



Ventilatory drive modulates the temporal evolution of multidimensional dyspnoea during constant-load exercise in healthy adults

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Abstract

How increased ventilatory drive shapes the temporal evolution and multidimensional experience of exertional dyspnoea remains incompletely understood. This study examined whether experimentally increasing ventilatory drive via dead-space loading (DSL) alters dyspnoea during constant-load exercise. Nine healthy adults (7 male; $\dot{V}O_{2\text{peak}}$ $100 \pm 16\%$ predicted) performed constant-load cycle ergometry to task failure at $50\%\Delta$ between the gas-exchange threshold and $\dot{V}O_{2\text{peak}}$ under control (CTRL) and DSL (15% vital capacity) conditions in a randomised crossover design. Dyspnoea intensity, dyspnoea unpleasantness, and leg discomfort were assessed using the Borg CR10 scale, and sensory-perceptual and affective-emotional dimensions using the Multidimensional Dyspnoea Profile. Compared with CTRL, DSL increased end-tidal CO_2 , minute ventilation, tidal volume, and inspiratory pressures without altering cardiometabolic responses, and reduced time to task failure (10.0 ± 2.3 vs. 13.8 ± 4.6 min; $p = .012$). Dyspnoea intensity rose more rapidly during DSL, but was similar at task failure, whereas dyspnoea unpleasantness was consistently higher without a distinct temporal divergence. Leg discomfort and dyspnoea descriptor frequencies did not differ between conditions. Post-exercise multidimensional profiling revealed greater breathing unpleasantness ($p = .008$), immediate perception scores ($p = .036$), respiratory work/effort ($p = .040$), and air hunger ($p = .027$), with no differences in emotional response scores. Greater iso-time increases in dyspnoea intensity and unpleasantness were associated with shorter time to task failure ($r = -.82$ to -0.88 ; $p \leq .007$). These findings suggest that increased ventilatory drive accelerates dyspnoea development and preferentially augments sensory-perceptual characteristics of dyspnoea, contributing to earlier task failure despite similar end-exercise symptom intensity.

Keywords Cycle ergometry · Exertional dyspnoea · Inspiratory muscle effort · Respiratory mechanics · Respiratory motor output · Ventilatory drive

Abbreviations

ANOVA Analysis of variance
CTRL Control
DSL Dead-space loading
 f_R Respiratory frequency

FVC Forced vital capacity
MDP Multidimensional Dyspnoea Profile
MVV Maximum voluntary ventilation
 $P_{\text{oe,exp}}$ End-expiratory oesophageal pressure
 $P_{\text{oe,insp}}$ End-inspiratory oesophageal pressure
 $P_{\text{oe,tidal}}$ Inspiratory tidal oesophageal pressure swing
 P_{ETCO_2} Partial pressure of end-tidal CO_2
 P_{Imax} Maximal inspiratory pressure
RER Respiratory exchange ratio
 S_{pO_2} Arterial oxyhaemoglobin saturation
 t_I/t_{TOT} Ratio of inspiratory time to total breath time
VC Vital capacity
 $\dot{V}_E$ Minute ventilation
 V_T Tidal volume
 $\dot{V}\text{CO}_2$ Carbon dioxide output

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VMR	Ventilatory muscle recruitment index
$\dot{V}O_2$	Oxygen uptake
V_T/t_I	Mean inspiratory flow

Introduction

Dyspnoea, or breathlessness, is a complex, multidimensional symptom that commonly arises during exercise (Parshall et al. 2012). In healthy individuals, exertional dyspnoea reflects an appropriate response to progressively increasing ventilatory demand, yet the mechanisms underlying its temporal development and contribution to exercise tolerance remain incompletely understood. Conceptual models distinguish between sensory-perceptual and affective-emotional dimensions of dyspnoea (Banzett et al. 2008; Lansing et al. 2009). The sensory-perceptual domain encompasses qualitative respiratory sensations such as work/effort, air hunger, and chest tightness, whereas the affective-emotional domain encompasses the unpleasantness associated with breathing and the subsequent emotional response evoked by the sensation. Evidence demonstrating partial dissociation between these dimensions highlights the limitations of unidimensional intensity scales and supports multidimensional assessment using instruments such as the Multidimensional Dyspnoea Profile (MDP) (Banzett et al. 2015; Ferguson et al. 2024, 2025; Williams et al. 2022). Characterising how these dimensions evolve throughout exercise is therefore important because end-exercise symptom ratings alone provide only limited insight into the temporal development of dyspnoea and its relationship with exercise tolerance.

Experimental manipulation of respiratory load or capacity has been widely used to investigate exertional dyspnoea. Load-increasing perturbations (e.g., resistive breathing and chest wall restriction) augment respiratory motor output (el-Manshawi et al. 1986; Mendonca et al. 2014), whereas load-reducing perturbations (e.g., mechanical ventilation and heliox) attenuate ventilatory demand (Harms et al. 2000; McClaran et al. 1999). Likewise, respiratory muscle training and experimentally induced respiratory muscle fatigue alter respiratory muscle capacity relative to ventilatory demand (Boyle et al. 2020; Ramsook et al. 2017). Interpretation of these perturbations is complicated, however, because they can also influence cardiovascular function and blood-flow distribution (Dominelli et al. 2017; Harms et al. 1997, 1998), making it difficult to isolate the perceptual consequences of changes in ventilatory drive.

Carbon dioxide loading provides a relatively drive-dominant perturbation in which chemoreceptor stimulation increases respiratory motor output and ventilation (Santin 2018). Dead-space loading (DSL), a practical approach to carbon dioxide loading, increases minute ventilation

primarily through increased tidal volume while imposing relatively little additional cardiometabolic stress (Jones et al. 1971; Kelman and Watson 1973; McClaran et al. 1999; McParland et al. 1991; Sackner et al. 1980; Ward and Whipp 1980). DSL also increases inspiratory pressure generation and dyspnoea intensity while largely preserving neuro-mechanical and neuro-ventilatory coupling (Jensen et al. 2011; O'Donnell et al. 2000), making it a useful model for investigating the perceptual consequences of increased ventilatory drive and respiratory motor output.

Despite these advantages, how increased ventilatory drive shapes the temporal evolution of dyspnoea and exercise tolerance remains incompletely understood. Previous incremental exercise studies using DSL have reported inconsistent effects on dyspnoea and exercise tolerance (Jensen et al. 2011; O'Donnell et al. 2000), possibly because differences in dead-space prescription contributed to inter-individual variability. Moreover, incremental exercise protocols combined with unidimensional symptom measures provide only limited insight into the temporal evolution and multidimensional experience of exertional dyspnoea. During incremental exercise, task failure may result from cardiovascular or locomotor limitations before dyspnoea becomes intolerable (Bassett and Howley 2000; Hamilton et al. 1996), potentially obscuring differences in the rate and pattern of symptom development. In contrast, constant-load exercise enables detailed characterisation of ventilatory, mechanical, and perceptual responses throughout exercise while permitting symptom comparisons at equivalent exercise durations. Recent work demonstrated that DSL progressively increased perceptions of breathing work/effort and unsatisfied inspiration or expiration during incremental exercise (Mitchell et al. 2026). However, its effects on the temporal evolution and multidimensional experience of dyspnoea during constant-load exercise remain unknown.

The aim of the present study was to determine how increased ventilatory drive influences the temporal evolution and multidimensional experience of exertional dyspnoea during severe constant-load cycle ergometry in healthy young adults. To address this aim, we combined DSL with serial assessments of dyspnoea intensity, dyspnoea unpleasantness, sensory descriptors, and post-exercise MDP responses to characterise the temporal evolution and multidimensional experience of dyspnoea during exercise. Although the respiratory system is not generally considered the primary limitation to exercise performance in healthy young adults, experimentally increasing ventilatory drive was expected to accelerate the development of dyspnoea and reduce exercise tolerance. Constant-load exercise allowed dyspnoea responses to be compared at equivalent exercise durations (iso-time), providing a basis for examining whether greater iso-time dyspnoea responses were

associated with earlier task failure. We therefore hypothesised that DSL would: (1) increase ventilatory drive and inspiratory pressure generation; (2) accelerate the temporal evolution of dyspnoea intensity and unpleasantness and augment the sensory-perceptual and affective-emotional dimensions of dyspnoea; and (3) reduce exercise tolerance, with greater iso-time dyspnoea intensity and unpleasantness associated with shorter time to task failure. As an exploratory secondary analysis, we examined whether the relationships between minute ventilation and dyspnoea intensity and unpleasantness differed between conditions to provide additional insight into the perceptual consequences of elevated ventilatory drive. Defining how increased ventilatory drive influences the development of exertional dyspnoea may improve understanding of the mechanisms by which respiratory loading contributes to exercise intolerance in health and respiratory disease.

Materials and methods

Compliance with ethical standards

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Brunel University of London Research Ethics Committee (45245-A-Jan/2024-4944-1). All participants provided written informed consent after receiving a detailed explanation of the study procedures and the associated risks and benefits.

Participants

Nine healthy adults (7 male) volunteered to participate. Inclusion criteria were: age 18–30 y; body mass index $< 25 \text{ kg} \cdot \text{m}^{-2}$; non-pregnant; nonsmoker; absence of injury, illness, or disease affecting cardiorespiratory or metabolic responses to exercise; engagement in $\geq 150 \text{ min/wk}$ of moderate-to-vigorous physical activity during the preceding 3 mo; normal pulmonary function, defined as forced expiratory volume in 1 s to forced vital capacity ratio (FEV_1/FVC) and total lung capacity (TLC) above lower limits of normal; no hypersensitivity to local anaesthetics or latex; and no nasal obstruction (e.g., congestion or deviated septum). Participants were instructed to abstain from strenuous exercise and alcohol for $> 24 \text{ h}$, caffeine for $> 12 \text{ h}$, and heavy meals for $> 3 \text{ h}$ before each laboratory visit.

