Dyspnea 2013 is supported by:
Welcome to Maine

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Denis O'Donnell
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Capucine Morélot-Panzini
Janelle Yorke

Meeting Organization
Robert Banzett (Chair)
Andrew Binks (Director)
Barbara Rogers (Consultant)
Meeting Information

Directions to Campus from Logan Airport:

Exit the airport toward I-93 North by following signs for Route 1A South and the Sumner tunnel. Pay toll and enter tunnel. Immediately upon exiting the tunnel follow the sign for 93 and enter the under pass and merge onto I-93 North. Take I-93 approximately 10 miles to Exit 37A and merge onto I-95 N following signs for Portsmouth, NH. Take I-95 N into Maine (approximately 40 miles). Follow Directions ‘Take the Maine Turnpike’ below...

Directions to Campus from Portland Jetport:

Exit the airport via the Jetport Access Road turning left past the Hilton Garden Inn and head toward Route 9. Cross over Route 9 at the lights and join I-95 S. Follow Directions ‘Take the Maine Turnpike’ below...

Take the Maine Turnpike (I-95) to Exit 32 (Biddeford). After the tollbooth, turn left at the traffic light intersection onto Route 111 (Alfred Street). Staying in the right lane to the intersection of Route 1, take a left onto Route 1 from the right-hand lane, and then an immediate right as Rt. 111 branches off to the right. Then continue to the next traffic light. Turn right onto Route 9/208 (Pool Street). Follow Route 9/208 approximately 4 miles to the University of New England sign on your left. Turn left at the sign to enter the campus.

Check-in upon arrival: Check-in will occur on the third floor of the Alfond Center for Health Sciences (#12 on campus map) between 2-7pm on the 10th and 8-9am on the 11th. Your check-in packet will include your hard-copy of the program and name badge as well your accommodation details if you have booked an on-campus room. Parking coupons will be available upon request.

Drinks and snacks will be served at the check-in area 4pm-5.45 before dinner.

Meeting Location: All meetings will take place on the third floor of the Alfond Center for Health Sciences (#12 on campus map). All presentations will be given in the third floor lecture room and posters will be presented in the atrium.

Posters will be displayed in the atrium outside of the meeting room for the duration of the meeting. You will be assigned a poster board number when you pick up your registration packet. Poster boards are 4x6’ horizontal.
Meals will be served in the Cafeteria in Decary Hall (#4 on the campus map) apart from the Lobster Bake on Tuesday evening which will occur in the River Tent (between #27 & #26 on campus map).

Snacks, sandwiches or beverages can be purchased outside of scheduled meals in the Windward Cafe located downstairs of the Ketchum Library (#6 on campus map).

Food, beer and wine can also be purchased at the Sea Star store near the campus entrance (junction of Hills Beach Road and Route 9).

On-campus accommodation is in Champlain Residence Hall (#15 on campus map). Details and keys will be provided when you check-in (see above).

WiFi connections are available in the residential rooms and the meeting rooms.

Parking can be found on numerous lots on campus, with two large lots opposite Alfond on the other side of Hills Beach Road being closest. A parking coupon can be collected at registration.

Local attractions include the campus beach which follows the Saco River as it enters the Atlantic. Shopping, restaurants and pubs can be found in Kennebunkport (approx. 9 miles down Route 9) and in Portland. If sufficient interest exists we can arrange group transport to either location.

Useful Phone Numbers

Andrew Binks (Meeting Host): (617) 281-4292
Conference Services on-call #: (207) 468-4075
Campus Security: (207) 602-2298 for non-emergency
Emergency: dial 366
Program
<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.00</td>
<td>Welcome</td>
</tr>
<tr>
<td>9.15</td>
<td><strong>Dyspnea: the patient's perspective.</strong></td>
</tr>
<tr>
<td></td>
<td>Speaker - Barbara Rogers (p40)</td>
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<tr>
<td>9.30</td>
<td><strong>Invited Speaker Session on Dyspnea in the Palliative Care setting and beyond</strong></td>
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<tr>
<td></td>
<td>‘Opioids and dyspnea: why, when, how and for whom?’</td>
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<td></td>
<td>Speaker - Amy Abernethy (p40)</td>
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<tr>
<td></td>
<td>Discussants - Pierantonio Laveneziana &amp; Marie Claude-Gregoire</td>
</tr>
<tr>
<td>10.15</td>
<td>Coffee Break</td>
</tr>
<tr>
<td>10.45</td>
<td><strong>Oral Presentations: Therapy and Management of Dyspnea</strong></td>
</tr>
<tr>
<td>10.45</td>
<td>Currow: The longitudinal pattern of response when morphine is used to treat chronic refractory dyspnoea (p12)</td>
</tr>
<tr>
<td>10.55</td>
<td>Russell: Daily hand-held spirometry for the monitoring of patients with idiopathic pulmonary fibrosis (p13)</td>
</tr>
<tr>
<td>11.05</td>
<td>Baeske: Perceived control increases effort in a breathing challenge despite increased perceived stimulus intensity and unpleasantness (p14)</td>
</tr>
<tr>
<td>11.15</td>
<td>Discussion</td>
</tr>
<tr>
<td>11.35</td>
<td>Pappens: The effect of interoceptive fear conditioning on the perception of dyspnea intensity in asthma patients and healthy controls (p15)</td>
</tr>
<tr>
<td>11.45</td>
<td>Dangers: Effects of Nefopam, a nonopioid analgesic, on experimental work/effort dyspnea in healthy volunteers: a laser-evoked potential study (p16)</td>
</tr>
<tr>
<td>11.55</td>
<td>Gilani: Antagonism of Substance P and Perception of Dyspnea and Pain in Patients with COPD (p17)</td>
</tr>
<tr>
<td>12.05</td>
<td>Subhan: Effect of inspiratory muscle training and de-training on dyspnea during bicycle ergometry in healthy subjects (p18)</td>
</tr>
<tr>
<td>12.15</td>
<td>Discussion</td>
</tr>
<tr>
<td>12.45</td>
<td>Lunch</td>
</tr>
</tbody>
</table>
## June 11th Afternoon Session

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
</table>
| 2.15-3.00 | **Invited Speaker Session on Assessment of dyspnea in the clinical field**  
              
              ‘Feasibility and clinical pertinence of a multidimensional approach to dyspnea measurement’  
              
              Speaker - Mark Parshall (p40)  
              
              Discussants - David Currow & Ginger Carrieri-Kohlman |
| 3.00-3.30 | Coffee Break |
| 3.00-5.30 | **Oral Presentations: Physiological & Psychological factors impacting Dyspnea**  
              
              3.30 Petersen : Geriatric dyspnea: doing worse, feeling better (p19)  
              
              3.40 Lavietes : Panic and dyspnea in acute asthma (p20)  
              
              3.50 Song : Air hunger is correlated with anxiety sensitivity and evokes greater anxiety in panic disorder than in healthy subjects (p21)  
              
              4.00 Discussion |
| 4.20 | O’Donnell: Affective Responses to Laboratory-Induced, Activity-Associated, and Clinical Dyspnea (p22) |
| 4.30 | Morélot-Panzini : Gender and age do not affect dyspnea response to an air hunger stimulus (p23) |
| 4.40 | Adler : “I breathe, therefore I am”: a pilot study linking breathing to self-consciousness (p24) |
| 4.50 | Discussion |
| 5.30 | **Spotlight: The 2012 Paris ERS Dyspnea Symposium**  
              
              Speaker - Pierantonio Laveneziana & Louis Laviolette (p41)  
              
              Discussants - Thomas Similowski & Bob Banzett |
| 6.30 | **Business Meeting of the Dyspnea Society** |
| 7.30 | Lobster Bake at the River Tent |
### June 12th Morning Session

