Lung volume recruitment acutely increases compliance in individuals with severe respiratory muscle weakness

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ONLINE SUPPLEMENT

METHODS

Respiratory System Compliance. During measurements of C_{rs}, subjects wore a nose clip and breathed through a low resistance (0.2-1.5 cmH_2O. $l^{-1}.s^{-1}$ at 0.5-10 $l.s^{-1}$) circuit with minimal dead-space (0.1 *l*). The breathing circuit was attached to a two-way pneumatic valve (Series-8600, Hans Rudolph, Shawnee, USA) with one end open to the atmosphere, and the other connected to a tank of compressed room air and a two-stage gas pressure regulator. Bi-directional flow ($\dot{V}$) was measured using a calibrated pneumotachograph (model-3813, Hans Rudolph, Shawnee, USA), and volume was obtained by numerical integration of the $\dot{V}$ signal. Mouth pressure (P_{mo}) was measured through a port in the mouthpiece using a calibrated differential pressure transducer (Series-1110, Hans Rudolph, Shawnee, USA). Measurements of C_{rs} were made using the pulse method, as previously described [1]. The pulse method of measuring compliance involves the delivery of a pulse of air at a constant $\dot{V}$ (~0.3 $l.s^{-1}$) over 2 seconds from end-expiratory lung volume, causing a progressive increase in P_{mo} that is inversely proportional to C_{rs} (**Figure E1** and **E2**). In order to trigger the pulse of air, the pneumatic valve was connected to a computer, and bespoke software was used to detect the end of an expiration then rapidly trigger the valve, thereby switching the valve position from open to the atmosphere to in-line with the tank of compressed gas. The valve was then switched back to the initial position exactly 2.25 seconds later. A 250 millisecond delay was built in to the valve control software in order to allow for the equilibration of $\dot{V}$ during the initial phase of the pulse. In all subjects, the desired $\dot{V}$ was achieved within 250 milliseconds of the onset of the pulse. For individuals in the RWM group with a VC <0.6 *l*, $\dot{V}$ was decreased in order to ensure that the inflations were delivered along the linear portion of the pressure-volume relationship of the respiratory system. To minimize the confounding influence of inspiratory muscle effort and glottic closure on C_{rs} measurement in awake individuals, subjects were instructed to remain as relaxed as possible with an open glottis and make no inspiratory effort during inflations. For each pulse, $\dot{V}$ and P_{mo} data were analysed within the 2 second window at the end of each 2.25 second pulse (**Figure E1**, **E2**, and **E3**). C_{rs} was then calculated based upon the following equation:

$$C_{rs} = \frac{\dot{V}}{P_M \div Time}$$

Manoeuvres were considered satisfactory if the slope of the P_{mo}-time curve was linear, as determined by having an $r^2 \geq 0.99$. Manoeuvres with non-linear P_{mo}-time curves, as reflected by an $r^2 < 0.99$, were rejected (**Figure E3**). Multiple measurements were made at each time point (Baseline, 0H, 1H, and 2H) until a minimum of five satisfactory measures were obtained. The pulse method of measuring compliance has been shown to closely agree with measures of compliance based on conventional breath interrupter techniques [1] as well as published values [2]. Moreover, the technique has previously been used to measure compliance in a wide variety of populations; C_{rs} and lung compliance in healthy individuals [1, 3], lung compliance and chest-wall compliance in obese individuals [3, 4], lung compliance in individuals with chronic obstructive pulmonary disease [3], lung compliance in individuals with pulmonary fibrosis [3], as well as lung compliance and C_{rs} in mechanically ventilated adults and newborns in the ICU [5-7].

Blood Pressure and Heart Rate. During LVR, continuous non-invasive beat-by-beat blood pressure and heart rate (HR) were measured using finger pulse photoplethysmography (Finometer, FMS, Arnhem, Netherlands). Finometer derived measures of arterial blood pressure have been shown to accurately represent direct measurements of arterial blood pressure using a radial arterial catheter [8]. We confirmed the accuracy of our MAP measurements during LVR by simultaneously measuring intra-arterial (radial) blood pressure in one control subject (**Figure E4**). Average measures of MAP and HR during LVR were calculated five seconds prior to each LVR manoeuver, during the entire plateau phase, and five seconds following each LVR manoeuver.