Experimental design and overview

A randomised, controlled, crossover design was used. Participants attended the Human Performance Laboratory at Brunel University on three occasions, each separated by

2–7 d, with all visits scheduled at the same time of day to minimise circadian variation. Visit 1 included pulmonary function testing, maximal ramp-incremental cycle ergometry, and familiarisation with all perceptual and physiological procedures. Visits 2 and 3 consisted of constant-load cycle ergometry performed to task failure under control (CTRL) and dead-space loading (DSL) conditions. During the experimental trials, participants were instrumented with a gastro-oesophageal balloon catheter for measurement of inspiratory mechanical responses. Dyspnoea intensity, dyspnoea unpleasantness, and dyspnoea descriptors were assessed at rest and throughout exercise using the Borg CR10 scale, whereas multidimensional dyspnoea was evaluated post-exercise using the Multidimensional Dyspnoea Profile (MDP). All testing was conducted in a temperature-controlled laboratory (21°C).

Pulmonary function testing

Spirometry and multi-breath N_2 washout (Ultima PFX, Medical Graphics, Tewksbury, UK) were performed according to international recommendations (Bhakta et al. 2023; Graham et al. 2019). Maximal inspiratory and expiratory mouth pressures were measured at residual volume and total lung capacity, respectively, using a handheld manometer (MicroRPM, Carefusion, Hoechberg, Germany) following established procedures (Laveneziana et al. 2019). Pulmonary function values were expressed in absolute terms and relative to predicted values using published reference equations (Bowerman et al. 2023; Evans and Whitelaw 2009; Hall et al. 2021). Maximum voluntary ventilation (MVV) was estimated as $\text{FEV}_1 \times 40$.

Exercise testing procedures

All exercise testing was performed on a calibrated electromagnetically braked cycle ergometer (Excalibur Sport, Lode, Groningen, NL) operating in hyperbolic mode. Saddle and handlebar positions were standardised across visits. Each exercise session comprised $\sim 3 \text{ min}$ of seated rest (respiratory exchange ratio [RER] < 0.90), followed by 3 min of unloaded cycling (0 W) and either ramp-incremental or constant-load exercise. Participants breathed through a flanged mouthpiece incorporating a saliva trap and bidirectional Pitot-tube flow sensor while wearing a nose clip. During the experimental trials (Visits 2 and 3), a two-way non-rebreathing valve (model 2700; Hans Rudolph, USA) was incorporated into the breathing circuit. Cycling cadence was maintained between 70 and 80 rpm. Task failure was defined as a sustained reduction in cadence $> 15 \text{ rpm}$ despite standardised verbal encouragement. Following exercise, participants completed 3 min of active recovery at 25 W.

Ramp-incremental exercise and familiarisation (Visit 1). Ramp rate was determined by dividing the difference between estimated $\dot{V}O_2$ during unloaded cycling and predicted $\dot{V}O_{2peak}$ by the product of metabolic efficiency ($10.3 \text{ ml} \cdot \text{min}^{-1} \cdot \text{W}^{-1}$) and a target test duration of 10 min (Sietsema et al. 2020). The calculated ramp rate was $24 \pm 6 \text{ W} \cdot \text{min}^{-1}$, resulting in an actual exercise duration of $10.4 \pm 1.2 \text{ min}$. Within 3 min of completing the incremental test, participants completed the MDP for familiarisation. Following recovery, participants performed constant-load exercise at a work rate corresponding to 50% of the difference between gas-exchange threshold and $\dot{V}O_{2peak}$ ($50\% \Delta$). To account for the delayed $\dot{V}O_2$ response during ramp exercise, the target work rate was reduced by two-thirds of the ramp rate (Whipp et al. 1981). This work rate was selected to target the severe domain (Lansley et al. 2011). If exercise duration was $< 5 \text{ min}$, the work rate was reduced to achieve the desired exercise duration.

Experimental Trials (Visits 2 and 3). Following catheter placement, participants performed five maximal sniff manoeuvres from relaxation volume through a patent nostril to determine maximal inspiratory pressure (P_{Imax}) (Miller et al. 1985). After 3 min of seated rest, participants completed 3 min of unloaded cycling followed by an immediate square-wave transition to the target work rate. Symptom ratings were obtained at rest and every 60–90 s during exercise. Verbal encouragement was restricted to cadence maintenance.

Dead-space loading

External dead space was increased by inserting 35-mm internal diameter tubing between the mouthpiece and non-rebreathing valve, with the additional volume individually adjusted to 15% of each participant's FVC. This volume was added to a fixed apparatus dead space (168 ml). A dead-space volume equivalent to 15% of FVC was selected because previous studies using comparable dead-space loading have demonstrated increases in ventilation, inspiratory pressure generation, and dyspnoea during exercise while remaining well tolerated (Jensen et al. 2011; McClaran et al. 1999; McParland et al. 1991; Mitchell et al. 2026; O'Donnell et al. 2000). Scaling the dead-space volume relative to FVC standardised the perturbation to lung size, thereby reducing potential inter-individual variability associated with fixed-volume approaches. Under CTRL conditions, the valve was connected directly to the mouthpiece–flow sensor assembly, while identical lengths of tubing were attached to the inspiratory and expiratory valve ports to ensure comparable apparatus resistance without introducing additional dead space (Ward and Whipp 1980). The tubing was partially enclosed within a rigid foam sheath and suspended from an

overhead support to minimise mechanical interference during cycling. Inspiratory resistance was estimated during the final 30 s of exercise as the ratio of tidal inspiratory mouth pressure to mean inspiratory flow.

Pressure measurements

Oesophageal (P_{oc}) and gastric (P_{ga}) pressures were measured using a dual-balloon catheter system (Guangzhou Yinghui Medical Equipment Ltd., Guangzhou, China). Prior to insertion, the nasal mucosa was anaesthetised with 1 ml of 2% lidocaine hydrochloride. The catheter was inserted per nasally and advanced into the stomach via peristalsis. Each balloon was connected via short rigid tubing to a differential pressure transducer (DP45-3, Validyne Engineering, Northridge, CA, USA), calibrated across the physiological range before each test using a digital manometer (C9553, JMW, Harlow, UK). Following catheter insertion, both balloons were briefly deflated using a Valsalva manoeuvre and subsequently reinflated to standardised volumes (0.5 ml for the oesophageal balloon and 1.2 ml for the gastric balloon). The catheter was withdrawn until the proximal balloon was positioned within the oesophagus and the distal balloon within the stomach, verified by characteristic pressure responses during sniff manoeuvres. The catheter was secured at the nose using medical tape. Mouth pressure was measured via a port within the mouthpiece connected to a third differential pressure transducer (DP45-3). All analogue signals were amplified (CD280, Validyne), sampled at 200 Hz (PowerLab 16/30 model ML880; ADInstruments, Colorado Springs, CO, USA), and recorded using LabChart software (v7, ADInstruments).

Cardiometabolic and ventilatory assessment

Cardiometabolic and ventilatory variables were measured breath-by-breath using an online system (Ultima PFX, Medical Graphics, Tewksbury, UK) equipped with a bidirectional Pitot-tube flow sensor and paramagnetic O_2 and infrared CO_2 analysers. Variables included O_2 uptake ($\dot{V}O_2$), CO_2 output ($\dot{V}CO_2$), respiratory exchange ratio (RER), minute ventilation ($\dot{V}_E$), tidal volume (V_T), respiratory frequency (f_R), inspiratory duty cycle (t_I/t_{TOT}), mean inspiratory flow ($\dot{V}_T/t_I$), ventilatory equivalent for CO_2 ($\dot{V}_E/\dot{V}CO_2$), and end-tidal CO_2 partial pressure (P_{ETCO_2}). The flow sensor and gas analysers were calibrated immediately before each test according to manufacturer specifications. Arterial oxyhaemoglobin saturation (S_pO_2) and heart rate were continuously assessed using finger pulse oximetry (7500, Nonin, MN, USA) and telemetry (HxM, Zephyr, MD, USA), respectively. Gas-exchange threshold was identified using established criteria (Beaver et al. 1986; Caiozzo et al. 1982), and

$\dot{V}O_{2\text{peak}}$ was defined as the highest 30-s mean $\dot{V}O_2$ attained during the incremental test. Gas-exchange threshold and $\dot{V}O_{2\text{peak}}$ were expressed relative to values derived from published reference equations (Gläser et al. 2013), with age fixed at 25 y for participants younger than 25 y.

Symptom evaluation

During the final minute of rest, the final minute of unloaded cycling, and at one-minute intervals during constant-load exercise, participants rated dyspnoea intensity, dyspnoea unpleasantness, and leg discomfort using Borg's modified category-ratio scale (CR10; Borg 1998). Standardised instructions were used to distinguish ratings of: (i) dyspnoea intensity ("how intense or strong is your breathing discomfort?"), (ii) dyspnoea unpleasantness ("how unpleasant or distressing is your breathing?"), and (iii) leg discomfort ("how intense is your leg discomfort?"). The distinction between intensity and unpleasantness was explained using the "radio analogy", contrasting loudness with disagreeableness (Banzett et al. 2015). Scale anchors were defined as 0 ("no sensation") and 10 ("the most intense sensation imaginable or ever experienced").

