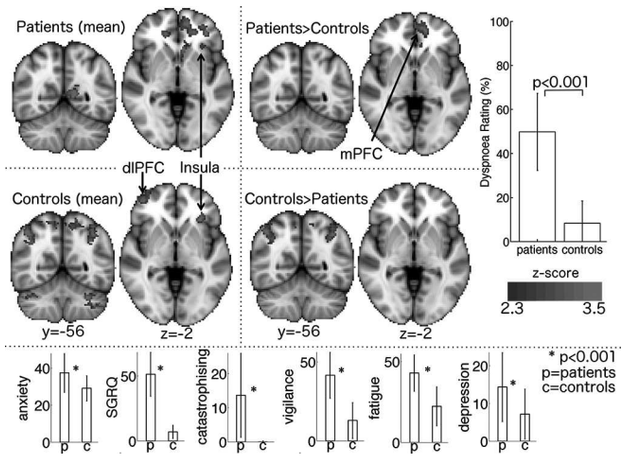
adapted this technique to identify brain areas responsible for breathlessness perception in COPD. We hypothesised that healthy controls would demonstrate brain patterns similar to that observed in previous FMRI studies in healthy volunteers. As psychological dysfunction is strongly associated with COPD we hypothesised that patients would show greater engagement of cognitive brain areas.

Methods 44 COPD patients and 40 matched controls undertook FMRI scanning (Siemens 3T), and psychological and physiological assessments. During scanning, participants were presented with previously validated breathlessness-related word cues and rated breathlessness on a visual analogue scale. FMRI analysis was performed with FSL (http://www.fmrib.ox.ac.uk/fsl). Significant activations were determined as $Z > 2.3$, with a cluster probability threshold of $P < 0.05$, corrected for multiple comparisons.

A modified shuttle walk test (MSWT) and spirometry were performed. The following questionnaires were administered: Center for Epidemiological Studies Depression Scale, Dyspnoea-12, State and Trait Anxiety Inventory, bespoke catastrophising and vigilance questionnaires, Fatigue Severity Scale and St Georges Respiratory Questionnaire.

Results Imaging and questionnaire results are displayed in the figure. MSWT values (mean ± SD) were 331 +/-193m (patients) and 804 +/-274m (controls) ($p < 0.001$). FEV1 (% predicted) was 0.6 ± 02(patients) and 1.0 ± 0.2(controls) ($p < 0.001$)

Conclusions We observed differing brain activation patterns in response to dyspnoea-related word cues between COPD patients and controls. The control group displayed a similar activation pattern to that observed in previous FMRI studies of breathlessness in healthy volunteers while COPD patients display significantly greater activation in the medial prefrontal cortex (emotion control and memory consolidation). Our behavioural data demonstrates greater psychomorbidity in patients. Taking our imaging and behavioural findings together, we propose that in COPD engagement of the medial prefrontal cortex distorts the processing of breathlessness sensations towards greater reliance on fear memories and expectations, contributing to a vicious circle of avoidance and fear.



Abstract S116 Figure 1.

S117 FACTORS DRIVING THE DEVELOPMENT OF CHRONIC RESPIRATORY FAILURE IN OBESE PATIENTS

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Introduction Currently, there are limited data reporting the pathophysiology of chronic respiratory failure in obese patients, the so called *Obesity Hypoventilation Syndrome* (OHS). Although a number of hypotheses have been proposed, there are no comprehensive data that have investigated the imbalance between respiratory muscle load, capacity and drive. We aimed to investigate the factors contributing to early chronic respiratory failure in obese patients including body habitus, upper airways obstruction, lower airflow obstruction and lung volume.

Methods A cross sectional study was performed in an obese group of subjects (BMI $>30 kg/m^2$) with and without early chronic respiratory failure. Early chronic respiratory failure was arbitrarily defined for this analysis as an arterial base excess > 2 mmol/l as this is a metabolic respiratory biomarker of 24-hour carbon dioxide levels. Arterial blood gas measurements were undertaken in the morning, after an overnight study to determine the 4% oxygen desaturation index and apnoeas hypopnoea index. An overnight auto titrating continuous positive airway pressure study (S9 ResMed, Oxfordshire, UK) was used as another measure of the severity of upper airways loading. Pulmonary function and the forced oscillation technique (MS-IOS, CareFusion, CA, USA) to measure of airway impedance were performed in the upright and supine position.