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.30-10.15</td>
<td><strong>Invited Speaker Session on Dyspnea in the Palliative Care setting and beyond</strong>&lt;br&gt;‘Is non-invasive ventilation a valid option to treat end-of-life dyspnea?&lt;br&gt;Speaker - Nicholas Hill (p41)&lt;br&gt;Discussants - Capucine Morélot &amp; Dean Hess</td>
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<tr>
<td>10.15-10.45</td>
<td>Coffee</td>
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<tr>
<td>10.45 - 12.45</td>
<td><strong>Oral Presentations: Neurophysiological Mechanisms of Dyspnea</strong></td>
</tr>
<tr>
<td>10.45</td>
<td>Evans: Hypercapnic induced dyspnea evokes exaggerated limbic cerebral blood flow in panic disorder (p25)</td>
</tr>
<tr>
<td>10.55</td>
<td>Dangers: Experimental air hunger inhibits laser-evoked potentials (p26)</td>
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<tr>
<td>11.05</td>
<td>Laviolette: Is experimental work/effort dyspnea mediated by muscles C-fibers? (p27)</td>
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<tr>
<td>11.15</td>
<td>Burki: The role of airway sensory nerves in the sensation of dyspnea (p28)</td>
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<tr>
<td>11.25</td>
<td>Discussion</td>
</tr>
<tr>
<td>11.50</td>
<td>Malher: Effect of Increased Blood Levels of Beta-endorphin on Perception of Breathlessness (p29)</td>
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<tr>
<td>12.00</td>
<td>Sevoz-Couché: Inspiratory threshold loading induces autonomic imbalance in healthy subjects</td>
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<tr>
<td>12.10</td>
<td>Laveneziana: Exertional dyspnea in patients with pulmonary veno-occlusive disease and idiopathic pulmonary arterial hypertension (p31)</td>
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<tr>
<td>12.20</td>
<td>Discussion</td>
</tr>
<tr>
<td>12.45 - 2.15</td>
<td>Lunch</td>
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<td>Time</td>
<td>Event Description</td>
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</tbody>
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| 2.15-3.00 | **Invited Speaker Session on Assessment of Dyspnea in the clinical field**  
‘Dyspnea in general practice and emergency settings’  
Speaker - Miriam Johnson (p41)  
Discussants - Christina Spengler and Kathy Baker |
| 3.00-3.30 | Coffee Break |
| 3.30-5.30 | **Oral Presentations: Dyspnea Measurement** |
| 3.30 | Currow: Feasibility of measurement of function in advanced cancer: Comparison of the 6-minute walk test, 2-minute walk test, isometric arm exercises and reading numbers aloud. (p33) |
| 3.40 | Persichini: Feasibility and performance of the Respiratory Distress Observation Scale (RDOS) to evaluate dyspnea upon admission in the intensive care unit (ICU) (p34) |
| 3.50 | Banzett: The Multidimensional Dyspnea Profile (MDP): What is good for? (p35) |
| 4.00 | Discussion |
| 4.20 | Baker: Comparison of Dyspnea MRC Rating to Risk of Adverse Events and Length of Stay (p36) |
| 4.30 | Johnson: Clinically important differences in chronic refractory breathlessness (p38) |
| 4.40 | Discussion |
| 5.30 | **Closing session**  
‘Observing Dyspnea - can we see what the patient feels?’  
Speaker - Margaret Campbell (p42) |
| 6.15-6.30 | Farewell, see you in 2017 |
Abstracts

listed in order of presentation
The longitudinal pattern of response when morphine is used to treat chronic refractory dyspnoea

David C. Currow¹, Stephen Quinn², Aine Greene³, Janet Bull ⁴, Miriam J Johnson⁵, Amy P. Abernethy¹,⁶

Affiliations
¹Discipline, Palliative and Supportive Services, Flinders University, Bedford Park, Australia.
²Flinders Centre for Clinical Effectiveness, Flinders University, Bedford Park, Australia.
³Southern Adelaide Palliative Services, Repatriation General Hospital, Daw Park, Australia.
⁴Four Seasons Hospice, Flatrock, North Carolina.
⁵Palliative Medicine, Hull and York Medical School, Hull, United Kingdom
⁶Division of Medical Oncology, Department of Medicine, Duke University Medical Centre, Durham, North Carolina, USA, USA 27710

Background
While evidence supports using sustained release morphine for chronic refractory breathlessness, little is known about the longitudinal pattern of breathlessness intensity as people achieve symptomatic benefit.

Methods
This secondary analysis used breathlessness intensity scores (100mm visual analogue scale (VAS)) from a prospective, dose increment study of once daily (morning) sustained release morphine for chronic refractory breathlessness. Participants who achieved <10% improvement over their own baseline at one week (10mg) were titrated to 20mg and, if no response, another week later to 30mg for one week. Time was standardised at the first day of the week in which participants responded generating twice daily data one week either side of symptomatic benefit. Analysis used random effect mixed modelling.

Results
Of the 83 participants, 17/52 responders required >10mg: 13 participants (20mg) and four (30mg), contributing 634 VAS observations. In the week leading to a response, average VAS scores worsened by 0.3mm/day (p=0.16); the average improvement in the first 24 hours of response was 10.9mm (7.0 to 14.7; p<0.00
Daily hand-held spirometry for the monitoring of patients with idiopathic pulmonary fibrosis

Russell AM\textsuperscript{1,2}, Fraser UH\textsuperscript{1}, Kokosi M\textsuperscript{1}, Renzoni EA\textsuperscript{1,2}, Wells AU\textsuperscript{1,2}, Maher TM\textsuperscript{1,2}

1 Interstitial Lung Disease Unit Royal Brompton Hospital, London.
2 National Heart Lung Institute, Imperial College, London

Introduction: Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive lung disease associated with high mortality. Breathlessness, fatigue and cough are the most frequently reported symptoms. Patients experience periods of relative disease stability punctuated by episodes of rapid decline (acute exacerbations) resulting in further disability. Daily hand-held spirometry has been shown to be an effective means of detecting acute rejection episodes in lung transplant recipients. This study aims to determine the utility of daily hand-held spirometry in IPF.

Methods: Patients with IPF were recruited from new referrals to our unit. Baseline severity was assessed by FVC, DLco and 6 minute walk. Patients were given a hand-held spirometer (Carefusion UK) and provided with instruction on how to self-administer spirometry and record daily FEV\textsubscript{1} and FVC values.

Results: 50 subjects have been recruited; 46 male, age 69 ± 9 years with moderate to severe disease: FVC 70.8 ± 18.8% predicted, DLco 38.6 ± 12.5% predicted and 6 minute walk distance 325±120m. Forty subjects have completed six months of diary monitoring. Mean hand held FVC correlates well with formal clinic spirometry (r\textsuperscript{2} 0.902). Reproducibility of daily FVC is good with mean variance 6.9% (range 3.0-12.1%).

Discussion: This small study suggests that daily spirometry can be reliably and reproducibly performed by patients with IPF. Further longitudinal data collection and analysis is ongoing. This will enable us to determine the value of recording daily FVC as a predictor of disease progression in IPF and hopefully detect, and thus treat, acute exacerbations early in their evolution.

Conclusion
When treating chronic refractory breathlessness with once daily sustained release morphine:
1. titrate to effect, since inadequate dose may generate no response; and
2. following an initial response, further dose increase should not occur for at least one week.

Whether further benefit would be derived beyond day 6 on the dose to which people respond, and what net effect a further dose increase would have are questions yet to be answered.
PERCEIVED CONTROL INCREASES EFFORT IN A BREATHING CHALLENGE DESPITE INCREASED PERCEIVED STIMULUS INTENSITY AND UNPLEASANTNESS

Jessica Baeske¹ & Sibylle Petersen²

1) University of Dortmund, Department of Rehabilitation Sciences
2) KU Leuven, Research Group on Health Psychology

Background: In research on perceived control and interoception we find a paradox: increasing perceived control over a stimulus can lead to increased ratings of stimulus intensity, particularly in individuals high in negative affect. However, little is known on effects of perceived control on stimulus-related behavior which could mediate the relationship between dyspnea and perceived control.

Methods: Participants (N=50) completed an assessment of maximal respiratory pressure and three breathing tasks with respiratory loads of 6, 9, and 16 cmH2O (order randomized). We measured respiratory flow and pressure breath by breath and participants rated stimulus intensity and unpleasantness. Furthermore, participants completed questionnaires on negative affect and locus of control. We manipulated perceived control by providing one group of participants (n=24, higher perceived control HPC) with extended information on the instruments, protocol, duration and procedure. The other group (lower perceived control LPC) received no such information.