At each time point, participants identified the most prominent dyspnoea descriptor relative to rest from the following options: (1) "my breathing requires more work and effort", (2) "I cannot get enough air in", (3) "I cannot get enough air out", or (4) "none apply" (Cory et al. 2015). Multiple selections were permitted when descriptors were considered equally applicable. The unsatisfied expiration descriptor was included primarily as a control descriptor.

Immediately following exercise cessation, participants identified the primary reason(s) for stopping exercise (breathing discomfort, leg discomfort, both, or other) and apportioned the relative contribution of breathing and leg discomfort to exercise termination as percentages summing to 100%. After 3 min of recovery, participants completed the MDP (Banzett et al. 2015), focusing on sensations experienced during the final moments of exercise. The MDP comprises 11 numerical rating items (0–10 scale), comprising five sensory quality items, one overall unpleasantness/discomfort item, and five affective-emotional items, together with five binary sensory descriptors. The questionnaire was self-administered and typically completed within 2 min. The validity, reliability, and responsiveness of the MDP for assessing exercise-related dyspnoea have been established (Williams et al. 2022; Zhang et al. 2020).

Data analysis

Maximal sniff oesophageal pressure was used as an index of maximal inspiratory pressure (P_{Imax}). Inspiratory and

expiratory oesophageal pressures were defined as peak oesophageal pressure during tidal inspiration ($P_{\text{oe, insp}}$) and expiration ($P_{\text{oe, exp}}$), respectively. Inspiratory tidal pressure swing ($P_{\text{oe, tidal}}$) was calculated as $P_{\text{oe, insp}} - P_{\text{oe, exp}}$ and expressed relative to P_{Imax} . Mechanical-ventilatory efficiency was quantified using the $P_{\text{oe, tidal}}/P_{\text{Imax}} : V_T/VC$ ratio, whereby higher values reflected reduced mechanical-ventilatory efficiency. Ventilatory muscle recruitment (VMR) was calculated as $(P_{\text{ga, insp}} - P_{\text{ga, exp}})/(P_{\text{oe, insp}} - P_{\text{oe, exp}})$, with more negative values indicating greater diaphragmatic contribution to inspiratory pressure generation (Martinez et al. 1990). Cardiometabolic, ventilatory, and pressure variables were averaged over the 30 s immediately preceding symptom assessment. Analyses were performed at rest (0 min), during minutes 1–6 of exercise, at iso-time (defined as the highest equivalent exercise time achieved under both conditions for each participant), and at task failure. For the MDP, item scores were averaged to generate sensory and affective domain scores. Responses were further summarised as: (i) the overall unpleasantness/discomfort score (A1); (ii) the immediate perception domain score, calculated as the mean of A1 and five sensory quality items (SQ); and (iii) the emotional response domain score, calculated as the mean of the five affective-emotional items (A2) (Banzett et al. 2015). Binary sensory descriptors were expressed as the percentage of trials in which each descriptor was selected.

Statistical analysis

Sample size estimation was performed using G*Power (v3.1.9.6; Faul et al. 2007) based on a paired-samples comparison of dyspnoea intensity between conditions at a standardised submaximal workload. Assuming an effect size of 1.2 (O'Donnell et al. 2000), $\alpha=0.05$, and power $(1-\beta)=0.80$, a minimum sample size of eight participants was required. Nine participants were recruited to accommodate potential attrition or missing data.

Statistical analyses were performed using SPSS (v29.0; IBM Corp., Armonk, NY, USA) and Python (v3.10). Normality was assessed using the Shapiro–Wilk test. Paired-samples *t*-tests were used to compare conditions at rest, iso-time, and task failure. Two-way repeated-measures ANOVA was used to evaluate the effects of condition (DSL vs. CTRL) and time (minutes 1–6), with Greenhouse–Geisser ($\epsilon \leq 0.75$) or Huynh–Feldt ($\epsilon > 0.75$) corrections applied where appropriate. Post-hoc comparisons were adjusted using the Benjamini–Hochberg false-discovery-rate procedure (Curran–Everett 2000). Effect sizes for

ANOVA were expressed as partial eta squared (η_p^2) (Cohen 1988). Dyspnoea descriptor frequencies were analysed using McNemar's mid-*p* test with false-discovery-rate correction

Table 1 Participant characteristics

	Measured value	Percent predicted
<i>Anthropometrics and cardiorespiratory fitness</i>		
Age (y)	26±11	
Stature (m)	1.74±0.11	
Body mass (kg)	71±14	
Body mass index (kg/m ²)	23.3±3.9	
PPO (W)	218±51	109±19
$\dot{V}O_{2peak}$ (L/min)	2.71±0.53	100±16
GET (L/min)	1.68±0.38	131±18
<i>Pulmonary function</i>		
FVC (L)	5.27±1.28	112±15
FEV ₁ (L)	4.38±1.19	109±14
FEV ₁ /FVC	0.83±0.08	97±8
TLC mb (L)	7.49±2.16	114±19
VC (L)	5.17±1.21	103±14
IC mb (L)	3.53±0.75	108±16
FRC mb (L)	3.96±1.62	123±34
ERV (L)	1.58±0.59	95±21
RV mb (L)	2.32±1.24	157±68
RV/TLC (%)	30±9	134±39
MVV (L/min)	175±47	109±14
MIP (cmH ₂ O)	-116±30	110±31
MEP (cmH ₂ O)	127±52	91±40

Values are means±SD for 9 participants (7 M, 2 F). Abbreviations: PPO, peak power output; $\dot{V}O_{2peak}$, peak oxygen uptake; GET, gas-exchange threshold; FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 s; TLC, total lung capacity; mb, multi-breath nitrogen washout; VC, vital capacity; IC, inspiratory capacity; FRC, functional residual capacity; ERV, expiratory reserve volume; RV, residual volume; MVV, maximum voluntary ventilation (FEV₁ × 40); MIP, maximal inspiratory mouth pressure; MEP, maximal expiratory mouth pressure. Reference values for exercise: Gläser et al. (2013). Reference values for pulmonary function: Bowerman et al. (2023), Hall et al. (2021), Evans and Whitelaw (2009)

(Fagerland et al. 2013). Differences in the reported reason for exercise termination between conditions were evaluated using an exact Bowker test of symmetry for paired categorical data. MDP outcomes were compared using paired-samples *t*-tests. Associations between the between-condition difference in exercise time to task failure and physiological or perceptual variables were assessed using Pearson product-moment correlations, with corresponding 95% confidence intervals (CI) calculated using Fisher's *z* transformation. As an exploratory secondary analysis, linear mixed-effects models were fitted to examine whether the associations between minute ventilation and dyspnoea intensity and unpleasantness differed between conditions. Minute ventilation, condition, and the ventilation × condition interaction were specified as fixed effects, with participant included as a random intercept to account for repeated measures. Data are presented as mean±SD. Statistical significance was accepted at *p* < .05 (two-tailed).

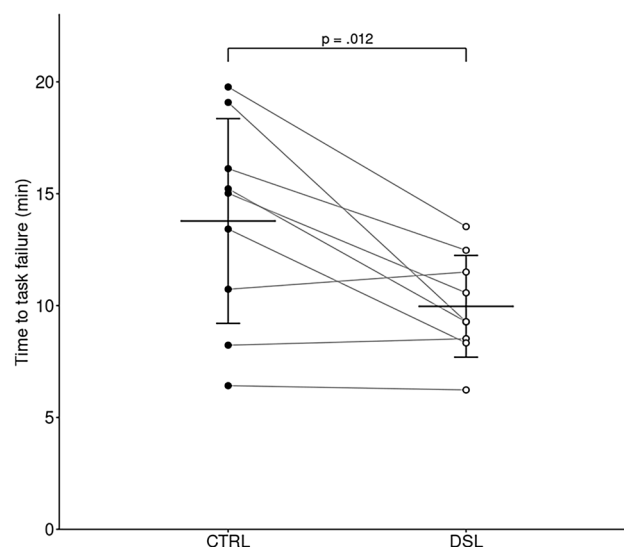


Fig. 1 Time to task failure during constant-load cycle ergometry under control (CTRL) and dead-space loading (DSL). Individual participant responses (*n*=9) are shown as points connected by lines. Group data are presented as mean±SD (horizontal bars and whiskers). Exercise time to task failure was significantly shorter during DSL compared with CTRL

Results

Participants

Participant characteristics are shown in Table 1. The cohort comprised young healthy adults with normal pulmonary function and aerobic capacity. Peak $\dot{V}O_2$ and peak power output during incremental exercise were numerically higher than predicted but did not differ significantly from predicted values (both *p* > .05). Gas-exchange threshold occurred at 63±9% peak $\dot{V}O_2$, with $\dot{V}O_2$ at threshold exceeding predicted values (*p* < .001). Peak responses included an RER of 1.21±0.10, $\dot{V}_E$ of 102±18 L·min⁻¹ (61±16% estimated MVV), S_pO_2 of 97±1%, and heart rate of 179±13 beats·min⁻¹ (97±9% predicted).

Exercise tolerance

Exercise intensity during constant-load exercise was identical between conditions (157±27 W; 68±3% peak power output). Despite identical exercise intensity, time to task failure was significantly shorter during DSL than CTRL (10.0±2.3 vs. 13.8±4.6 min; *p* = .012), representing a mean reduction of 3.8±3.5 min (−23±21%; range: +7 to −51%). Time to task failure was shorter during DSL in seven of the nine participants (Fig. 1).