RESULTS

Breathing Patterns. Data relating to breathing patterns and dyspnoea are presented in **Table E1**. At rest, subjects in the RMW group had a more rapid and shallow breathing pattern relative to controls, as evidenced by a significantly higher breathing frequency (f_B) and significantly lower tidal volume (V_T) (both $p<0.001$), while minute ventilation ($\dot{V}_E$) was not different between groups ($p=0.19$). There were no significant within-group changes following LVR in V_T, f_B, and $\dot{V}_E$ relative to baseline at any time point in either group (all $p>0.05$), indicating that LVR did not have an effect on resting breathing pattern.

Respiratory System Compliance. A total of 691 pulse manoeuvres to measure C_{rs} were performed across all time points for the subjects in the RMW group, of which 55% were acceptable (**Table E2**). A total of 768 pulse manoeuvres were performed across all time points for subjects in the control group, of which 40% were acceptable (**Table E2**). Given their normative respiratory muscle function, and the fact that controls were unfamiliar with the feeling of passive lung inflation, they had a significantly lower success rate and average number of rejected manoeuvres than individuals in the RMW (both $p<0.05$). The average within-subject coefficient of variation in C_{rs} at baseline was 16.5±3.2% and 18.2±3.1% in the RMW and control groups respectively.

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Supplemental Figures

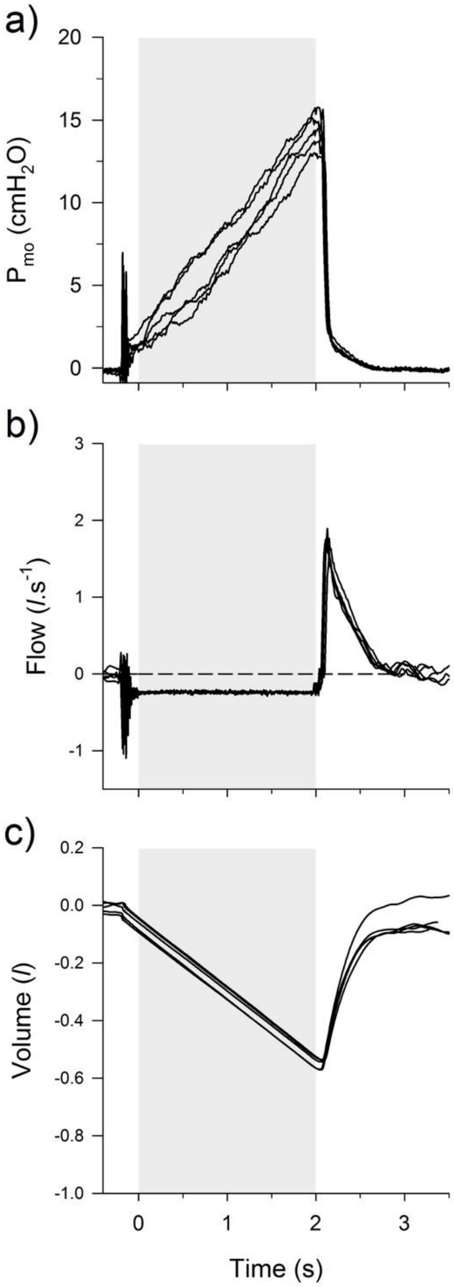

Figure E1. Raw P_{mo}, $\dot{V}$, and volume traces during 5 individual pulse manoeuvres for C_{rs} measurement at baseline in one representative subject in the RMW group. In panels a), b), and c), the portion of time from which data is used to calculate C_{rs} is outlined by the grey shaded area. Panel a) shows the changes in P_{mo} as a function of time. Each P_{mo}-time curve within the grey shaded area had an $r^2 \geq 0.99$. Panel b) shows the changes in $\dot{V}$ as a function of time. The average $\dot{V}$ was constant at 0.3 l.s^{-1} within the grey shaded area. Panel c) shows changes in volume as a function of time. P_{mo}, mouth pressure; $\dot{V}$, flow.