Results: In the HPC group, ratings of stimulus intensity and unpleasantness were higher than in the LPC group. However, in the HPC group inspiratory pressure and flow were also higher indicating higher effort. Trait anxiety and locus of control had no significant influence on stimulus ratings after controlling for respiratory parameter.

Conclusion: Results suggest that higher perceived control is related to higher effort invested in a breathing task despite increased perceived stimulus intensity and unpleasantness. Results are of clinical relevance for respiratory rehabilitation programs.
THE EFFECT OF INTEROCEPTIVE FEAR CONDITIONING ON THE PERCEPTION OF DYSPNEA INTENSITY IN ASTHMA PATIENTS AND HEALTHY CONTROLS

Meike Pappens, Thomas Janssens, Geert Verleden, & Ilse Van Diest

University of Leuven

The high comorbidity between asthma and some psychiatric disorders suggests that psychological factors might play a role in asthma. In this study we wanted to investigate the influence of fear conditioning on self reported dyspnea intensity. The conditioned stimulus (CS) was a small respiratory load that creates a mild dyspneic feeling; the unconditional stimulus (US) was a breathing occlusion. 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, 27-30s). 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 received 6 CS-only trials. After each trial participants were asked to rate their dyspnea intensity during the CS. Three CS pre-exposure trials were given before acquisition, after which a dyspnea intensity rating was also registered. Results show that all groups reported significantly 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. Our findings might shed an important light on the role of safety learning in asthma.
EFFECTS OF NEFOPAM, A NON OPIOID ANALGESIC, ON EXPERIMENTAL WORK/EFFORT DYSPNEA IN HEALTHY VOLUNTEERS: A LASER-EVOKED POTENTIAL STUDY

Laurence Dangers 1*, Louis Laviolette 1*, Beny Charbit 2, Thomas Similowski 1, Capucine Morelot-Panzini 1

* equal contribution to the work.

1 Pneumologie et Réanimation Médicale, Groupe Hospitalier Pitié-Salpêtrière and ER10, Université Paris 6 Pierre et Marie Curie, Paris, France
2 Centre d’investigation Clinique Paris Est UPMC/INSERM UMR S_956, Groupe Hospitalier Pitié-Salpêtrière, Paris, France

Rationale. Counter-irritation is the attenuation of a painful sensation by a superimposed heterotopic noxious stimulus. It arises from C-fiber stimulation. Dyspnea-pain counter-irritation has been described with experimental dyspnea of the work/effort type, which inhibits laser evoked cortical potentials (LEPs). We therefore hypothesized that experimental dyspnea (work/effort) might be relieved by a non-opioid analgesic, in which case the effect of dyspnea on LEPs should be lessened.

Methods. In this randomized, double-blind, placebo-controlled cross-over study, a non opioid analgesic (nefopam) was administrated by intravenous infusion over 30 min to fifteen healthy naïve male subjects. The N2P2 component of LEPs was obtained using CO2 laser stimulation on the hand and recorded using EEG. LEPs were acquired during three conditions: spontaneous breathing, spontaneous breathing under nefopam/placebo and experimental dyspnea induced by inspiratory threshold loading under nefopam/placebo.

Results. The intensity of experimental dyspnea was not different (p=0.88) between nefopam and placebo (VAS rating 3.7 ± 2 cm versus 4 ± 1.9 cm). The amplitude of N2P2 during experimental dyspnea was reduced by 35 ± 18% and 25 ± 21% (Δ = 37%, p = 0.23) with placebo and nefopam respectively (power 0.74).

Conclusion. There was no statistically significant effect of nefopam on experimental dyspnea, and on dyspnea-pain counter-irritation assessed through LEPs, but the study was markedly underpowered.
Antagonism of Substance P and Perception of Dyspnea and Pain in Patients with COPD

Donald A. Mahler, M.D.¹ Alex H. Gifford, M.D.¹ Laurie A. Waterman, M.S.² Aamir Gilani, M.D.¹ Brian R. Kupchak, Ph.D.³ William J. Kraemer, Ph.D.³

¹Section of Pulmonary & Critical Care Medicine, Geisel School of Medicine at Dartmouth, Hanover, NH
²Pulmonary Function & Cardiopulmonary Exercise Laboratories, Dartmouth-Hitchcock Medical Center, Lebanon, NH
³Department of Kinesiology and Department of Physiology and Neurobiology, University of Connecticut, Storrs, CT

Background: Substance P, an excitatory neuropeptide, is present along with its receptor neurokinin (NK)-1 in the peripheral and central nervous systems and augments respiratory rhythm in animal preparations. The primary objective of this study was to investigate whether substance P modulates the perception of dyspnea by administering aprepitant, a selective antagonist that blocks NK-1 receptor signaling.

Methods: Sixteen patients (age, 70 ± 6 years) with chronic obstructive pulmonary disease (COPD) inspired through resistances during practice sessions to identify an individualized target load that provoked breathlessness ≥ 50 mm on a 100 mm visual analog scale. At intervention visits, aprepitant (125 mg) or placebo was administered orally, and patients rated the intensity and unpleasantness of breathlessness during resistive load breathing (RLB) and of pain during immersion of the hand into cold water. Blood levels of substance P and beta (β)-endorphin were measured.

Results: After aprepitant, but not with placebo, there were significant increases in substance P (+54 ± 39 %) and β-endorphin (+27 ± 17 %); these changes were significantly correlated (Spearman r = 0.62; p = 0.01). There were no differences in ratings of breathlessness during RLB and of pain during cold water immersion between aprepitant and placebo.

Conclusions: Our results do not support a role for the substance P-NK-1 pathway in the perception of dyspnea or pain in patients with COPD. These findings may be explained by opposing effects of excitatory (substance P) and inhibitory (β-endorphin) neuropeptides, released after administration of aprepitant, that affect perception of noxious stimuli.
Effect of inspiratory muscle training and de-training on dyspnea during bicycle ergometry in healthy subjects

MMF Subhan¹, Mohsin Yakub², MN Khan¹, HR Ahmad³
¹Arabian Gulf University, Manama, Bahrain, ²Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA, ³Ziauddin Medical University, Karachi, Pakistan

Previous literature has shown that inspiratory muscle training (IMT) decreases dyspnea in patients and controls. However, de-conditioning is a common path for many patients after completing a rehabilitation programme. The present study was undertaken to investigate the effect of IMT and its de-conditioning on breathlessness during exercise.

Twelve healthy sedentary males, aged 17 to 27 years undertook a progressive exercise test to a symptom limited maximum, during the course of which breathlessness was estimated each minute using the visual analogue scale (VAS). Subjects were studied once every two weeks over a period of 16 weeks. For 8 weeks, subjects used an IMT device on a supervised daily basis. After 8 weeks subjects discontinued the use of the IMT device. The difference in the slope and intercept of the breathlessness (VAS) and expired pulmonary ventilation (Ve) relationship was assessed. A paired t-test was used for statistical analysis and the level of probability taken as significant was 5% (p<0.05). The study was approved by the Human Subject Protection Committee, Aga Khan University, Pakistan.

The plot of VAS against Ve was effectively linear with a mean r² value of 0.97. After 8 weeks, the mean VAS/Ve intercept showed a significant increase (p<0.05). Data for the de-conditioning will be presented along with heart rate indices and blood lactate measurements to see whether any training effect was produced or not. In summary, our results agree with previous data confirming that IMT reduces dyspnea.

The study was supported by a grant from the Aga Khan University, Pakistan.
Geriatric dyspnea: doing worse, feeling better

Sibylle Petersen¹, Andreas von Leupoldt¹,², Omer Van den Bergh¹

¹ KU Leuven, Research Group on Health Psychology
² University of Hamburg, Department of Psychology

Background: In higher age, dyspnea perception and self-report is reduced despite age-related decline in the physiological capacity of the respiratory system. Reduction of dyspnea self-report is related to increased rates of under-diagnosis and misdiagnosis of respiratory disease in higher age. Also in Chronic Obstructive Pulmonary Disease (COPD), large proportions of (typically older) patients report no symptoms despite strong physical impairments. We suggest that the seemingly contradiction of reduced dyspnea in the face of age-related physiological decline might partly be explained by increased emotion regulation skills in higher age extending to the regulation of bodily discomfort. As a first test of this hypothesis, we examined the combined effects of age and anxiety on dyspnea report in patients with COPD.