Cardiometabolic and ventilatory responses

Cardiometabolic and ventilatory responses at rest, iso-time, and task failure are presented in Table 2, with temporal profiles shown in Fig. 2 (A–D) and omnibus ANOVA results provided in Table S1 (Online Resource 1). Relative to CTRL, DSL increased P_{ETCO_2} and $\dot{V}_E$ at rest, iso-time, and task failure. Across minutes 1–6, P_{ETCO_2} was higher throughout DSL, with between-condition differences evident from minute 2 onwards. Ventilation increased progressively in both conditions but was higher throughout DSL, with the temporal profile differing between conditions. The greater ventilatory response during DSL was attributable primarily to higher V_T , which remained higher throughout exercise while exhibiting a broadly similar temporal trajectory between conditions. Respiratory frequency increased progressively in both conditions and was modestly higher during DSL, with a similar temporal trajectory between conditions. Consistent with these ventilatory responses, mean inspiratory flow (V_T/t_I) and ventilatory demand ($\dot{V}_E/\dot{V}_{\text{CO}_2}$) were higher during DSL. In contrast, no meaningful main or interaction effects were observed for t_I/t_{TOT} , $\dot{V}_{\text{O}_2}$, $\dot{V}_{\text{CO}_2}$, RER, $S_p\text{O}_2$, or heart rate.

Inspiratory mechanical responses

Inspiratory mechanical responses are shown in Table 3; Fig. 2 (E–F), with omnibus ANOVA results shown in Table S1 (Online Resource 1). Respiratory pressure data from one female participant were excluded due to signal artefact. DSL increased the magnitude of inspiratory pressure generation during exercise, as indicated by greater inspiratory $P_{\text{oe, tidal}}$

and higher $\%P_{\text{Imax}}$. End-inspiratory P_{oe} was more negative during DSL across all time points, whereas end-expiratory P_{oe} was more positive during exercise but not at rest. Across minutes 1–6, inspiratory pressure generation increased progressively over time and was higher during DSL, with no evidence of a condition $\times$ time interaction. A similar pattern was observed for the mechanical-ventilatory efficiency index ($P_{\text{oe, tidal}}/P_{\text{Imax}} : V_T/VC$), which was higher during DSL, with no evidence of a condition $\times$ time interaction. The $P_{\text{oe, tidal}}/V_T$ ratio was more negative during DSL than CTRL at iso-time only, with no difference at task failure. The VMR index was negative in both conditions and became progressively less negative over time, without meaningful between-condition differences. Total inspiratory resistance did not differ between DSL and CTRL (0.50 ± 0.12 vs. 0.46 ± 0.09 $\text{cmH}_2\text{O} \cdot \text{L}^{-1} \cdot \text{s}^{-1}$; $p = .370$).

Perceptual responses during exercise

Temporal perceptual responses are shown in Fig. 3, with omnibus ANOVA results provided in Table S1 (Online Resource 1). Dyspnoea intensity increased progressively throughout exercise in both conditions but rose more rapidly during DSL, with the temporal profile diverging from minute 3 onwards. Across minutes 1–6, dyspnoea intensity was higher overall during DSL, with between-condition differences emerging from minute 3 onwards. At discrete time points, dyspnoea intensity was numerically higher during DSL at rest (mean difference 0.61 ± 0.82 , $p = .056$) and iso-time (1.67 ± 2.18 , $p = .051$), although neither comparison reached statistical significance. No difference was evident at task failure (0.22 ± 1.30 , $p = .622$), despite the shorter

Table 2 Effects of dead-space loading on cardiometabolic and ventilatory responses at discrete time points during constant-load exercise

Variable	Rest			Iso-time			Task failure		
	CTRL	DSL	<i>p</i> -value	CTRL	DSL	<i>p</i> -value	CTRL	DSL	<i>p</i> -value
Time (min)	–	–	–	8.8 $\pm$ 2.3	8.8 $\pm$ 2.3	–	13.8 $\pm$ 4.6	10.0 $\pm$ 2.3	0.012
$\dot{V}_{\text{O}_2}$ (L/min)	0.41 $\pm$ 0.10	0.46 $\pm$ 0.16	0.384	2.54 $\pm$ 0.49	2.61 $\pm$ 0.54	0.179	2.52 $\pm$ 0.50	2.61 $\pm$ 0.55	0.279
$\dot{V}_{\text{CO}_2}$ (L/min)	0.33 $\pm$ 0.08	0.34 $\pm$ 0.14	0.906	2.49 $\pm$ 0.45	2.60 $\pm$ 0.47	0.126	2.48 $\pm$ 0.45	2.56 $\pm$ 0.44	0.302
RER	0.82 $\pm$ 0.12	0.73 $\pm$ 0.09	0.060	0.96 $\pm$ 0.06	1.00 $\pm$ 0.06	0.100	0.94 $\pm$ 0.07	1.00 $\pm$ 0.06	0.065
$\dot{V}_E$ (L/min)	13 $\pm$ 3	24 $\pm$ 6	0.003	83 $\pm$ 14	116 $\pm$ 21	<0.001	90 $\pm$ 13	115 $\pm$ 21	<0.001
$\dot{V}_E/\text{MVV}$ (%)	8 $\pm$ 2	14 $\pm$ 4	0.004	49 $\pm$ 8	68 $\pm$ 14	<0.001	54 $\pm$ 10	68 $\pm$ 14	<0.001
V_T (L)	1.02 $\pm$ 0.29	1.89 $\pm$ 0.5	0.002	2.28 $\pm$ 0.43	2.81 $\pm$ 0.64	0.003	2.09 $\pm$ 0.51	2.77 $\pm$ 0.62	<0.001
f_R (breaths/min)	13.6 $\pm$ 2.1	13.2 $\pm$ 3.9	0.720	37.7 $\pm$ 5.5	42.2 $\pm$ 8.8	0.070	45.0 $\pm$ 11.9	42.6 $\pm$ 8.6	0.104
t_I/t_{TOT}	0.30 $\pm$ 0.04	0.29 $\pm$ 0.03	0.461	0.37 $\pm$ 0.02	0.37 $\pm$ 0.02	0.845	0.37 $\pm$ 0.01	0.36 $\pm$ 0.02	0.164
V_T/t_I (L/s)	0.75 $\pm$ 0.14	1.37 $\pm$ 0.31	0.002	3.74 $\pm$ 0.68	5.22 $\pm$ 0.83	<0.001	3.98 $\pm$ 0.64	5.23 $\pm$ 0.85	<0.001
$\dot{V}_E/\dot{V}_{\text{CO}_2}$	41.5 $\pm$ 4.7	76.3 $\pm$ 21.1	0.001	33.4 $\pm$ 4.0	44.9 $\pm$ 5.8	<0.001	36.9 $\pm$ 5.6	45.2 $\pm$ 5.5	<0.001
P_{ETCO_2} (mmHg)	35.5 $\pm$ 4.1	40.2 $\pm$ 4.4	0.010	36.6 $\pm$ 4.1	43.0 $\pm$ 3.6	0.004	34.1 $\pm$ 3.9	43.1 $\pm$ 3.8	<0.001
$S_p\text{O}_2$ (%)	98 $\pm$ 1	96 $\pm$ 2	0.069	96 $\pm$ 1	94 $\pm$ 6	0.191	95 $\pm$ 3	94 $\pm$ 6	0.491
Heart rate (beats/min)	82 $\pm$ 11	82 $\pm$ 11	0.865	175 $\pm$ 13	174 $\pm$ 14	0.494	176 $\pm$ 12	174 $\pm$ 14	0.116

Values are means $\pm$ SD for 9 participants. Abbreviations: CTRL, control condition; DSL, dead-space loading condition; $\dot{V}_{\text{O}_2}$, oxygen uptake; $\dot{V}_{\text{CO}_2}$, carbon dioxide output; RER, respiratory exchange ratio; $\dot{V}_E$, minute ventilation; MVV, estimated maximal voluntary ventilation; V_T , tidal volume; f_R , respiratory frequency; t_I/t_{TOT} , inspiratory duty cycle; V_T/t_I , mean inspiratory flow; P_{ETCO_2} , partial pressure of end-tidal CO_2 ; $S_p\text{O}_2$, oxyhaemoglobin saturation. Values in bold represent significant difference vs. CTRL at respective time point ($p < .05$; paired *t*-test)

