Abstract S46 Table 1 Values Δ AUC dose – response to ADP (0–10 μ M)

	Placebo	Fostair
p-selectin expression (%) baseline	–21.6, +140.6 ($p = 0.2$)	+5.8, +140.6 ($p = 0.03$)*
Platelet fibrinogen expression (%) baseline	–136.0, +169.1 ($p = 1.0$)	–52.5, +252.6 ($p = 0.3$)
PMA (%) baseline	–168.3, +92.4 ($p = 0.8$)	–116.7, +144.1 ($p = 1.0$)

Conclusion The effects of B/F in this study may represent delivery of corticosteroid to the peripheral airways ameliorating local injury and altering platelet activation. Bronchodilation may represent an effect on the small airways in IPF. Whether these effects are important in disease progression remains to be established.

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The breath of life: respiratory physiology

S47 NEURAL RESPIRATORY DRIVE RESPONSES TO INCREASES IN CONTINUOUS POSITIVE AIRWAY PRESSURE IN HEALTHY SUBJECTS

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Introduction Dynamic hyperinflation (DH) is characterised by an increase in end-expiratory lung volume (EELV) and contributes to exercise limitation in Chronic Obstructive Pulmonary Disease (COPD) patients. Neural respiratory drive (NRD) directly reflects the load-capacity relationship of the respiratory system and is therefore expected to increase with DH. However, there are limited data investigating the effects of isolated increases in EELV on NRD. We hypothesised that 1) increases in EELV induced by continuous positive airway pressure (CPAP) would increase NRD in healthy subjects and 2) with the change in lung volume, NRD to the parasternal intercostal muscles would increase to a greater extent than that to the diaphragm at higher levels of CPAP.

Method CPAP was applied to healthy subjects at 0, 4, 8, 12 and 16 cmH₂O in a random order and inspiratory capacity (IC) measured at each CPAP level as an indicator of EELV. Trans-diaphragmatic pressure swings (ΔP_{di}), tidal volume (V_T) and respiratory rate (RR) were measured. NRD was assessed with second intercostal space parasternal muscle electromyography (EMG_{para}) and diaphragm electromyography (EMG_{di}) using surface electrodes and a multipair oesophageal electrodes, respectively. EMG_{para}/EMG_{di} ratio was calculated.

Results 10 healthy subjects were recruited. Increasing levels of CPAP led to a reduction in IC ($p < 0.0001$, Table 1). Both EMG_{para} and EMG_{di} increased with progressive increases in CPAP (Table 1). Interestingly, respiratory rate and tidal volume

did not change with the increases in CPAP. Similarly, EMG_{para}/EMG_{di} ratio and ΔP_{di} remained unchanged.

Conclusion This detailed physiological study has demonstrated that escalating levels of CPAP increased EELV, shown by the reduction in IC, in healthy subjects. The increase in EELV was associated with an increase in NRD to both the parasternal intercostal muscles and to the diaphragm. However, contrary to the original hypothesis and observations in COPD patients (O'Donoghue *et al.*, Thorax 2001), NRD was not preferentially distributed to the parasternal intercostal muscles at higher lung volumes. These data indicate that the differential NRD to the parasternal and diaphragm in COPD patients is not solely a consequence of a rise in EELV and alternative mechanisms for the differential NRD should be sought.

Abstract S47 Table 1 Changes in neural respiratory drive and other physiological parameters during CPAP titration between 0 and 16 cmH₂O