Methods: 258 COPD patients (age 33-85 years) reported dyspnea at rest, after exercise, and retrospectively for everyday activities. Furthermore, we assessed anxiety. Analyses of covariance compared dyspnea-report between older and younger patients with high versus low levels of anxiety while controlling for exercise capacity and lung function.

Results: Older patients with low anxiety levels reported less dyspnea after exercise and retrospectively compared to younger patients high or low in anxiety. A substantially larger proportion of older patients with low compared to high anxiety levels reported no or only very mild dyspnea.

Conclusions: Older COPD patients with low anxiety levels are at risk for reduced dyspnea-report which might contribute to inadequate treatment and less favorable prognosis. Results are discussed with reference to a general model on dyspnea in higher age.
PANIC AND DYSPNEA IN ACUTE ASTHMA

Marc H Lavietes MD

New Jersey Medical School, Newark New Jersey

Background   The link between asthma, anxiety and panic while long appreciated by clinicians has never been studied in the emergency room setting. The literature draws no distinction between panic disorder in general and the acute panic of the severely ill patient. This study categorizes and quantifies both panic and dyspnea in acutely ill asthmatic patients prior to treatment and repeats these measures soon after therapy. The goal: to explore the linkage of dyspnea with acute panic, altered lung function and anxiety (a basic component of personality) in acute asthma.

Methods   Spirometry was performed, dyspnea quantified and a specialized measure of acute panic (acute panic inventory, API) was administered to 32 asthmatics immediately upon their arrival for emergency service care and again after treatment. Outcome measures include: lung function tests (peak flow, FEV1, inspiratory capacity), the API and a quantitative measure of dyspnea (Borg scale score).

Results   A multiple linear regression model showed that measures of the API, the peak expiratory flow rate and gender taken together accounted for 41% of dyspnea (Borg scale score) in acute asthma. By contrast, when the API is taken as the dependent variable, only dyspnea contributed to the outcome. After treatment, only the API predicted dyspnea in the 32 subjects.

Conclusions Panic and bronchoconstriction account for the dyspnea in acute asthma. The self report of dyspnea differs in its interpretation between acutely ill and stable asthmatic patients. This supports the notion that subjective history will not substitute for spirometry for the serial evaluation in asthma.
Air hunger is correlated with anxiety sensitivity and evokes greater anxiety in panic disorder than in healthy subjects

Tian-Yue Song¹, Achint Patel¹, Kimberley Glover¹, Richard J. McNally², Karleyton C. Evans¹

1. Department of Psychiatry, Massachusetts General Hospital, Boston, MA
2. Department of Psychology, Harvard University, Cambridge, MA

Background
Hypercapnic challenge via inhaled to carbon dioxide (CO₂) reliably provokes panic attacks in patients with panic disorder (PD) but not healthy controls (HCs). The False Suffocation Alarm Theory, a leading theory for PD pathophysiology, suggests PD patients have deranged afferent circuitry that renders them hypersensitive to suffocation/air hunger stimuli. Since air hunger comprises distinct quantifiable sensory and affective dimensions, we hypothesized that: (1) compared to HCs, PD patients would have similar sensory intensity (SI), yet exaggerated anxious responses (A₂) to air hunger; and that (2) the Anxiety Sensitivity Index (ASI), a measure of fear/anxiety of interoceptive bodily sensations, would predict A₂ responses.

Method
Psychometric screening (including the ASI) was performed in Forty-seven subjects (27-PD/20-HC). The subjects subsequently underwent hyperoxic (~30% inspired O₂), fixed mechanical ventilation via mouthpiece (0.17 L/min/Kg) and rated SI (0-10 scale) as PCO₂ was systematically varied by 4-20 mmHg above baseline. Each PCO₂ level was held 2.5 minutes. The magnitude of A₂ (0-10 scale) was assessed immediately after the breathing trial that evoked maximum SI.

Results
The regression slope of air hunger SI responses as a function of PCO₂ level was similar between groups; however, the maximum A₂ response was significantly greater for the PD group than for the HC group. ASI was significantly correlated with A₂ responses.

Conclusion
The present findings suggest PD patients have normal afferent sensory perception, but aberrant affective processing of air hunger stimuli and that the ASI is predictive of the exaggerated affective responses.
Affective Responses to Laboratory-Induced, Activity-Associated, and Clinical Dyspnea

CR O’Donnell ScD, M. Parshall PhD RN, R Lansing PhD, RB Banzett PhD

Division of Pulmonary, Critical Care and Sleep Medicine, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA; University of New Mexico College of Nursing, Albuquerque, NM

Introduction: Much of our knowledge about dyspnea is derived from laboratory models, raising questions such as: “does laboratory dyspnea evoke different emotional responses than dyspnea experienced by patients?”

Methods: We assessed affective responses to: moderate and high laboratory dyspnea stimuli in healthy and COPD subjects as well as dyspnea induced by activities of daily living (ADL) in the same COPD subjects. We also assessed patients with acute episodes of dyspnea as the chief complaint motivating an Emergency Room (ER) visit. Subjects rated immediate unpleasantness of the dyspnea experience (A1) and associated emotional responses such as anxiety (secondary affective or A2). Responses to A2 items were expressed relative to the rating of A1.

Moderate and High laboratory stimuli evoked A1 ratings of 60% and 90% full scale. Anxiety rating during laboratory dyspnea did not differ significantly between patients and healthy subjects. COPD patients limited their exertion during ADL, resulting in A1 and anxiety ratings equivalent to moderate laboratory stimulus. ER patients prior to treatment reported A1 and anxiety nearly equivalent to the high laboratory stimulus. A1 was reduced by ER treatment, but anxiety remained disproportionately high. (see figure).

We conclude that anxiety associated with breathing discomfort does not differ between COPD subjects and healthy volunteers or between lab and home under non-emergent conditions such as self limited ADL. For a given perceived level of breathing discomfort, acute, emergent dyspnea is associated with substantially greater anxiety and fear than dyspnea induced in the laboratory or by ADL, either of which can be readily alleviated.

Supported by NIH grant NR10006
GENDER AND AGE DO NOT AFFECT DYSPNEA RESPONSE TO AN AIR HUNGER STIMULUS.

C. Morelot-Panzini1,3, CR O’Donnell1,2, RW Lansing1, DM Beach1,2, RM Schwartzstein1,2, RB Banzett1,2,

1Pulmonary Division, Beth Israel Deaconess MC, Boston, MA, 02215. 2Harvard Med School Boston, MA, 02115 USA, 3ER10, University Pierre & Marie Curie, Paris, France.

Rationale: Age and gender may affect the perceived unpleasantness of dyspnea and the emotional response to dyspnea. Women report a greater perception of dyspnea in asthma and in COPD; however, it is difficult to know whether pathophysiological impairment is truly similar. We employed controlled laboratory dyspnea to allow precise matching of afferent input in the assessment of the effect of gender and age on perception of air hunger.

Methods: We studied healthy men and women repeatedly. Inspired P\textsubscript{CO\textsubscript{2}} was controlled to achieve steps of end-tidal P\textsubscript{CO\textsubscript{2}} from eucapnia to maximum tolerable. Minute ventilation was limited during hypercapnia to 0.13 L/min/kg. Subjects rated their “breathing discomfort” (BDVAS). Immediately after each dyspnea challenge, subjects completed the Multidimensional Dyspnea Profile (MDP) to rate their air hunger intensity, immediate discomfort (A1), and emotional responses during the final 30 sec of the trial.

Results: A similar high level of breathing discomfort (BDVAS\geq85\% full scale) was achieved in all subgroups by increasing PET\textsubscript{CO\textsubscript{2}}. There was no difference related to gender or age (20 to 35 years : n=12 vs 50 to 65 years : n=8) in the 3 outcome variables at high level of breathing discomfort: air hunger intensity rating, anxiety rating and fear rating.