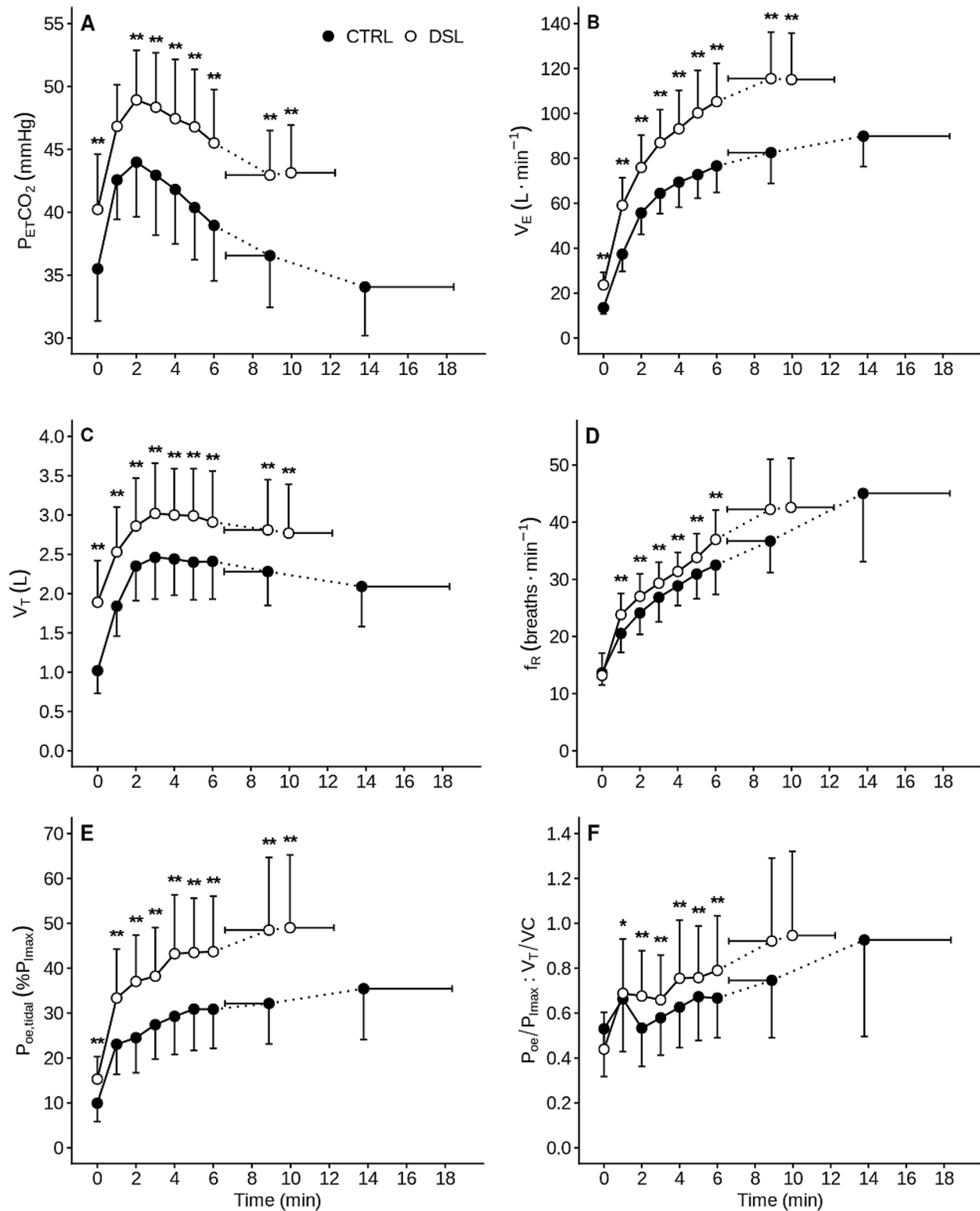


Fig. 2 Ventilatory and inspiratory mechanical responses during constant-load cycle ergometry under control (CTRL) and dead-space loading (DSL). Variables are shown at rest (0 min), during minutes 1–6 of exercise, at iso-time, and at task failure: end-tidal CO_2 partial pressure ($P_{\text{ET-CO}_2}$) (A), minute ventilation ($\dot{V}_E$) (B), tidal volume (V_T)

(C), respiratory frequency (f_R) (D), inspiratory tidal oesophageal pressure swing ($P_{\text{oe, tidal}}$) (E), and mechanical-ventilatory efficiency index ($P_{\text{oe, tidal}}/P_{\text{Imax}} : V_T/VC$) (F). Data are presented as mean $\pm$ SD for 9 participants in panels A–D and 8 participants in panels E–F. * $p < .05$, ** $p < .01$ vs. CTRL at the corresponding time point

Table 3 Effects of dead-space loading on respiratory mechanical responses at discrete time points during constant-load exercise

Variable	Rest			Iso-time			Task failure		
	CTRL	DSL	<i>p</i> -value	CTRL	DSL	<i>p</i> -value	CTRL	DSL	<i>p</i> -value
$P_{oe, insp}$ (cmH ₂ O)	-11.4±3.9	-14.5±2.5	0.047	-21.2±4.9	-25.6±4.5	0.001	-21.7±5.1	-25.8±4.5	<0.001
$P_{oe, exp}$ (cmH ₂ O)	-4.2±2.5	-3.4±1.7	0.246	2.4±3.3	10.0±6.1	0.004	4.3±4.9	10.2±6.0	0.001
$P_{oe, tidal}$ (cmH ₂ O)	-7.2±2.2	-11.1±1.7	0.001	-23.5±2.7	-35.6±7.3	0.001	-26.0±4.5	-36.0±7.1	<0.001
$P_{oe, tidal}$ (% $P_{I_{max}}$)	9.9±4.1	15.3±5.0	0.004	32.1±9.0	48.5±16.2	0.004	35.4±11.3	49.0±16.2	<0.001
$P_{oe, tidal}/V_T$ (cmH ₂ O/L)	-7.8±2.9	-6.5±2.7	0.279	-10.6±2.8	-13.3±4.7	0.044	-13.3±5.1	-13.6±4.6	0.676
$P_{oe, tidal}/P_{I_{max}} : V_T/VC$	0.53±0.21	0.44±0.17	0.316	0.75±0.26	0.92±0.37	0.077	0.93±0.43	0.95±0.38	0.676
VMR index	-0.93±0.46	-0.92±0.36	0.933	-0.49±0.12	-0.57±0.18	0.127	-0.54±0.19	-0.57±0.18	0.429

Values are means±SD for 8 participants. Abbreviations: CTRL, control condition; DSL, dead-space loading condition; $P_{oe, insp}$, end-inspiratory oesophageal pressure; $P_{oe, exp}$, end-expiratory oesophageal pressure; $P_{oe, tidal}$, inspiratory tidal oesophageal pressure swing; $P_{I_{max}}$, maximal inspiratory (oesophageal) pressure; VC, vital capacity; VMR index, ventilatory muscle recruitment index. Values in bold represent significant difference vs. CTRL at respective time point ($p < .05$; paired *t*-test)

exercise duration during DSL. Dyspnoea unpleasantness also increased progressively during exercise and was higher overall during DSL; however, the temporal trajectory of dyspnoea unpleasantness was similar between conditions, with no evidence of a condition time interaction. At discrete time points, unpleasantness did not differ between DSL and CTRL (rest: 0.44 ± 1.36 , $p = .354$; iso-time: 1.50 ± 2.72 , $p = .136$; or task failure: -0.06 ± 1.78 , $p = .928$). Leg discomfort likewise did not differ between conditions (rest: -0.22 ± 0.44 , $p = .169$; iso-time: 0.89 ± 2.15 , $p = .249$; task failure: -0.78 ± 1.30 , $p = .111$), and the temporal trajectory was comparable between conditions.

Ventilation–dyspnoea relationships

Exploratory linear mixed-effects modelling demonstrated that minute ventilation was strongly associated with dyspnoea intensity and dyspnoea unpleasantness (both $p < .001$; Fig. S1). For dyspnoea intensity, neither a main effect of condition ($p = .192$) nor a significant ventilation × condition interaction ($p = .062$) was observed, providing no evidence that the ventilation-dyspnoea relationship differed between conditions. In contrast, although no main effect of condition was evident for dyspnoea unpleasantness ($p = .385$), a significant ventilation × condition interaction was observed ($p = .015$), indicating that dyspnoea unpleasantness increased more steeply with increasing minute ventilation during DSL than CTRL.

Dyspnoea descriptors during exercise

Dyspnoea descriptor selection frequencies are shown in Fig. 4. The qualitative profile of dyspnoea varied over time in both conditions, with broadly similar patterns but a greater numerical prevalence of “I cannot get enough air in” during DSL. The descriptor “my breathing requires more work and effort” was generally the most frequently selected descriptor during exercise in both conditions. Sensations consistent

with unsatisfied inspiration (“I cannot get enough air in”) were numerically more prevalent at earlier time points and more frequently selected during DSL, whereas this descriptor was selected less commonly during CTRL. Reports of expiratory difficulty (“I cannot get enough air out”) were infrequent in both conditions. Despite these numerical differences, no between-condition differences in descriptor selection frequencies were observed at any time point (all adjusted mid- $p > .05$).

Perceived reasons for exercise termination

Perceived reasons for task failure showed different descriptive patterns between conditions (Fig. 5). During CTRL, task failure was attributed predominantly to leg discomfort alone (67%), with the remaining 33% reporting combined contributions from leg and breathing discomfort. During DSL, responses were distributed across leg discomfort (56%), breathing discomfort (33%), and combined contributions (11%). Although these descriptive patterns suggested a greater perceived contribution of respiratory factors during DSL, the distribution of reported reasons for task failure did not differ significantly between conditions (exact Bowker test, $p = .500$). Ratings of the relative attribution of breathing and leg discomfort to exercise termination were consistent with this descriptive pattern. During CTRL, participants attributed a greater proportion of limitation to leg discomfort than breathing discomfort (68 ± 16 vs. $32 \pm 16\%$, $p = .010$), whereas contributions were more balanced during DSL (54 ± 17 vs. $46 \pm 17\%$, $p = .523$). Between-condition comparisons of these relative attributions did not reach statistical significance (both $p = .051$).