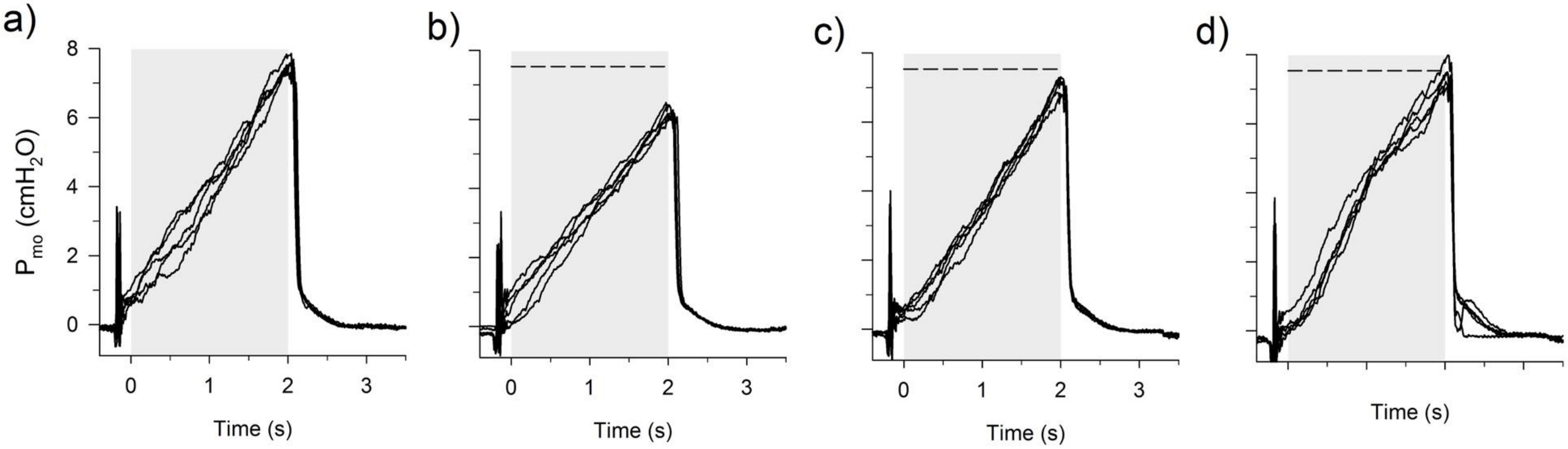

Figure E2. Raw P_{mo}, traces as function of time for one representative subject in the RMW group during 5 individual pulse manoeuvres for C_{rs} measurement at baseline (Panel a), 0H (Panel b), 1H (Panel c), and 2H (Panel d). In each panel the portion of time from which data is used to calculate C_{rs} is outlined by the grey shaded area. In panels b), c), and a), the dashed line represents the average peak P_{mo} during five pulse manoeuvres at baseline (Panel a), reflecting an 18% increase in C_{rs} at 0H relative to baseline, and no significant change relative to baseline at 1H and 2H. All P_{mo}-time curves within the grey shaded area in each panel had an $r^2 \geq 0.99$. The $\dot{V}$ for all pulse manoeuvres was constant at 0.3 $l.s^{-1}$ within the grey shaded area, and by association, the delivered volume over 2 seconds was 0.6 *l*. P_{mo}, mouth pressure; $\dot{V}$, flow; C_{rs}; compliance of the respiratory system.