Conclusion: These pilot laboratory results suggest that the perceptual and emotional response to dyspnea sensation per se is not inherently different between these groups. The overall experience of disease including, for instance, impairment of life activities and underlying the sensation of dyspnea may differently affect gender and age groups. Supported by NIH-NRI 2009, NR10006, Fonds de Dotation Recherche en Santé Respiratoire & CARDIF.
“I breathe, therefore I am”: a pilot study linking breathing to self-consciousness

Dan Adler (1), Thomas Similowski (2,3), Bruno Herbelin (4), Olaf Blanke (4)

(1) Division of Pulmonary Diseases, Geneva University Hospitals, Geneva, Switzerland
(2) Paris 6 university, ER10 research unit
(3) Assistance Publique - Hôpitaux de Paris, Pitié-Salpêtrière hospital, Department of Respiratory and Critical Care Medicine
(4) Laboratory of Cognitive Neurosciences, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

Background:
Bodily self-consciousness can be studied experimentally by using conflicting visual-somatosensory inputs in virtual reality (VR) to disrupt unity between the body and the self. Faced with multisensory conflicts, subjects identify with a virtual body (VB) projected in front of them and mislocalize themselves towards it. A host of experiments, in various settings have led the understanding that sense of self is dependent upon multisensory integration of bodily signals. We hypothesized that breathing and self-consciousness are intimately intertwined.

Methods:
VR and illumination of a VB or a neutral object synchronously or asynchronously to breathing was used to immerse 17 healthy subjects (M:9, F:8) in a state of illusory self-identification. Self-location was measured (in seconds) using the mental ball drop task (MBD). A specific questionnaire was used to measure self-identification to VB/neutral object.

Results:
Breathing-synchronized illumination resulted in a displacement of self towards VB or object, as demonstrated by a longer MBD time in both conditions when compared to asynchronous illumination (+0.045sec, 95%CI0.013-0.08, p=0.007 for body condition, respectively +0.037sec, 95%CI0.007-0.067, p=0.016 for object condition). Synchronous illumination also resulted in positive changes in self-identification questionnaires in both body and object conditions.

Conclusion:
Breathing contributes to the maintenance of the interface between the self and the outside world. Of major importance, the subjects self-identified to a breathing object assuming that synchronous breathing inputs were provided. Self-identification to a non-human form has never been observed before. It suggests that breathing is an extremely powerful element of brain’s representation of self.
Hypercapnic induced dyspnea evokes exaggerated limbic cerebral blood flow in panic disorder

Karleyton C. Evans1, Tian-Yue Song1, Donald G. McLaren2

1. Department of Psychiatry, Massachusetts General Hospital, Boston, MA
2. Department of Neurology, Massachusetts General Hospital, Boston, MA

Background:
The anxiogenic response to hypercapnia is one of the most replicated, but poorly understood findings in panic disorder (PD) research. Given the prevailing cortico-limbic circuit theory for anxiety, this pulsed arterial spin labeled (pASL)-fMRI study employed hypercapnic stimuli to test for differential interoceptive (dyspnea) responses in cortico-limbic circuitry, specifically the amygdala. We hypothesized that compared to healthy controls (HCs), PD patients would have similar ventilatory and dyspnea responses but exaggerated anxious and amygdalar regional cerebral blood flow (rCBF) responses.

Method:
Dyspnea and ventilatory stimulus-responses to hypercapnia were determined in 22 medication-free PD patients and 18 matched HCs prior to scanning. Subjects subsequently underwent 3-Tesla pASL-fMRI (TR/TE/TI1/Tl2 = 3000/15/600/1600 ms) during alternating hypercapnic (5% CO2; titrated to 8 mmHg above baseline)/eucapnic periods for 15.5 min. Voxel-wise whole brain and small volume correction (SVC; amygdala) image analyses were performed with SPM8 to test effects of: hypercapnia, ventilation, dyspnea (modeled from pre-scan data).

Results:
Systematic elevation of PCO2 (8 mmHg) evoked comparable increases in ventilation (60.5%), dyspnea (40%), and global CBF (28.3%) for both groups. However, PD patients had greater anxiety/panic responses. SVC image analyses identified greater rCBF in the left amygdala/nucleus accumbens of PD patients during periods of hypercapnic induced dyspnea. Potential between-group differential effects related directly to hypercapnia or ventilation failed to reach statistical significance on whole brain analysis.

Conclusion:
The findings provide the first evidence for an exaggerated limbic response to hypercapnia in PD and lend support to the cortico-limbic circuit model for PD.
EXPERIMENTAL AIR-HUNGER INHIBITS LASER-EVOKED POTENTIALS

Laurence Dangers*
Louis Laviolette*
Thomas Similowski
CapucineMorelot-Panzini

*equal contribution to the work.

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

Rationale: Counter-irritation is the attenuation of a painful sensation by a superimposed heterotopic noxious stimulus. Dyspnea-pain counter-irritation has been described with experimental dyspnea of the excessive effort type, which inhibits both the nociceptive spinal reflex (RIII, about 50% reduction in amplitude) and laser evoked cortical potentials (LEPs, about 35% reduction in amplitude). In contrast, experimental air-hunger has no influence on the RIII reflex. Its effects on LEPs are unknown.

Methods: LEPs were obtained using a CO2 laser stimulator in twelve healthy naïve subjects (age range = 21-29 years), during eupneic ventilator controlled breathing with a FiCO2 of 0% (VC condition) and after inducing air hunger by increasing FiCO2 at a fixed level of ventilator controlled ventilation (VC-CO2 condition).

Results: Air hunger was intense in the VC-CO2 condition (VAS rating = 6.3 ±0.6, mean ± SD, p < 0.05 vs. VC). Concomitantly, the amplitude of the N2P2 component of the LEPs was reduced in comparison to the VC condition (-22.6% ± 17.8%, p<0.05).

Discussion: Although seemingly to a lesser extent than excessive effort type dyspnea, air-hunger dyspnea does inhibit LEPs. This contrasts with the lack of inhibition of the RIII reflex with air-hunger dyspnea, a difference that could be in line with the central components of LEPs. Air hunger may have some nociceptive characteristics, which could potentially open novel therapeutic avenues.
IS EXPERIMENTAL WORK/EFFORT DYSPNEA MEDIATED BY RESPIRATORY MUSCLE C-FIBERS?

Louis LAVIOLETTE 1 Marie-Cécile NIÉRAT 1 Anna L. HUDSON 1,2 Thomas SIMILOWSKI 1,3

1 Université Paris 6, ER10UPMC, Paris, France
2 Neuroscience Research Australia and University of New South Wales, Sydney, Australia
3 Assistance Publique-Hôpitaux de Paris, Groupe Hospitalier Pitié-Salpêtrière, Service de Pneumologie et Réanimation Médicale, Paris, France

Introduction. Dyspnea of the work effort type is thought to involve respiratory muscle C-fibers, because it induces pain counter-irritation. The occurrence of wind-up (progressive increase in perception with constant stimulus) would lend support to this notion, as would the gating of dyspneic sensations by non-nociceptive cutaneous stimulation in the appropriate dermatome (C4 for the diaphragm).

Methods. Nine healthy subjects (9 women, 24 ± 4 years), naïve to the study objectives, were exposed to ITL in association with transcutaneous electric nerve stimulation (TENS) in C4 or L3 (control). Two sessions (C4 and L3), comprising three, 5-minute periods (resting ventilation, ITL alone and ITL-TENS) were completed according to a randomized, single blind design. Breathing pattern and dyspnea were recorded continuously during all sessions.

Results. Compared to resting condition, ITL induced a decrease in breathing frequency (F), and increases in inspiratory time (TI), total cycle time (TTOT), tidal volume (VT) and dyspnea (all p<0.001). In all trials, dyspnea exhibited a two-phase increase, with a prompt initial rise in response to ITL, followed by a slow sustained increase, suggestive of wind-up. TENS did not significantly alter breathing pattern or dyspnea.