Multidimensional components of dyspnoea at task failure

Multidimensional Dyspnoea Profile responses are presented in Fig. 6. At the item level, DSL increased ratings for “my

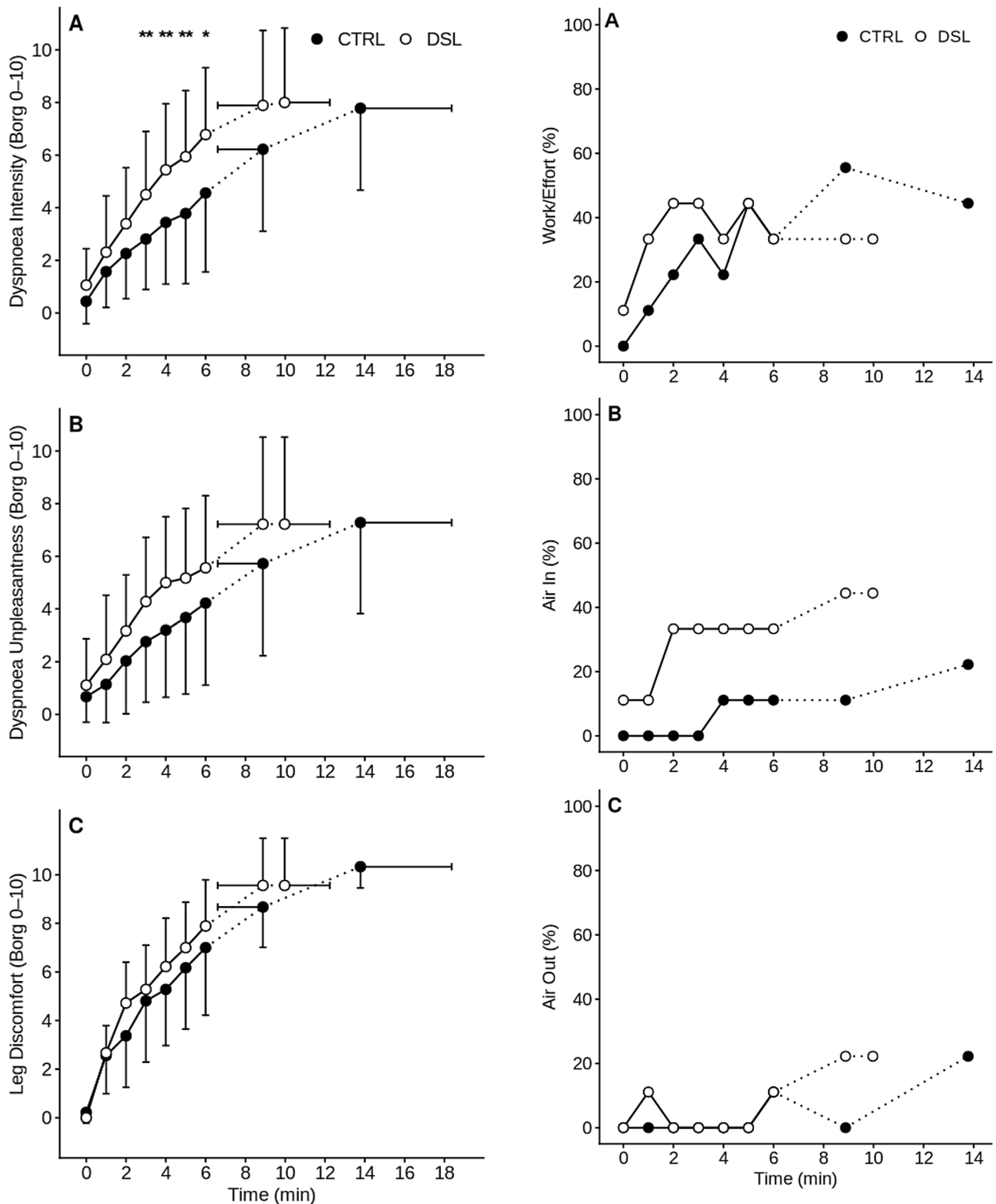


Fig. 3 Perceptual responses during constant-load exercise under control (CTRL) and dead-space loading (DSL). Dyspnoea intensity (A), dyspnoea unpleasantness (B), and leg discomfort (C) are shown at rest (0 W), during minutes 1–6 of exercise, at iso-time, and at task failure. Data are presented as mean $\pm$ SD for 9 participants. * $p < .05$, ** $p < .01$, vs. CTRL at the corresponding time point

breathing requires muscle work or effort" (6.4 ± 2.1 vs. 5.3 ± 2.3 , $p = .040$) and "I am smothering or I feel hunger for air" (5.2 ± 2.5 vs. 3.3 ± 2.7 , $p = .027$). Ratings for "I am breathing a lot" were numerically higher during DSL but did not differ significantly

Fig. 4 Selection frequency (%) of the most prominent dyspnoea descriptors during constant-load cycle ergometry under control (CTRL) and dead-space loading (DSL). Panels show the percentage of participants selecting: “my breathing requires more work and effort” (A), “I cannot get enough air in” (B), and “I cannot get enough air out” (C). Data are presented descriptively for 9 participants at rest (0 min), during minutes 1–6 of exercise, at iso-time, and at task failure. Statistical comparisons were performed on the underlying frequency counts and revealed no significant between-condition differences at any time point (all adjusted mid- $p > .05$)

between conditions (7.6 ± 1.8 vs. 6.6 ± 1.9 , $p = .053$). Selection frequencies for the sensory-quality items did not differ between conditions. No between-condition differences were observed for individual affective-emotional items or for the overall emotional-response domain score. Nevertheless, breathing unpleasantness/discomfort was higher during DSL (6.8 ± 2.0 vs. 5.1 ± 1.8 , $p = .008$), accompanied by a higher immediate-perception domain score (5.6 ± 1.5 vs. 4.5 ± 1.8 , $p = .036$). Overall, DSL augmented sensory-perceptual responses, whereas affective-emotional responses were largely unchanged.

Correlates of exercise performance

Greater increases in dyspnoea intensity and unpleasantness at iso-time (DSL v. CTRL) were associated with shorter time to task failure when expressed in either absolute terms (dyspnoea intensity: $r = -.82$, 95% CI -0.96 to -0.34 , $p = .007$; dyspnoea unpleasantness: $r = -.88$, 95% CI -0.97 to -0.52 , $p = .002$; Fig. 7) or relative terms (dyspnoea intensity: $r = -.87$, 95% CI -0.97 to -0.49 , $p = .003$; dyspnoea unpleasantness: $r = -.82$, 95% CI -0.96 to -0.34 , $p = .007$). Changes in dyspnoea intensity and unpleasantness were also strongly related ($r = .86$, 95% CI 0.46 to 0.97 ; $p = .003$). In contrast, changes in leg discomfort and MDP outcomes were not significantly associated with time to task failure (all $p > .15$). Among the physiological indices, only changes in $P_{ET}CO_2$ were significantly associated with a perceptual measure, demonstrating an inverse relationship with changes in MDP-derived breathing unpleasantness ($r = -.77$, 95% CI -0.95 to -0.22 , $p = .016$).

Discussion

The present study showed that DSL elicited physiological responses consistent with increased ventilatory drive, accelerated the temporal evolution of dyspnoea, preferentially augmented sensory-perceptual characteristics, and reduced exercise tolerance during constant-load exercise in healthy young adults. Dyspnoea intensity diverged during the middle stages of exercise but did not differ at task failure, despite a markedly shorter time to task failure during DSL,

indicating that the trajectory of dyspnoea development provides a more informative marker of exercise tolerance than conventional end-exercise symptom ratings. Although dyspnoea unpleasantness was also higher overall, its temporal profile differed from that of dyspnoea intensity, and multidimensional profiling suggested selective amplification of sensory-perceptual components without parallel increases in affective-emotional responses. Together, these findings provide insight into how increased ventilatory drive shapes the multidimensional experience of dyspnoea and contributes to exercise tolerance.

Dyspnoea time course and multidimensional responses

A principal finding was that DSL altered the temporal profile of dyspnoea during exercise. Dyspnoea intensity increased more rapidly during DSL, diverging during the middle stages of exercise but not differing at task failure. This dissociation between the rate of symptom accumulation and end-exercise symptom magnitude demonstrates that similar end-exercise ratings can arise from markedly different trajectories of symptom development. The present findings therefore extend previous incremental exercise studies (Jensen et al. 2011; O'Donnell et al. 2000) by demonstrating that increased ventilatory drive alters not only the magnitude of dyspnoea, but also its temporal evolution during constant-load exercise.

Although dyspnoea unpleasantness was higher overall during DSL, it did not exhibit the same condition-dependent temporal divergence observed for dyspnoea intensity. Instead, its temporal profile was broadly similar between conditions despite higher ratings throughout exercise during DSL. This distinction highlights the multidimensional nature of dyspnoea and suggests that different dimensions of the symptom may not respond identically to increased ventilatory drive during exercise. Consistent with this interpretation, post-exercise MDP assessment demonstrated greater breathing unpleasantness, higher immediate perception domain scores, and increased ratings of respiratory effort and air hunger during DSL, whereas affective-emotional responses were unchanged. These findings are consistent with contemporary models proposing partial dissociation between sensory-perceptual and affective-emotional dimensions of dyspnoea (Banzett et al. 2008; Lansing et al. 2009; Mitchell et al. 2025).

