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Early View

Research letter

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Heightened ventilatory response during stair climbing in individuals with dysfunctional breathing

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INTRODUCTION

Dysfunctional breathing, defined as an alteration in the normal pattern of breathing,[1,2] is recognised to be an important differential diagnosis for individuals with 'unexplained' dyspnoea. It is estimated that dysfunctional breathing is present in up to 10% of the general population[3] and is a prevalent co-morbid finding in individuals with airways disease, acting to amplify symptom burden and to confound accurate assessment of disease control.[1,3,4]

Individuals with dysfunctional breathing often report disproportionate symptoms,[5] such as the breathlessness at the onset of every-day activities. Tasks that typically cause breathlessness include a change in posture, such as when bending forward or starting to climb stairs.[5] Although, there is currently no gold-standard means for the assessment of exertion-related aspects of dysfunctional breathing, when studies have employed standard laboratory-based exercise assessments (e.g. using an incremental exercise protocol with cardiopulmonary exercise testing [CPET]), overall exercise capacity appears to be preserved in those with dysfunctional breathing.[6]

To evaluate the apparent discrepancy between subjective and objective findings, in individuals with dysfunctional breathing, we evaluated cardiopulmonary and ventilatory response during a more pragmatic or 'real-life' exercise challenge, i.e. during a stair-climb. We hypothesised that the ventilatory response to exercise would be disordered in individuals with dysfunctional breathing, when comparing with an age-matched control group.

METHODOLOGY

Study design and participants

Patients prospectively attending the unexplained breathlessness service at the Royal Brompton Hospital, between May and September 2019, were invited to undertake a stair-climb CPET assessment, as described below. Participants were recruited if they were diagnosed with dysfunctional breathing; based on the positive identification (by a senior respiratory physiotherapist) of a series of typical characteristics of dysfunctional breathing[4,5] and having had other relevant pathologies excluded (e.g. with pulmonary function tests, imaging and cardiac investigations, as indicated). In addition, a laboratory-based CPET revealed no significant cardiorespiratory abnormality. Age- and sex matched individuals, with no history of cardiorespiratory illness were recruited as a control group. All participants provided written consent for this ethically approved study (Local REC Project reference: 18/WM/0268).

Study measurements

Participants initially completed dyspnoea-related questionnaires (Dyspnoea-12[7] and Nijmegen[8]), spirometry and a stair-climb exercise test with a portable CPET device (Oxycon Mobile, CareFusion, USA) and heart rate belt (Polar T31 transmitter). Baseline data were collected with subjects in the seated position for two minutes. Resting respiratory rate was reported as the mean of a 30 second period after one minute rest. Participants were then instructed to climb four flights of stairs consisting of eleven steps (rise 160 mm; total elevation gain 7.04 m), at their own pace. Recovery data was collected for two minutes in a seated position. Ratings of breathlessness and muscular exertion were obtained at rest and upon end of exercise bout, using the modified BORG Dyspnoea Scale and Rate of Perceived Exertion (CR10) Scales (0-10).[9] Independent t-test and Mann-Whitney U test were used as appropriate to test for differences between groups. A Chi-

squared test or Fisher's Exact test were used for binary variables. All analyses were performed using IBM SPSS statistics version 26.0. A p-value of < 0.05 was considered significant.

RESULTS

A total of 24 subjects completed assessment. Patients (n=11) and controls (n=13) were well matched for age and sex, although patients had a slightly greater BMI (Table 1). Patients reported higher baseline dyspnoea scores than controls; Dyspnoea-12 ($P < 0.01$) and Nijmegen ($P < 0.01$)(Table 1). Patients also had a slightly higher breathing frequency than controls at rest ($P = 0.01$), but a similar minute ventilation ($P = 0.36$) (Table 1). Resting spirometric indices were normal in both groups (Table 1). Patients with dysfunctional breathing had a predicted peak VO_2 of 97 % (n = 3, peak < 80 %), from their laboratory-based CPET.

The end stair climb oxygen consumption and heart rate at the end of the challenge was similar between patients and controls (Table 1, all $P > 0.05$). At end-exercise, patients reported a higher BORG dyspnoea rating ($P < 0.01$), with 91% reporting the challenge as BORG $\geqq 3$ (rating as moderate to severe), in contrast, only 8% of controls reported the same severity rating. At the end of the stair climb, breathing frequency was approximately 10 breaths per minute higher ($P < 0.01$) in patients, but with a similar tidal volume ($P = 0.87$), when compared with controls.

DISCUSSION

The ventilatory response to a simple, every-day physical activity challenge appears to be amplified in individuals with dysfunctional breathing when compared with a matched control group, despite a similar cardiac and metabolic demand. Specifically, in individuals with dysfunctional breathing,

stair-climbing was associated with a heightened end stair climb-exercise ventilation, arising from seemingly excessive exertional hyperpnoea. These findings align with patients' subjective reports of breathlessness in response to this type of activity and a sensation of ‘faster breathing’ during simple activities.

Stair climbing is an important daily activity for most people, but represents a ‘composite’ physiological challenge, with a requirement for synchronous changes in not only respiratory patterns but also muscular tone and vascular and cardiac responses.[10] The mechanisms relating to metabolic and respiratory control during exercise remain debated and feed-forward, anticipatory responses are likely to be relevant[11]. The disordered ventilatory response we observed during exercise in patients with dysfunctional breathing, aligns with our previous work[6] which indicated that individuals with this condition appear to have a chaotic and amplified ventilatory response during CPET testing. Further mechanistic work is needed to determine if this amplified response pattern is centrally-controlled and/or is potentially arising from alterations in chemo-sensitivity, oxygen extraction, central control or aberrant autonomic control mechanisms.[12,13] These are important mechanistic considerations that need to be explored in future studies, to help provide targeted treatments.