Discussion. The presence of wind-up during constant load ITL is compatible with an implication of respiratory muscle C-fibers in the genesis of dyspnea. The failure of C4 TENS to attenuate dyspnea goes against this notion, but could be explained by C-fiber contribution from inspiratory muscles other than the diaphragm.
The role of airway sensory nerves in the sensation of dyspnea

Nausherwan Burki\textsuperscript{1} and Lu-Yuan Lee\textsuperscript{2}

\textsuperscript{1} Department of Medicine, University of Connecticut Health Center, Farmington, CT; \textsuperscript{2} Department of Physiology, University of Kentucky Medical Center, Lexington, KY.

Central mechanisms and pathways of dyspnea remain poorly defined. One pathway which we have identified is via pulmonary vagal C fibers (J Appl Physiol. 2005;98:180-5). However, the central connections and pathways of this sensation remain shrouded in mystery (Chest. 2010;138:1196-201).

Intravenous adenosine is dyspnogenic and we attribute this to A1 and possibly A2 receptors on pulmonary vagal C fibers; our animal studies (J Physiol. 1998;508(1):109-118; J Appl Physiol 2003;953:1315-1324), as well as blockade of with lidocaine or aminophylline (Pulm Pharmacol Ther. 2008;21:208-13; Pulm Pharmacol Ther. 2010;23:279-82) appear to support our interpretation.

However, inhaled or intravenous capsaicin, which is known to stimulate transient receptor potential vanilloid type 1 (TRPV1) receptors expressed on C fibers, induces cough, but not dyspnea (Pulm Pharmacol Ther 2007 204 319-324; Clin Sci (Lond) 1986 715 519-526). Studies with phenylbiguanide, another substance that acts on pulmonary C fibers by selective 5-hydroxytryptamine subtype 3 (5-HT3) receptor stimulation, have also not reported any breathlessness (Clin Sci 1972 422 163-177). Finally, lobeline is believed to stimulate vagal C fibers; however, IV injection of lobeline produces cough but not dyspnea (Pulm Pharmacol Ther. 2007;204 319-324; J Physiol 1998 511 pt 1 289-30; Respir Physiol Neurobiol 2009 1671 36-44; J Physiol 2001 534pt 2 583-593).

Our recent single fiber electrophysiologic studies, indicating differential activation of bronchial and pulmonary C fibers by adenosine, may provide a possible explanation for these apparent discrepancies. The pathways involved may serve to illustrate further the mechanisms of the dyspnogenic sensation attributed to vagal C fibers.
Effect of Increased Blood Levels of Beta-endorphin on Perception of Breathlessness

Donald A. Mahler, M.D., 1  Alex H. Gifford, M.D.1  Laurie A. Waterman, M.S.2  Joseph Ward, RCPT2  William J. Kraemer, Ph.D.3  Brian R. Kupchak, Ph.D.3  Andrew Harver, Ph.D.4

1 Section of Pulmonary & Critical Care Medicine Geisel School of Medicine at Dartmouth, Hanover, NH, 2 Pulmonary Function & Cardiopulmonary Exercise Laboratories, Dartmouth-Hitchcock Medical Center; Lebanon, NH 3 Department of Kinesiology and Department of Physiology and Neurobiology University of Connecticut, Storrs, CT 4 Department of Public Health Sciences, University of North Carolina at Charlotte, Charlotte, NC

Background: Although opioid receptors are expressed broadly in the central nervous system (CNS) and in peripheral sensory nerve endings including bronchioles and alveolar walls of the respiratory tract, it is unknown whether the modulatory effect of endogenous opioids on breathlessness occurs in the central or peripheral nervous system. The purpose of this investigation was to examine whether increased blood levels of beta-endorphin modify breathlessness by a putative effect of binding to peripheral opioids receptors in the respiratory tract.

Methods: Twenty patients (10 female/10 male; age, 70 ± 8 years) with chronic obstructive pulmonary disease inspired through resistances during practice sessions to identify an individualized target load that caused ratings of intensity and unpleasantness of breathlessness > 50 mm on a 100 mm visual analog scale.

At two interventions, blood levels of beta-endorphin and adrenocorticotropic hormone (ACTH) were measured, ketoconazole (600 mg) or placebo was administered orally, and patients rated the two dimensions of breathlessness each minute during resistive load breathing (RLB).

Results: By inhibiting cortisol synthesis, ketoconazole led to significant increases in beta-endorphin (mean change = 20 ± 4%) and ACTH (mean change = 21 ± 4%) compared to placebo. Intensity and unpleasantness ratings of breathlessness and endurance time during RLB were similar between interventions.
Conclusions: The previously demonstrated modulatory effect of endogenous opioids on breathlessness appears mediated by binding to receptors within the CNS rather than peripheral opioid receptors in the respiratory tract. An alternative explanation is that the magnitude of beta-endorphin response was inadequate to affect peripheral opioid receptors.
INSPIRATORY THRESHOLD LOADING INDUCES AUTONOMIC IMBALANCE IN HEALTHY SUBJECTS

Caroline SEVOZ-COUCHE1 Anna L. HUDSON2,3 Marie-Cécile NIÉRAT2,4 Thomas Similowski2,4 Louis LAVIOLETTE2,4

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

Rationale
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.

Methodology
Eleven naive healthy subjects (9 women, age 29 ± 7 years, mean ± SD) were exposed in random order to 3 levels of inspiratory threshold loading (ITL, 5 minutes 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 within the frequency ranges of 0.04 - 0.15 Hz (low frequency, LF) and 0.15 - 0.4 Hz (high frequency, HF, an index of parasympathetic activity). The LF-to-HF ratio (LF/HF), an index of sympathetic activity, 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, LF and LF/HF increased, while HF and RSA decreased compared to baseline spontaneous ventilation values. Maximal increases (+15%, +75% and +161%, respectively) and decreases (-35% and -15%, respectively) were found after the first ITL load, independently of its magnitude. Values returned to baseline during recovery.

Conclusion
First exposure to ITL induced both an increase in sympathetic activity and a decrease in parasympathetic tone. 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.
Exertional dyspnea in patients with pulmonary veno-occlusive disease and idiopathic pulmonary arterial hypertension

Authors:
Pierantonio Laveneziana1,2,3,4, David Montani1,2,5, Peter Dorfmuller1,2, Olivier Sitbon1,2,5, Xavier Jaïs1,2,5, Laurent Savale1,2,5, Thomas Similowski4, Gérald Simonneau1,2,5, Marc Humbert1,2,5, Gilles Garcia1,2,3.

Affiliations:
1Université Paris-Sud, Faculté de médecine, Le Kremlin-Bicêtre, 94276, France; 2INSERM U999, Centre Chirurgical Marie Lannelongue, Le Plessis-Robinson, 92350, France; 3Assistance Publique Hôpitaux de Paris, Service d’Explorations Fonctionnelles Respiratoires, Centre de Référence de l’Hypertension Pulmonaire Sévère, DHU TORINO "Thorax Innovation", Hôpital Universitaire de Bicêtre, Le Kremlin-Bicêtre, 94270, France; 4Université Pierre et Marie Curie (Paris VI), Equipe de Recherche ER 10 UPMC, Laboratoire de Physio-Pathologie Respiratoire, Faculté de Médecine Pierre et Marie Curie (site Pitié-Salpêtrière), Paris, 75013, France; 5Assistance Publique Hôpitaux de Paris, Service de Pneumologie et Soins Intensifs Thoraciques, Centre de Référence de l’Hypertension Pulmonaire Sévère, DHU TORINO "Thorax Innovation", Hôpital Universitaire de Bicêtre, Le Kremlin-Bicêtre, 94270, France.

