s during dyspnea induction, (2) immediately after each trial, (3) after the experiment, and (4) after 2 weeks. **Results.** Concurrent breathlessness ratings did not differ between groups. Retrospective ratings of experienced dyspnea were significantly overestimated during recall by both high and low habitual symptom reporters ($p < .001$). Furthermore, overestimation tended to increase over time (immediate vs. follow-up ratings) in HSR ($p = .06$), while it remained constant in LSR. **Discussion.** Memory for experienced breathlessness is overall inaccurate and overestimated. However, with the passing of time, HSR tend to increase their overestimation. Furthermore, the findings show that retrospective evaluations are biased immediately after the end of experience. The present findings are important for diagnostic assessment based on symptom reporting.

Separation of respiratory modulations from the tachogram for the classification of mindfulness

Devy Widjaja[1,2], *Elke Vlemincx*[3], *Ilse Van Diest*[3], *Sabine Van Huffel*[1,2]

[1]*KU Leuven, Department of Electrical Engineering (ESAT), SCD-SISTA, Kasteelpark Arenberg 10, Box 2446, 3001 Leuven, Belgium*[2]*iMinds Future Health Department, Kasteelpark Arenberg 10, box 2446, 3001 Leuven, Belgium*[3]*KU Leuven, Department of Psychology, Health Psychology, Tiensestraat 102, 3000 Leuven, Belgium*

Background. Respiration is one of the main modulators that cause variations in the heart rate (HR). Although most studies focus on this phenomenon of RSA, we will analyze variations in HR that cannot be coupled to the dominant HR modulations due to respiration. Recent research already showed that these variations unrelated to respiration (=residual tachogram) can be successfully used to classify rest and stress states. We aim to expand these results to the application of mindfulness. Data from a study that investigates the effects of induced worry and mindfulness on respiratory variability (RV) are used. No differences between baseline recordings and mindfulness on RV were found. Therefore we want to examine whether the residual tachogram is able to classify those two states. **Method.** Separation of respiratory influences from the tachogram is performed via orthogonal subspace projection. This method projects the tachogram (RRoriginal) onto a basis that is constructed from the respiratory signal. In this way, a tachogram that contains HR variations related to respiration is constructed. The HR variations that cannot be related to respiration comprise the residual tachogram (RRresidual). From each tachogram, several spectral features are computed using standardized frequency bands, and based on these features the classification between baseline and mindfulness is carried out. **Results.** Classification based on RRoriginal and RRresidual shows an average accuracy of 53.47% and 90.41%, respectively. Further inspection reveals that both LF and HF power from RRresidual seem to be important features in the classification. **Discussion.** These results confirm the findings obtained when classifying rest and stress, i.e., features derived from the residual tachogram are able to classify different mental states, whereas this was not possible when RRoriginal was used. Moreover, the same spectral features seemed to be important. However, future studies should focus on the physiological interpretation of features from RRresidual.

The influence of respiratory dynamics on relaxation and cardiorespiratory parameters

R. Wuyts, *E. Vlemincx*, *I. Van Diest*, *O. Van den Bergh*

Research Group on Health Psychology, University of Leuven, Belgium

Background. Whereas slow regular breathing instructions are often included in relaxation training, the clinically validated effects of breathing techniques on stress-related disorders are not well understood. From a dynamic systems perspective, healthy breathing is characterized by complex variability balancing correlated and random variability, while a lack of structured variability or excess random variability is indicative of unhealthy breathing. In this study we wanted to explore whether slow regular vs. normal regular breathing patterns differentially influence subjective relaxation and cardiorespiratory parameters, and how stress-reactivity is influenced by these patterns. **Method.** A slow regular (8 bpm) and a normal regular (14 bpm) breathing pattern was induced in each participant by means of auditory pacing. Respiratory and cardiovascular parameters were continuously recorded using the LifeShirt System. After each breathing pattern

a mental stressor was introduced followed by a recovery period. Self-reported relaxation in response to the breathing patterns was assessed, and total respiratory variability and structured variability of minute ventilation were indexed by the coefficient of variation (CV) and autocorrelation (AR), respectively. This protocol was repeated after a 4-week daily training period in one of both breathing patterns. **Results.** We will address (1) within-subject differences in subjective relaxation and respiratory variability in response to the breathing patterns; (2) the differential influence of both patterns on the physiological response to the stressor and recovery thereof; and (3) the effect of training in one of both breathing patterns. First results show a tendency for subjective relaxation to be higher during slow breathing than during the normal breathing condition. **Discussion.** Results will possibly help to resolve conflicting conceptions about healthy breathing and treatment practices.