Despite greater dyspnoea during DSL, the qualitative profile of respiratory sensations was broadly similar between conditions. Work/effort remained the dominant descriptor throughout exercise, although sensations consistent with unsatisfied inspiration were reported earlier and more frequently during DSL. Descriptor selection frequencies did

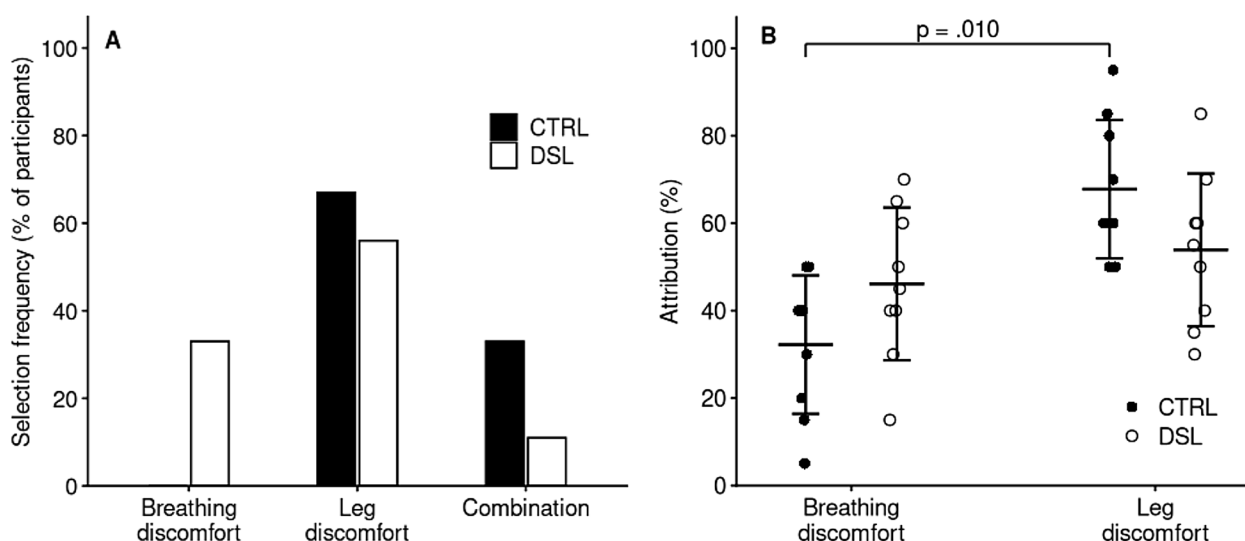


Fig. 5 Reported reasons for exercise termination during constant-load cycle ergometry under control (CTRL) and dead-space loading (DSL). **Panel A** shows the selection frequency for reported reasons for exercise termination. **Panel B** shows the relative attribution of breathing

discomfort and leg discomfort to exercise termination. The bracket indicates a significant within-condition difference between breathing and leg discomfort attribution in CTRL only. Data in panel B are presented as mean ± SD for 9 participants

not differ significantly between conditions, although the modest sample size limits confidence in the absence of genuine condition-related differences. The relative preservation of the qualitative descriptor profile, despite greater overall dyspnoea and selective increases in MDP ratings for respiratory effort and air hunger, suggests that increased ventilatory drive may primarily amplify the intensity of existing respiratory sensations rather than fundamentally alter the qualitative character of those sensations. Taken together, these findings indicate that increased ventilatory drive primarily modified the intensity and temporal expression of established respiratory sensations, with less evidence for a fundamental alteration in the qualitative or affective-emotional character of dyspnoea.

Perceptual correlates of exercise tolerance

A central observation was the strong association between changes in dyspnoea and exercise tolerance. Larger increases in iso-time dyspnoea intensity and unpleasantness were associated with earlier task failure. The corresponding coefficients of determination indicate that these associations accounted for approximately two-thirds to three-quarters of the variance in time to task failure, although these estimates should be interpreted cautiously given the modest sample size and exploratory nature of the correlational analyses. The strength of the associations suggests that individual differences in the perceptual response to increased ventilatory drive may be relevant to the extent of exercise intolerance produced by DSL.

The reported reasons for exercise termination provided additional, although descriptive, insight into the perceptual responses to DSL. Under control conditions, task failure was attributed predominantly to leg discomfort, whereas respiratory factors were more prominent among the reported reasons for exercise termination during DSL. Similarly, participants attributed a greater proportion of exercise termination to leg discomfort than breathing discomfort under control conditions, whereas these contributions were more balanced during DSL. However, neither the categorical distribution of reported reasons for termination nor the relative attribution ratings differed statistically between conditions. Thus, these findings provide descriptive evidence of a greater perceived respiratory contribution to exercise termination during DSL but should be interpreted cautiously given the modest sample size.

Although increased respiratory muscle work may impair locomotor performance through activation of a respiratory muscle metaboreflex (Dominelli et al. 2019; Harms et al. 1997, 2000; Romer et al. 2006), the present findings provide limited support for this mechanism as the dominant explanation for reduced exercise tolerance. Leg discomfort did not differ between conditions, and changes in leg discomfort were not significantly associated with time to task failure. Moreover, substantial ventilatory reserve remained during DSL, making critical ventilatory constraint an unlikely explanation for task failure. Instead, the strong associations between changes in dyspnoea and time to task failure, together with the earlier development of dyspnoea during DSL, support dyspnoea as the prominent perceptual correlate of the reduction in exercise tolerance. This

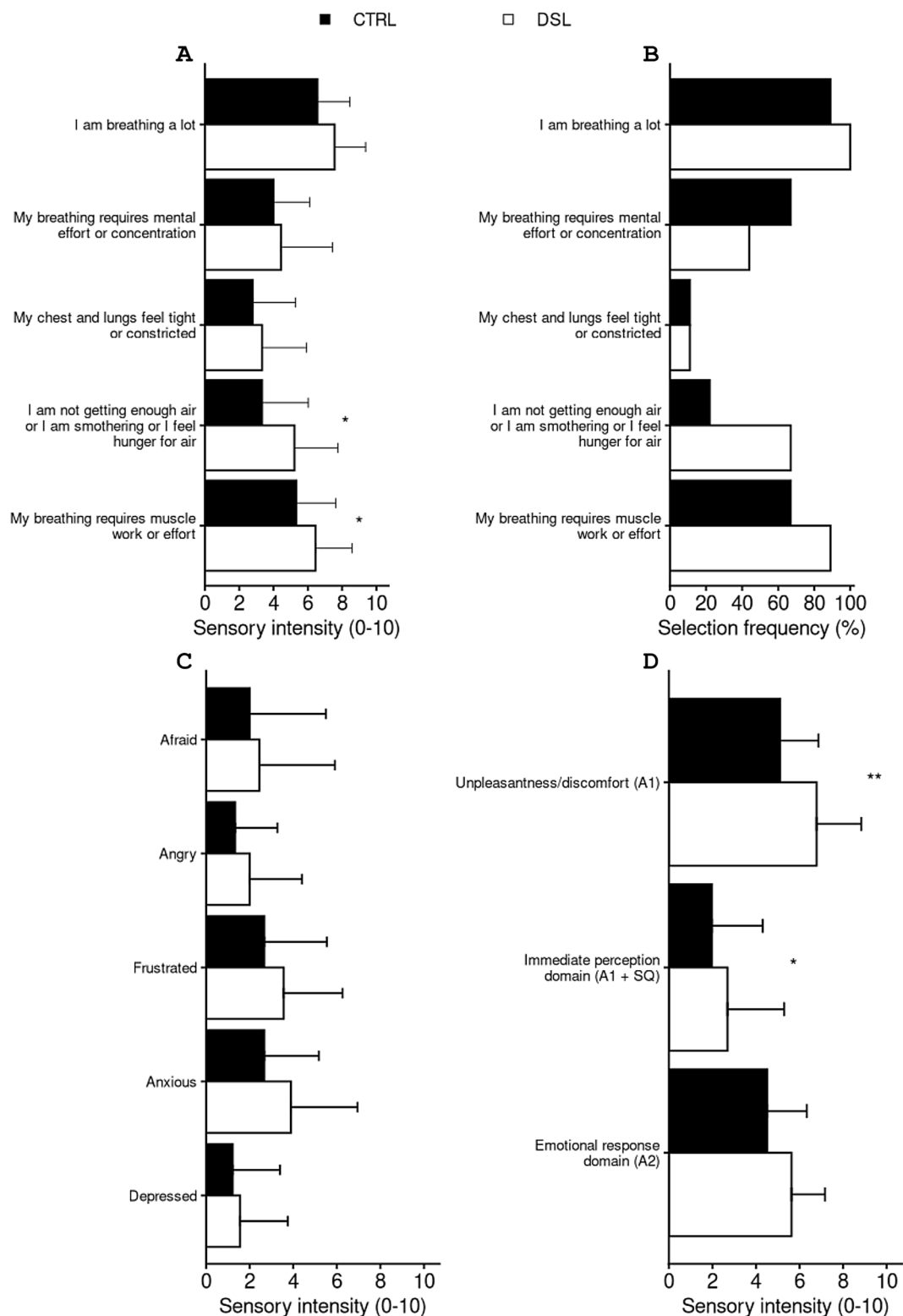
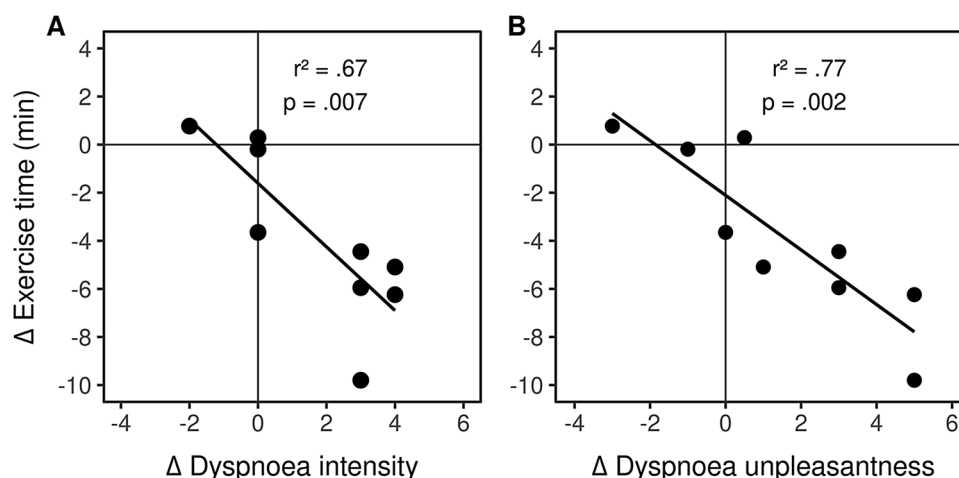