ABSTRACT
Rationale: Exertional dyspnea curtails daily-living activities in patients with pulmonary veno-occlusive disease (PVOD). Its mechanisms are incompletely understood.
Objectives: To compare the perceptual and ventilatory response to cardiopulmonary exercise testing (CPET) between PVOD and pulmonary arterial hypertension (PAH) patients.
Methods: Thirteen PVOD and 13 idiopathic or heritable PAH patients matched for aging, sex and resting hemodynamics and pulmonary function performed a CPET to the limit of tolerance. Ventilation (VE), oxygen uptake (VO2), dyspnea intensity (by Borg scale), arterial partial pressure of O2 and CO2 (PaO2 and PaCO2, respectively) and the gradient between alveolar and PaO2 [P(A-a)O2] were measured throughout CPET.
Results: Compared with PAH, PVOD patients presented greater VE at rest and at any given VO2 during CPET. Dyspnea intensity (Borg scale) was increased in PVOD compared with PAH. Peak VE was similar between PVOD and PAH despite peak VO2 was reduced to greater extent in PVOD than in PAH patients [41 ± 15 vs 55 ± 10%predicted, respectively]. PaO2 and PaCO2 were significantly lower at rest and at peak exercise in PVOD. P(A-a)O2 was significantly increased at rest and at peak exercise in PVOD compared with PAH.
Conclusions: The more deranged ventilation/perfusion unevenness due to the greater gas exchange inefficiency likely contributed to the increased ventilatory demand which, in turn, contributed to the greater dyspnea intensity found in PVOD patients compared with PAH. CPET may help clinicians better orientating their clinical suspects toward a PVOD profile.
Feasibility of measurement of function in advanced cancer: Comparison of the 6-minute walk test, 2-minute walk test, isometric arm exercises and reading numbers aloud.

Ms Kahren White (1), A/Professor Meera Agar (2,3), Professor David Currow (2).

1. Consultant Occupational Therapist, Marrickville NSW
2. Department of Palliative and Supportive Services, Flinders University, SA
3. Braeside Hospital, Department of Palliative Care, Prairiewood NSW

Background: The pattern in which functional decline in people living with advanced cancer occurs has been described as an initial period of reasonably stable function, followed by more rapid functional deterioration with a defined terminal phase. However little is known about the more subtle changes in function in the more advanced stages of cancer, and the role that breathlessness plays in functional changes. The aim of this pilot study is to compare the feasibility of conducting a range of standardised assessments at different levels of performance status in people with advanced cancer.

Methods: A consecutive cohort was recruited to a cross sectional study from three large palliative care units in metropolitan Sydney. Participants completed four breathlessness-inducing assessments: Six-minute Walk Test Two-minute Walk Test, Isometric Upper limb Exercises and Reading Numbers Aloud. A range of performance status and breathlessness assessments were also completed.

Results: The results of the pilot study have allowed a comparison of the four methods of breathlessness-inducing exercise by functional status in 37 people with advanced cancer. Median scores for performing breathlessness-inducing exercise by level of function where ≥80% of people could complete the tasks will also be presented.

Conclusion: This oral presentation will highlight the pilot study results and the feasibility of using these assessments in research and clinical practice, to improve the assessment of functional capacity and breathlessness in people living with advanced cancer. There is currently limited evidence into how function can be assessed in advanced cancer when breathlessness is present.
Feasibility and performance of the Respiratory Distress Observation Scale (RDOS) to evaluate dyspnea upon admission in the intensive care unit (ICU)

Romain Persichini (1,2), Frédérick Gay (3), Mathieu Schmidt (1,2), Alexandre Duguet (1,2), Alexandre Demoule (1,2), Thomas Similowski (1,2)

(1) Paris 6 university, ER10 research unit ; (2) Assistance Publique - Hôpitaux de Paris, Pitié-Salpêtrière hospital, Department of Respiratory and Critical Care Medicine and (3) Department of Parasitology, Paris, France

ICU admitted patients are at high risk of dyspnea, and of not being able to describe it using a mere visual analog scale (VAS). This study assessed the respiratory distress observation scale (RDOS), a hetero-evaluation dyspnea scale validated in palliative care, in "day one" ICU patients.

In 193 patients admitted to a 16-bed ICU (4 months), we recorded dyspnea, anxiety and pain VAS, RDOS components (breathing frequency, heart rate, accessory muscle activity, nasal flaring, abdominal paradox, expiratory grunting, restlessness, frightened look), various physiological data and disease and treatment descriptors. VAS and RDOS were compared using Spearman's correlation. RDOS ability to detect a VAS>3 was studied using ROC curves. A principal component analysis (PCA) was conducted with the aim of developing a ICU-adapted RDOS.

VAS proved impossible in 73 patients. In the remaining 120, RDOS was weakly correlated with VAS (\(\rho = 0.45\), 95\% CI 0.29-0.58, \(p<0.01\)) (Figure). RDOS>3 had a 95.5\% specificity (95\% CI 87.5-99.1) to predict VAS>3. In PCA, two vectors explained 36.2\% of the data set variability. F1 (25.9\%) included breathing frequency, accessory muscle activity, nasal flaring, and a frightened look. F2 (10.3\%) included abdominal paradox, restlessness, a frightened look, and breathing frequency.

RDOS only weakly correlates with VAS in ICU. However, RDOS>3 should raise the question of dyspnea. Preliminary PCA suggests that re-weighting the RDOS components could be useful to build an adapted score that would then have to be tested. The usefulness of such a modified RDOS in non communicant patients will have to be determined.
THE MULTIDIMENSIONAL DYSPNEA PROFILE (MDP): WHAT IS IT GOOD FOR?

RB Banzett¹,², CR O'Donnell¹,², RM Schwartzstein¹,², RW Lansing¹, PM Meek³, MB Parshall⁴, RH Gracely⁵

¹Beth Israel Deaconess Medical Ctr, Boston, MA ²Harvard Med Sch Boston, MA, ³University of Colorado, Denver, CO ⁴University of New Mexico, Albuquerque, NM, ⁵Univ North Carolina, Chapel Hill, NC.
Supported by NIH NR10006

The concept of multiple dimensions of dyspnea goes back decades (e.g., Gift et al, 1986, Carrieri-Kohlman et al, 1996). Comprehensive multidimensional instruments for pain are well accepted, but comprehensive dyspnea instruments lag behind. We developed the Multidimensional Dyspnea Profile based on a pain measurement model, and incorporated recent improvement in understanding of the sensory qualities of dyspnea.

The MDP assesses the sensory qualities and affective components of dyspnea with 12 rating scales and 1 forced choice item. We designed it to assess individual components of a specific dyspnea experience ('focus period') in both laboratory and clinical settings. The superficially similar Dyspnoea-12, was designed with a very different objective: to combine ratings of several components of dyspnea into one stable overall measurement of recent experience (“these days”), rather than to detect differences in the separate components between diseases or between intervention groups at specific time points (e.g., “when you arrived at the ED”).

Initial published studies in laboratory and clinical settings have shown the ability of the MDP to 1) differentiate both qualities and affective components of different forms of laboratory-induced dyspneas (Banzett et al, 2008), 2) differentiate immediate unpleasantness from emotional response following opioid treatment (Banzett et al, 2011), 3) differentiate "immediate perception" from “emotional response” in ED patients (Meek et al, 2012), 3) reliably assess individual items in short-term recall in ED patients (Parshall 2012), 4) compare COPD patients with healthy subjects in the laboratory and compare COPD patients in the laboratory setting to home setting (O'Donnell et al, 2013).
Comparison of Dyspnea MRC Rating to Risk of Adverse Events and Length of Stay.

K. Baker\textsuperscript{3}, RB Banzett\textsuperscript{1,2}, MD Howell\textsuperscript{1,2}, CR O’Donnell\textsuperscript{1,2}, RW Lansing\textsuperscript{1}, RM Schwartzstein \textsuperscript{1,2}, J. Barsamian\textsuperscript{3}, D. Leone\textsuperscript{3}, B. Donovan\textsuperscript{3}, D. Williams\textsuperscript{3}, K. Carnevale\textsuperscript{3}.

\textsuperscript{1}Pulmonary Division, Beth Israel Deaconess MC, Boston, MA, 02215. \textsuperscript{2}Harvard Medical School Boston, MA, 02115 USA, \textsuperscript{3}Dept of Nursing, Beth Israel Deaconess MC, Boston, MA, 02215.

Problem: Dyspnea is a symptom commonly seen in acutely ill patients that causes considerable suffering. The assessment of dyspnea has always been important for the treatment of causes and symptom management. It is an important independent predictor of adverse outcomes including morbidity and mortality in specific patient populations (Nishimura, 2002, Abidov, 2005).