Abstract S117 Table 1. Anthropometric and physiological characteristics of the patients without and with evidence of a metabolic compensation for increased CO_2 levels.

	Base excess ≤2 mmol/l (n= 22)		Base excess >2 mmol/l (n= 32)	
	Mean	Standard deviation	Mean	Standard deviation
BMI (kg/m^2)	44.6	9.8	48.3	9.64
Epworth Sleepiness Score (ESS)	12.3	5.45	12.8	5.28
$PaCO_2$ (kPa)	5.05	0.5	5.94	1.6
HCO_3^-(mmol/l)	24.6	1.2	27.7	1.6
Base excess (mmol/l)	0.27	1.3	3.8	1.8
Oxygen Desaturation Index (ODI; events/hr)	40.4	27.5	51.0	40.1
Apnoea-Hypnoea Index (AHI; events/hr)	24.7	29.1	30.1	29.3
Mean oxygen saturations (SpO_2) overnight (%)	89.3	1.7	89.1	6.9
AutoCPAP pressure (cmH_2O)	12.4	2.4	12.4	2.8
Upright FEV_1 % predicted	107.2	22.1	91.5	19.2
Upright FVC % predicted	107.4	23.0	95.5	17.4
Supine FEV_1 % predicted	89.7	21.3	77.4	18.5
Supine FVC % predicted	92.2	21.3	80.2	22.0
Upright Expiratory reserve volume (ERV) (mls)	534	360	497	290
Supine ERV (mls)	187	166	152	187
Upright Airway Impedance at FRC (mmHg /l/s)	0.55	0.38	0.83	0.66
Supine Airway Impedance at FRC (mmHg/l/s)	1.44	0.73	1.68	0.84

Results 54 patients, aged 51.9 ± 9.08 years, were recruited with BMI of 46.4 ± 9.53.

Conclusion We are finding considerable heterogeneity in terms of anthropometric and physiological findings within obese subjects with and without early chronic respiratory failure. We have shown that subjects with early chronic respiratory failure,

compared to subjects without, have lower lung volumes (upright and supine), a greater airway impedance (seen in FOT at FRC, both upright and supine), and a larger fall in their ERV on lying down. All these differences may be due to the higher BMI, and in particular differences in distribution of fat in subjects with early chronic respiratory failure. However, these obesity differences were not reflected in large differences in the AHI or ODI between the groups.

S118 THE VENTILATORY RESPONSE TO CO2 WITHIN OBSTRUCTIVE SLEEP APNEA PATIENTS

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Introduction Obstructive Sleep Apnea (OSA) is a condition defined by the collapse of the upper airway and cessation of respiration during sleep. The resulting hypoventilation leads to intermittent nocturnal hypoxia and increased arterial pCO_2 (hypercapnia). Control of ventilation is largely dependent on two interactive pathways, the central and peripheral chemoreceptors. Both chemoreceptors' respond to H^+ ions liberated as a result of the presence of CO_2. However, the peripheral chemoreceptors also respond to hypoxia particularly when PaO_2 falls below 70 Torr. Hypoxia has a synergistic effect on the ventilatory response to CO_2. Our study therefore investigated the ventilatory response to CO_2 with and without the presence of moderate hypoxia to determine whether the central and/or peripheral chemoreflex response to CO_2 is modified with the development of OSA.
Methods The ventilatory response to CO_2 amongst 33 newly diagnosed male OSA patients (AHI: 32.6 ± 24.8; age: 53.1 ± 10.3 years, BMI: 36.4 ± 6.8 kg/m^2) was measured whilst breathing four different gas mixtures balanced with N_2 (Mixture 1: ambient air; mixture 2: 25% O_2/6% CO_2; mixture 3: 13% O_2; mixture 4: 13% O_2/6% CO_2). The minute ventilation of each participant, normalised by their body surface area (BSA), was recorded with subjects blinded to the order of test gases. Additionally, fasted venous blood samples were taken to assess plasma leptin concentrations.
Results Mild and moderate OSA patients (AHI: 13.76 ± 7.01) revealed a significantly (p <.01) greater change in their ventilatory response to the hyperoxic-hypercapnic gas mixture (5.22 ± 1.95 l x min^{-1} x BSA^{-1}) compared to severe OSA patients (AHI: 55.31 ± 18.25) (3.26 ± 1.64 l x min^{-1} x BSA^{-1}). There was no significant change in ventilation between the hyperoxic and hypoxic-hypercapnic conditions in both groups. A significant negative correlation (r = -0.39; p <.05) was found between AHI and ventilation change (l x min^{-1} x BSA^{-1}) to the hyperoxic-hypercapnic gas mixture.
Conclusion These findings suggest the reduced ventilatory response to hypercapnia amongst severe OSA patients is likely a result of adaptation to the central chemoreceptors.