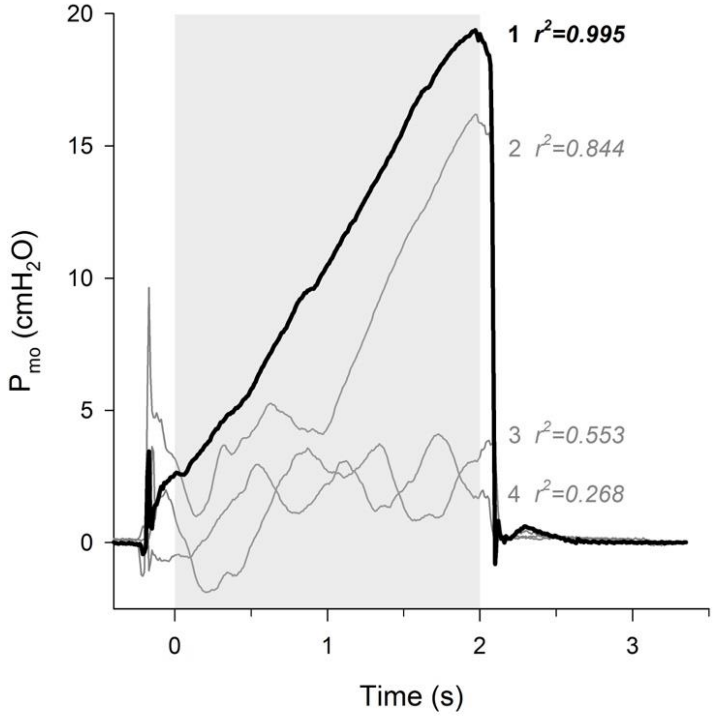

Figure E3. Raw P_{mo} traces during four individual pulse manoeuvres for C_{rs} measurement at baseline in one representative subject in the RMW group. The portion of time from which data is used to calculate C_{rs} is outlined by the grey shaded area. The manoeuvre labelled “1”, depicted by the thick black line, had a P_{mo}-time curve that had an $r^2 \geq 0.99$, and therefore was acceptable. Manoeuvres labelled “2”, “3”, and “4” depicted by the thin dark grey lines had P_{mo}-time curves that had an $r^2 < 0.99$, and therefore were rejected. For all four pulse manoeuvres, the average $\dot{V}$ was constant at 0.3 *l*.s^{-1} within the grey shaded area, and by association, the delivered volume over 2 seconds was 0.6 *l*. P_{mo}, mouth pressure; $\dot{V}$, flow; C_{rs}; compliance of the respiratory system.

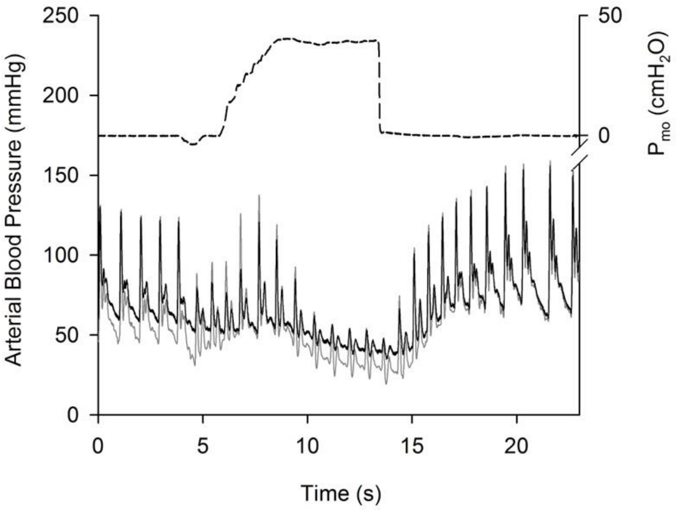

Figure E4. Raw P_{mo}, and arterial blood pressure data during a single LVR manoeuver in single control subject. The black dashed line represents P_{mo}, the black solid line represents arterial blood pressure data from the Finometer, and the grey solid line represents arterial blood pressure data sampled from a radial artery catheter. All data presented are raw traces. P_{mo}, mouth pressure.

Supplemental Tables

Table E1. Breathing patterns and dyspnoea prior to and following LVR.

	Baseline	0H Post	1H Post	2H Post
RMW				
V_T, *l*	0.41±0.03*	0.44±0.04*	0.43±0.07*	0.41±0.06*
f_B, bpm	27±2*	24±4*	26±5*	28±3*
$\dot{V}_E$, *l*.min^{-1}	10.6±0.6	10.1±0.8	11.1±0.5	11.4±0.9
Dyspnoea, *Borg Scale*	0.92±0.31	1.06±0.32	0.92±0.22	0.75±0.24
Controls				
V_T, *l*	0.96±0.06	0.94±0.06	1.02±0.10	1.00±0.09
f_B, bpm	14±2	13±2	14±1	13±1
$\dot{V}_E$, *l*.min^{-1}	12.6±1.3	12.4±1.1	14.3±1.5	13.0±1.1
Dyspnoea, *Borg Scale*	0.00±0.00	0.08±0.06	0.00±0.00	0.00±0.00

Values are presented as mean±SEM. V_T, tidal volume; f_B, breathing frequency; $\dot{V}_E$, minute ventilation. *p<0.05 for RMW versus control subjects.

Table E2. Pulse method of compliance measurement data

	RMW	Controls
Total manoeuvres accepted, *n*	370	284
Average manoeuvres accepted, *n*	27±4	24±4
Total manoeuvres rejected, *n*	321	484
Average manoeuvres rejected, *n*	31±2*	40±7
Total manoeuvres, *n*	691	768
Average manoeuvres, *n*	58±4	64±6
Average success rate (%)	55±4*	40±4

Values are presented as mean±SEM. *p<0.05 for RMW versus control subjects.