Previous studies have quantified dysfunctional breathing using different techniques, including the Self-Evaluation of Breathing Questionnaire (SEBQ), manual assessment of respiratory motion (MARM), end-tidal carbon dioxide measurement and the breathing pattern assessment tool (BPAT) measurement.[4] These assessment tools fail to adequately evaluate breathing patterns on exertion; a relevant consideration in dysfunctional breathing. This study therefore potentially establishes a

protocol that could now be used to assess dysfunctional breathing and responsiveness to intervention, e.g. with physiotherapy. Our findings also highlight the need for targeted intervention to help alleviate the breathlessness arising from this type of challenge. In this context, an energy conserving, pacing strategy has been successfully employed to help patients with COPD[14] during stair-climbing and a similar approach may prove beneficial in dysfunctional breathing. Future work should also explore relationships between stair climbing breathing response and the different phenotypes of dysfunctional breathing.[5]

We acknowledge several methodological limitations. Firstly, the sample size is small, and subjects were recruited from a single specialist centre and we do not have CPET data in a standard laboratory test from the control group. Our ability to recruit more subjects was unfortunately curtailed by the COVID-19 pandemic. Future studies should increase subject numbers and ideally aim to provide a comparator with standard laboratory CPET in both groups. It is also possible that some of the findings are explained by minor differences in BMI between the groups and ability to regulate their self-determined pace on stair climbing. i.e. the control group had a lower stair climb time. The use of non-standardized exercise test protocols warrants a need for caution in the interpretation of some aspects of the results, however self-paced protocols are commonly used to assess exertional performance (e.g. the 6 minute walking test). The choice of the protocol described in the current work, was determined by our desire to deliver a pragmatic design, but future work could explore differences in breathing control with a regulated pace; indeed this approach likely underpins some approaches to pacing that are used to help manage dyspnoea.

A second important consideration relates to the methodology used to diagnose dysfunctional breathing. As outlined in the introduction, there is currently no gold-standard means for establishing this diagnosis and accordingly we utilised the type of approach used to identify individuals with dysfunctional breathing, that would be undertaken in standard clinical practise. There may also be value in evaluating the recovery profile in respiratory rate on exercise cessation, to provide insight regarding resumption of 'normal' breathing control following exercise.

In conclusion, this study of individuals with dysfunctional breathing, provides physiological insight to support the subjective report of an abnormal or heightened ventilatory response to exercise and demonstrates commensurate, objective alterations in ventilatory response. This pragmatic approach to assessing ventilatory response in dysfunctional breathing, now needs to be validated and standardized in larger multiple centre studies.

TABLE HEADERS

Table 1. Baseline data and cardiopulmonary response to stair climbing

	CONTROL (N = 13)	PATIENTS (N = 11)	P-VALUE	
Sex: M:F	3:10	5:6	0.25	
Age	49 (8.0)	54 (9.9)	0.19	
BMI	26 (5.2)	29 (3.0)	0.047	*
Nijmegen (/64)	3.5 (4.7)	23 (9.8)	< 0.01	**
Dyspnoea-12 (/24)	0.0 (0)	15.7 (8.6)	< 0.01	**
FEV1 % predicted	99.4 (16)	109 (10)	0.23	
FVC % predicted	101 (18)	115 (12)	0.04	*
Rest Measurements:				
V_E Rest (L/min)	11 (4.1)	12 (4.9)	0.36	
BF Rest (1/min)	17 (3.3)	22 (5.0)	0.01	*
VO_2 Rest (mL/min/kg)	4.5 (1.2)	3.8 (0.7)	0.91	
V_{tex} Rest (L/min)	0.69 (0.2)	0.59 (0.1)	0.09	
HR Rest (1/min)	78 (14)	78 (9.5)	0.73	
PetCO2 rest (kPa)	4.4 (0.3)	4.0 (0.4)	< 0.01	**
RER rest	0.92 (0.1)	0.88 (0.2)	0.15	
Dyspnoea, Rest (BORG CR10)	0.0 (0.0)†	0.5 (1.0)†	0.02	*
RPE, Rest (BORG CR10)	0.0 (0.0)†	1.0 (1.0)†	0.02	*
End Stair Climb Measurements:				
V_E (L/min)	24 (8.6)	36 (9.0)	< 0.01	**
V_E % Of max (%)	22 (5.9)	31 (9.7)	0.02	*
BF (1/min)	21 (4.1)	31 (11)	< 0.01	**
VO_2 (mL/min/kg)	13 (2.6)	14 (3.0)	0.57	
BF Change (1/min)	4 (4.2)	10 (8.6)	0.21	
V_{tex} (L/min)	1.3 (0.4)	1.3 (0.4)	0.87	
HR (1/min)	121 (19)	116 (17)	0.65	
Dyspnoea (BORG CR10)	0.5 (0.5)†	4.0 (2.0)†	0.00	**
RPE (BORG CR10)	1.0 (1.5)†	3.0 (4.0)†	0.00	**
Stair Climb Time (Sec)	35.6 (9.0)	48.3 (21)	0.04	*

Numbers are mean (SD) unless otherwise stated. M:F: Male:Female; BMI: body mass index, VE: exhaled volume/ breath; BF: breathing frequency; VO_2: Oxygen consumption/min; V_{tex}: tidal volume; HR: heart rate; RPE: Rate of perceived exertion; SD: standard deviation, †Median (IQR),* P < 0.05, ** P < 0.01

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