S119 IS THE HYPERCAPNIC VENTILATORY RESPONSE STILL RELEVANT TO CENTRAL SLEEP APNOEA IN THE ERA OF MODERN HEART FAILURE MANAGEMENT?

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Introduction A brisk ventilatory response to carbon dioxide (CO_2) is integral to the development of central sleep disordered breathing (SDB) in heart failure (HF) patients. Modern treatments for HF enhance cardiac function and many improve central SDB. The role of hypercapnic ventilatory responses (HCVR) in central SDB in HF patients managed according to modern guidelines is unclear. For example, adaptive servoventilation (ASV), used to treat central SDB, both improves cardiac function and reduces hypercapnic ventilatory responses (HCVR), suggesting that heightened chemosensitivity in HF may relate to cardiac impairment.
Objective To test the hypothesis that there would be no difference in HCVR between optimally treated patients with HF and central SDB (HF-CSA), and those with HF alone (HF-noSDB).
Method Measurements of resting expired CO_2 (awake) and evening and morning HCVR, using the Read rebreathe technique, were undertaken in patients optimally treated for HF. Patients also underwent overnight polysomnography. Sample size calculations (using data from Javaheri, NEJM 1999) showed 10 patients were needed in each group. Statistical analyses were undertaken using SPSS. The study received ethical approval.
Results Twenty-six HF patients were studied (11 with HF-CSA: median (IQR) age 68 (58–78) and 15 with HF-noSDB: age 72 (67–78)years). Left ventricular ejection fraction was: HF-CSA 32 (20–40)% and HF-noSDB 40 (27–47)%. The apnoea hypopnoea index was: HF-CSA 14.6 (12.9–37.1)/hr and HF-noSDB 5.0 (3.2–6.0)/hr. The HF-CSA group had lower median resting expired CO_2 than the HF-noSDB group (end tidal CO_2: 30.6 (28.6–37.3) vs. 36.2 (35.2–40.4)mmHg, p = 0.02). There was no significant difference between the HF-CSA and HF-noSDB in evening HCVR (2.15 (1.70–2.74) vs. 1.99 (1.60–3.33)L/min/mmHg $ETCO_2$, p = 0.53) or morning HCVR (2.71 (1.43–4.88) vs. 2.20 (1.00–3.00)L/min/mmHg $ETCO_2$, p = 0.23). Resting expired CO_2 in the total study population correlated negatively with morning, but not evening, HCVR.
Conclusion The results of this small study suggest that modern HF management may have an effect on ventilatory stability via changes in HCVR. The timing of the HCVR tests may be a factor. We speculate that overnight disturbances in breathing may promote ventilatory instability in the morning, rather than the evening.

S120 HYPERPOLARISED 3HE DIFFUSION MRI AND MULTIPLE BREATH INERT GAS WASHOUT IN PATIENTS WITH ASTHMA

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Background Multiple breath inert gas washout (MBW) is a technique for detecting abnormal ventilation distribution in patients with asthma and other airway diseases. S_{cond} and S_{acin} are measures of convective-dependent inhomogeneity (CDI) and diffusion-convection-dependent inhomogeneity (DCDI) respectively. Hyperpolarised ^{3}He diffusion magnetic resonance imaging (^{3}He-MRI) may be used to probe lung microstructure at a variety of length scales, with short timescale (14 ms) apparent diffusion coefficient (ADC) corresponding to diffusion within an alveolus or a single acinar airway, and long timescale (1.5s–6s) ADC