Methods: We used a modified Medical Research Council (MRC+2) scale to assess dyspnea within the past day on 507 patients admitted to a large urban medical center over a seven week period. We then examined the medical records to determine the occurrence of at least one serious adverse event: the need for a rapid response team, a transfer to an ICU, or death. We also examined length of stay in these patients.

Results: 22\% of patients reported dyspnea while undressing, eating or talking, or at rest (MRC+2 Grade 5-7) upon admission. This cohort of patients experienced a greater incidence of adverse events and had longer hospital stays than their counterparts who rated their dyspnea

![Prevalence of Dyspnea by MRC+2 Grade](image-url)
with more strenuous activity (see graph below).

Conclusions: Early and routine, quantitative assessment of dyspnea is feasible for nurses and presents an opportunity to optimize care and improve symptom management. The presence of dyspnea at rest or with minimal activity is easy to measure at admission and has the potential to predict risk outcomes. Supported by NIH-NR 10006, NR 12009.
Clinically important differences in chronic refractory breathlessness

Authors: Johnson MJ\textsuperscript{1}, Bland JM\textsuperscript{2}, Oxberry SG\textsuperscript{3}, Abernethy AP\textsuperscript{4,5}, Currow DC\textsuperscript{5}

\textsuperscript{1} Hull York Medical School, University of Hull, UK
\textsuperscript{2} Department of Health Sciences, University of York, Heslington, York, UK
\textsuperscript{3} Kirkwood Hospice, Huddersfield, UK
\textsuperscript{4} Duke University Medical Centre, Durham, USA.
\textsuperscript{5} Discipline, Palliative and Supportive Services, Flinders University, Adelaide, Australia.

Background: The minimal clinically important difference (MCID) in chronic refractory breathlessness is ill-defined, but is a key concept for effective clinical practice and trial design.

Methods: A retrospective data analysis from 213 datasets from four clinical trials for refractory breathlessness. Linear regression was used to explore the relationship between study effect size and change in breathlessness score (0 – 100mm visual analogue scale) and to estimate the change in score equivalent to small, moderate and large effect sizes. Pooled individual blinded patient preference data from three randomized controlled trials were analysed. The difference between the mean change in day 4 minus baseline scores between preferred and non-preferred arms was calculated.

Results: There was a strong linear relationship between change in breathlessness intensity score and effect size, \(p=0.001; R^2=0.98\), giving VAS change values for small, medium and large effects as \(-5.5\text{mm}, -11.3\text{mm} \text{ and } -18.2\text{mm}\) respectively. The participant preference change in VAS was \(-9\text{mm} (95\% \text{ CI } -15.8 \text{ to } -2.1) (p = 0.008)\).

Conclusions: This larger dataset supports an MCID of 10mm VAS in chronic refractory breathlessness and studies should be powered to detect this difference.
Meet the Faculty

Listed in order of appearance
Barbara Rogers is President of Respiratory Resources, Inc. and President and CEO the National Emphysema/COPD Association. She is a consultant and advisor to clinicians, corporations and facilities and as a ventilator user for the past 25 years she brings a unique viewpoint. As a leading and nationally recognized COPD and ventilator patient advocate she has presented at public hearings for the Centers for Medicare & Medicaid Services and the Food and Drug Administration and recently completed an appointment as a member of Department of Health and Human Services (DHHS), Centers for Medicare & Medicaid Services (CMS) Program Advisory and Oversight Committee (PAOC). She serves on several Advisory Committees and Industry Boards, was the 2003 recipient of the American Respiratory Care Foundation’s Dr. Charles H. Hudson Award for Cardiopulmonary Public Health and was honored as the recipient of the CHEST 2010 Margaret Pfrommer Memorial Lecture in Long-term Mechanical Ventilation, being the first non-physician to receive this honor.

Amy P. Abernethy, MD, a palliative care physician and hematologist/oncologist, is Director of the Duke Center for Learning Health Care (CLHC) in the Duke Clinical Research Institute and an internationally recognized expert in symptom control clinical trials, health services research, and translational informatics. She is Co-Chair of the National Institutes of Health-funded Palliative Care Research Cooperative Group, an appointee to the Institute of Medicine’s National Cancer Policy Forum, and President of the American Academy of Hospice & Palliative Medicine. Relevant clinical research includes clinical trials, systematic reviews, and evidence implementation studies in opioids and oxygen for the management of refractory dyspnea.

Dr. Parshall, PhD RN has research interests in dyspnea and exacerbations of chronic cardiopulmonary diseases, especially in emergency department patients and hospital inpatients. He also has expertise in questionnaire development and is among the investigators developing the Multidimensional Dyspnea Profile (MDP). He co-chaired the American Thoracic Society (ATS) writing group for the 2012 Statement: Update on the mechanisms, assessment, and management of dyspnea.

(http://www.thoracic.org/statements/resources/other/update-on-mamd.pdf )
**Louis Laviolette, Ph.D.** is currently a postdoctoral fellow at Université Pierre et Marie Curie in Paris where his research interests focus on the neurophysiological aspects of dyspnea. He has also investigated exertional dyspnea and limb muscle fatigue in patients with COPD.

**Pierantonio Laveneziana, M.D., PhD** is a pulmonologist currently at the Université Pierre et Marie Curie in Paris. His research has focused on the ventilatory responses to exercise and activity limitation in COPD, aging and obesity as well as the language of dyspnea used by asthmatics. Pierantonio has worked in prominent research labs in Italy, Canada, the USA and France.

**Nicholas Hill, M.D.** is Chief of the Division of Pulmonary, Critical Care and Sleep Medicine at Tufts Medical Center in Boston and Professor of Medicine at Tufts University School of Medicine. A Dartmouth Medical School graduate, he did his Internal Medicine training at Tufts-New England Medical Center and the Boston VA Medical Center, a year of Cardiovascular Medicine fellowship at the University of Massachusetts and a fellowship in Pulmonary and Critical Care Medicine Boston University. He has done extensive research and writing in the fields of noninvasive ventilation and pulmonary hypertension. He is a former Eli Lilly Distinguished Scholar of the Chest Foundation, and recipient of an Excellence in Pulmonary Hypertension Care from the Pulmonary Hypertension Association. He is a past President of the American Thoracic Society and an Associate Editor of Chest.

**Professor Miriam Johnson, M.D.** is Co-director of the Supportive care, Early Diagnosis, and Advanced disease (SEDA) research group at Hull York Medical School (University of Hull), UK. Her research interests include the mechanisms and management of chronic refractory breathlessness in advanced disease, collaborating with partners across different disciplines. Studies range from projects looking at mechanisms, prevalence and patient experience, as well as clinical trials of drug or complex interventions, and secondary data analysis.
Margaret L. Campbell, Ph.D. RN, FPCN is an Associate Professor in the Office of Health Research at the College of Nursing at Wayne State University in Detroit, MI, USA. Her research is currently focused on assessment and treatment of dyspnea among patients at the end of life. She developed and rigorously tested the only known tool for assessing respiratory distress when the patient is unable to report dyspnea.
List of Attendees

| Amy Abernethy | Marie-Claude Gregoire | Donald Mahler |
| Dan Adler     | Ingrid Harle          | Cassandra Mendonca |
| Sharon Baer   | Yvonne Heijdra        | Capucine Morelott |
| Fiona Bailey  | Dean Hess             | Carl O'Donnell    |
| Kathy Baker   | Elizabeth Hill        | Claudine Peiffer  |
| Robert Banzett| Nicholas Hill         | Meike Pappens     |
| Andrew Binks  | Jenny Hoit            | Mark Parshall     |
| Naushenwan Burki | Doris Howell     | Sibyli Petersen   |
| Margaret Campbell | Dennis Jensen | Barbara Rogers   |
| Ginger Carrier-kohlman | Miriam Johnson | Anne-Marie Russell |
| David Currow  | Jeff Kepler           | Sami Simons       |
| Laurence Dangers | Robert Lansing | Tian Yue Song    |
| DorAnne Donesky | Marc H Lavietes | Christina M. Spengler Walder |
| Karl Evans    | Pierantonio Laveneziana | Thomas Similowski |
| Aamir Gilani  | Louis Laviolte        | Mirza Subhan      |

Program Artwork by Ruth Fryhle