	CPAP 0 cmH ₂ O	4 cmH ₂ O	8 cmH ₂ O	12 cmH ₂ O	16 cmH ₂ O	<i>p</i> value for trend
EMG _{para} (μ V)	5.82 (2.25)	6.07 (2.29)	6.97 (2.61)	7.90 (2.93)	10.3 (6.4)*	<0.001
EMG _{di} (μ V)	12.75 (5.03)	14.19 (5.04)	18.27 (8.57)	22.64 (10.33)*	33.2 (25.2)*	<0.001
EMG _{para} /EMG _{di} ratio	0.56 (0.38)	0.50 (0.27)	0.49 (0.28)	0.39 (0.16)	0.38 (0.23)	0.29
RR (/min)	14.9 (2.9)	13.5 (2.8)	12.3 (2.9)	14.4 (3.5)	14.9 (4.2)	0.95
IC (L)	2.50 (0.49)	2.38 (0.48)	2.13 (0.45)	1.79 (0.44)*	1.57 (0.71)*	<0.0001
IC %predicted	90.3 (14.3)	85.6 (11.6)	76.6 (12.5)	64.4 (11.0)*	55.2 (17.9)*	<0.0001
V_T (L)	0.57 (0.10)	0.58 (0.13)	0.62 (0.19)	0.61 (0.32)	0.59 (0.23)	0.95
ΔP_{di} (cmH ₂ O)	11.2 (4.4)	9.2 (2.4)	9.8 (4.2)	9.6 (4.2)	10.3 (3.8)	0.37
ΔP_{oes} (cmH ₂ O)	7.6 (2.5)	5.9 (1.5)	7.0 (1.5)	6.7 (2.1)	7.4 (1.6)	0.14

RR: respiratory rate, IC: inspiratory capacity, V_T : tidal volume, ΔP_{di} : transdiaphragmatic inspiratory pressure swing; ΔP_{oes} : oesophageal inspiratory pressure swing. * $p < 0.05$ compared with value at CPAP 0 cmH₂O.

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S48 CONTINUOUS POSITIVE AIRWAY PRESSURE TITRATION IN AWAKE OBESE SUBJECTS WITH OBSTRUCTIVE SLEEP APNOEA AND ITS IMPACT ON NEURAL RESPIRATORY DRIVE AND BREATHLESSNESS

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Background Continuous positive airway pressure (CPAP) is an effective treatment for obstructive sleep apnoea (OSA). We assessed neural respiratory drive (NRD), as measured by the surface electromyogram of the parasternal intercostals (sEMG_{para}),

during awake CPAP titration to quantify the effect of chest inflation on the load of the respiratory system.

Patients and methods Obese patients (body-mass-index, BMI >30) with confirmed obstructive sleep apnoea (OSA) were studied and NRD (sEMG_{para}) and the surface EMG of the external oblique (sEMG_{abd}) were recorded and normalised to baseline activity (awake, supine). The apnoea-hypopnoea index (AHI) and 95th percentile of CPAP were determined in sleep studies. The patients were then studied whilst awake and breathing on CPAP (4–20 cmH₂O, increments of 2 cmH₂O/3 mins), with the modified Borg score (mBorg) recorded.

Results 15 patients (age 48 ± 10 years, 12 male, BMI 38.9 ± 5.8) suffering with moderate-severe OSA (AHI 32.2 ± 21.1/h, 95th percentile nocturnal CPAP 14.1 ± 3.8 cmH₂O) were studied. Awake, sEMG_{para} declined by 15.1 ± 1.5% from baseline when CPAP was applied, with the nadir at a CPAP of 10.6 ± 3.4 cmH₂O (p = 0.026). Further increase in CPAP levels led to a rise in sEMG_{para} and breathlessness (mBorg at lowest sEMG_{para} 0.9 ± 0.8 points, at CPAP of 20 cmH₂O 2.7 ± 2.7 points, p = 0.02).

Conclusion The respiratory system is maximally offloaded with subtherapeutic CPAP levels in OSA. Levels of NRD observed at effective CPAP levels are associated with breathlessness which can impact on CPAP compliance.

S49

VENTILATORY IRREGULARITY QUANTIFIED BY APPROXIMATE ENTROPY IDENTIFIES DISORDERED BREATHING IN PATIENTS WITH UNEXPLAINED DYSPNOEA

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Introduction Patients with idiopathic persistent exertional dyspnoea are often labelled as having a breathing pattern disorder (BPD). There are no agreed objective diagnostic measures for BPD, which complicates its characterisation and response to therapy. Approximate entropy (ApEn) is a measure of unpredictability, based on chaos theorem, which quantifies the degree of irregularity in time-series data.

Objectives To measure ApEn of ventilatory variables during a cardiopulmonary exercise test (CPET) in patients referred with unexplained dyspnoea. We hypothesised that ApEn of tidal volume and breathing frequency would be greater (i.e. more irregular) in patients with BPD than healthy controls.