Fig. 6 Multidimensional Dyspnoea Profile responses following constant-load cycle ergometry under control (CTRL) and dead-space loading (DSL). Panels show sensory intensity ratings for dyspnoea qualities (A), selection frequency of dyspnoea sensory descriptors (B), affective-emotional intensity ratings (C), and multidimensional dyspnoea domain scores (D). Panels A and B correspond to the five sensory quality (SQ) items, whereas panel C corresponds to the five emotional-response (A2) items. In panel D, breathing unpleasantness/discomfort

(A1) represents the immediate unpleasantness associated with breathing sensations; the immediate-perception domain (A1 + SQ) represents the combined sensory-perceptual burden calculated from A1 and the five SQ intensity ratings; and the emotional-response domain score (A2) represents the affective-emotional response calculated from the five emotion ratings. Data in panels A, C, and D are presented as mean $\pm$ SD for 9 participants. * $p < .05$, ** $p < .01$ vs. CTRL

Fig. 7 Relationships between changes in time to task failure and dyspnoea responses at iso-time. Absolute changes in exercise time to task failure are plotted against absolute changes in dyspnoea intensity (A) and dyspnoea unpleasantness (B) during dead-space loading (DSL) relative to control (CTRL). Both relationships demonstrate significant inverse correlations, indicating that greater increases in dyspnoea were associated with larger reductions in exercise tolerance



interpretation is consistent with integrative models in which exercise tolerance reflects the interaction of multiple sensory and physiological signals rather than a single limiting factor (Hureau et al. 2018; Sheel et al. 2011).

Physiological basis for exertional dyspnoea

The physiological responses observed during DSL help explain the accompanying perceptual findings. Current models of exertional dyspnoea conceptualise symptoms as arising from interactions between ventilatory demand, inspiratory neural drive, respiratory mechanics, and the capacity of the respiratory system to satisfy increasing ventilatory requirements (Hijleh et al. 2026). DSL increased end-tidal CO_2 , minute ventilation, tidal volume, inspiratory flow, ventilatory equivalent for CO_2 , and inspiratory oesophageal pressure while producing minimal changes in indices of whole-body cardiometabolic stress. These findings are consistent with previous studies using DSL (Jensen et al. 2011; O'Donnell et al. 2000) and indicate that the perceptual responses occurred in the context of increased ventilatory demand and inspiratory pressure generation without a corresponding increase in systemic metabolic strain.

The exploratory ventilation–dyspnoea analyses provide further insight into these relationships. The ventilation–dyspnoea intensity relationship did not differ between conditions, with no significant ventilation $\times$ condition interaction. In contrast, the ventilation–dyspnoea unpleasantness relationship was steeper during DSL than CTRL, with a significant ventilation $\times$ condition interaction, indicating that dyspnoea unpleasantness increased more steeply with increasing ventilation during DSL. One plausible explanation for this latter observation is that dyspnoea unpleasantness was additionally influenced by the greater inspiratory pressure generation and mild hypercapnia accompanying DSL, although their independent contributions cannot be distinguished in the present design.

The greater ventilatory responses during DSL were accompanied by larger tidal volumes and substantially greater inspiratory oesophageal pressure swings. These mechanical responses closely paralleled higher MDP ratings for respiratory effort and “breathing a lot”, consistent with the concept that respiratory effort reflects awareness of the neural and mechanical demands of breathing (Lansing et al. 2009; Parshall et al. 2012). However, because neural respiratory drive was not assessed directly, oesophageal pressure should be interpreted as an indirect index of inspiratory muscle pressure generation rather than a direct measure of neural respiratory drive (Hudson et al. 2025).

Hypercapnia may also have contributed to the perceptual responses. End-tidal CO_2 was consistently elevated during DSL, and hypercapnia is known to stimulate chemoreceptor pathways capable of evoking air hunger (Banzett et al. 1990; Binks et al. 2014; Buchanan and Richerson 2009). This interpretation is supported by the higher MDP ratings for air hunger and the descriptively earlier and more frequent reporting of unsatisfied inspiration during DSL. However, because DSL simultaneously increased ventilatory drive and CO_2 retention, the present design cannot distinguish the independent contributions of respiratory motor output and hypercapnia. Hypercapnia may also influence dyspnoea through cerebrovascular and cerebral metabolic effects (Battisti-Charbonney et al. 2011; Caldwell et al. 2024). Accordingly, the perceptual effects observed during DSL likely reflect the combined influence of increased ventilatory demand, respiratory motor output, and hypercapnia.

Overall, the physiological profile was not consistent with critical ventilatory constraint. Ventilatory reserve remained substantial, ventilation increased predominantly through tidal volume expansion, inspiratory resistance was unchanged, the ventilatory muscle recruitment index remained negative, and no progressive deterioration in mechanical ventilatory efficiency was observed. Instead, the findings resemble the “excessive breathing” phenotype

described by Hijleh et al. (2026), whereby increased inspiratory muscle activation enabled ventilation to be augmented in the relative absence of major mechanical constraint.

Thus, DSL increased ventilatory demand while largely preserving respiratory mechanical capacity, with the accompanying perceptual effects occurring in the context of greater inspiratory pressure generation and mild hypercapnia. The absence of changes in affective-emotional MDP responses further suggests that the increase in ventilatory drive accompanying DSL preferentially amplified sensory-perceptual, rather than affective-emotional, dimensions of dyspnoea in healthy adults.

Methodological considerations

The randomised crossover design allowed direct within-participant comparison of physiological and perceptual responses while minimising inter-individual variability. The use of severe constant-load exercise enabled the temporal development of dyspnoea to be characterised throughout sustained high-intensity exercise and allowed comparisons at equivalent durations between conditions. Exercise intensity was individualised relative to gas-exchange threshold to target the severe-intensity domain, in which ventilatory demand progressively increases towards maximal values. This experimental approach provided a controlled approach for examining the development of dyspnoea during sustained exercise and extends previous work based primarily on incremental exercise. Scaling the dead-space volume to individual FVC also standardised the perturbation relative to lung size, addressing variability inherent in fixed-volume dead-space approaches. Finally, the combination of serial assessments of dyspnoea intensity, unpleasantness, and descriptors with post-exercise multidimensional assessment, together with concurrent ventilatory and respiratory mechanical measurements, allowed the perceptual responses to be interpreted alongside the physiological determinants of dyspnoea.

The sample size represents an important limitation. Although the study was powered for the primary perceptual outcome, it was not specifically powered for the secondary physiological, multidimensional, or correlational analyses. These findings should therefore be interpreted cautiously and regarded as hypothesis-generating. The predominance of male participants limits generalisability and precluded examination of sex-specific responses despite recognised differences in respiratory mechanics and dyspnoea perception (Ekström et al. 2017; Schaeffer et al. 2014). Menstrual cycle phase was not controlled and may have contributed additional variability (Behan and Wenninger 2008; Slatkowska et al. 2006). Participants were not blinded to condition. Although they were naïve to the study hypotheses

and exposed to matched external resistance, awareness of altered breathing sensations may nevertheless have influenced perceptual responses. Respiratory muscle pressure generation was assessed using mechanical pressure-based indices rather than direct electrophysiological measures of neural respiratory drive, limiting mechanistic specificity regarding the neural component of respiratory motor output. Moreover, because DSL simultaneously increased ventilatory drive and produced hypercapnia, their independent contributions to the observed dyspnoea responses could not be distinguished. Psychological traits known to influence dyspnoea perception were not assessed and may have contributed to inter-individual variability in symptom responses. Finally, the study was conducted in healthy, physically active young adults during laboratory-based cycle exercise. Whether the findings generalise to older adults, highly trained athletes, or individuals with cardiopulmonary disease, in whom respiratory mechanics, ventilatory control, and symptom perception may differ substantially, remains to be determined.

Conclusion

In healthy adults performing severe constant-load cycle ergometry, relative dead-space loading elicited physiological responses consistent with increased ventilatory drive, accelerated the development of dyspnoea, preferentially augmented sensory-perceptual characteristics, and reduced time to task failure without differences in end-exercise ratings of dyspnoea intensity or unpleasantness. Although dyspnoea unpleasantness was higher overall during exercise, it did not exhibit the same condition-dependent temporal divergence as dyspnoea intensity, whereas multidimensional profiling demonstrated no corresponding augmentation of affective-emotional responses. Dyspnoea intensity was similar at task failure despite the shorter exercise duration during DSL, suggesting that the trajectory of dyspnoea development may be more closely related to exercise tolerance than end-exercise symptom intensity. Together, these findings indicate that increased ventilatory drive accelerates the temporal evolution of dyspnoea and preferentially augments its sensory-perceptual characteristics, with the rate of symptom development emerging as an important perceptual correlate of exercise tolerance.

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Author Contributions All authors contributed to the conception and design of the study. Material preparation, data collection, and data analysis were performed by Leah Mann and Lee Romer. The initial draft of the manuscript was prepared by Leah Mann. All authors criti-

cally reviewed and revised the manuscript. All authors approved the final version for submission and agree to be accountable for all aspects of the work.

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Data availability The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Competing Interests The authors have no competing interests to declare that are relevant to the content of this article.

Ethics Approval The study was conducted in accordance with the principles of the Declaration of Helsinki. Approval was granted by the ethics committee of Brunel University of London (45245-A-Jan/2024-4944-1).

Consent to Participate Written informed consent was obtained from all participants.

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