Methods We studied 20 adults (14 female) with unexplained dyspnoea referred for CPET and diagnosed with BPD (by a senior respiratory physiotherapist blinded to ApEn data) and 15 age-gender- and BMI-matched healthy controls. Underlying cardiorespiratory disease was excluded using various investigations (e.g. imaging and echocardiography) prior to referral, in addition to tests performed on the day of CPET; namely pulmonary function and blood gas analysis. ApEn of various ventilatory parameters including tidal volume, breathing frequency and minute ventilation was calculated at rest and during a cycle-ergometer CPET.

Results BPD patients had greater dyspnoea (modified BORG) at rest (1.4 ± 1.2 vs 0.2 ± 0.6; P < 0.01) and lower peak oxygen uptake (VO₂) (P < 0.01; Table 1). Peak exercise respiratory exchange ratio was similar between groups (1.14 ± 0.17 vs 1.13 ± 0.08, P = 0.84) as were nadir values for ventilatory

equivalent for CO₂ (28.5 ± 5.2 vs 25.5 ± 3.6, P = 0.07) and end-exercise arterial PCO₂ (4.21 ± 0.68 vs 4.1 ± 0.67, P = 0.68). ApEn was significantly greater in the BPD cohort for the duration of the test (Table 1); however differences were not apparent at rest. There was no relationship between ApEn and baseline symptom scores.

Conclusion Measurement of ventilatory ApEn in patients referred with unexplained dyspnoea quantified irregularity of breathing pattern and was significantly greater (more irregular) in BPD than controls. These differences were not apparent from resting phase analysis. Quantifying increased dys-regulation in exercise hyperpnoea using ApEn can be applied to ventilatory variables collected during standard CPET, and thus could aid in diagnosis and evaluating treatment response in BPD. Further work should explore how ventilatory ApEn relates to perception of symptoms.

Abstract S49 Table 1 Participant characteristics and exercise responses

	BPD (N = 20)	Healthy Controls (N = 15)
Age (years)	49 (14)	50 (18)
BMI (kg/m ²)	26.0 (5.0)	24.5 (3.7)
FEV ₁ (% predicted)	107 (18)	95 (18)*
FEV ₁ /FVC	0.78 (0.06)	0.75 (0.12)
VO ₂ /kg Peak (ml/min/kg)	20.7 (7.1)	37.9 (14.9)**
VO ₂ Peak (% Predicted)	79.8 (17.5)	124.8 (27.3)**
ApEn Tidal Volume	1.31 (0.23)	1.04 (0.28)**
ApEn Breathing Frequency	1.42 (0.22)	1.24 (0.24)*
ApEn Minute Ventilation	1.01 (0.29)	0.64 (0.22)**

S50

UNDERSTANDING HEROIN OVERDOSE: A STUDY OF THE ACUTE RESPIRATORY DEPRESSANT EFFECTS OF INJECTED PHARMACEUTICAL HEROIN

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Introduction and objectives Opioids are respiratory depressants and heroin/opioid overdose is a major contributor to the excess mortality of heroin addicts. The individual and situational variability of respiratory depression caused by intravenous heroin is poorly understood. The aim of this study was to use advanced physiological monitoring to follow the time course and severity of acute opioid-induced respiratory depression.

Methods 10 patients (9/10 with chronic airflow obstruction) undergoing supervised injectable opioid treatment for heroin addiction received their usual prescribed dose of injectable opioid (diamorphine or methadone) (IOT), and their usual prescribed dose of oral opioid (methadone or sustained release oral morphine) after 30 min. The main outcome measures were pulse oximetry (SpO₂%), end-tidal CO₂% (ETCO₂%) and neural respiratory drive (NRD) (quantified using parasternal intercostal muscle electromyography). Significant respiratory depression was defined as absence of inspiratory airflow >10s, SpO₂% <90% for >10s and ETCO₂% per breath >6.5%.

Results ETCO₂% indicated significant respiratory depression following IOT in 8/10 patients, with levels increasing from baseline 4.7 (4.5 to 5.4)% to 5.4 (5.1 to 5.7)% at 30 min, p = 0.01. The median (range) peak ETCO₂% per breath was 6.9% (5.2 to 7.8).