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Does wearing a facemask decrease arterial blood oxygenation and impair exercise tolerance?

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Keywords: COVID-19 facemask
N95
Surgical facemask
Cycle exercise
Submaximal
Maximal
Exhaustion
Exercise-induced arterial hypoxemia
Cardiovascular responses
Rating of perceived exertion
Dyspnea

1. Introduction

Wearing a mask that covers the mouth and nostrils, along with social distancing and frequent handwashing, represents the first line of defense against the spread of COVID-19 (Leung et al., 2020) and WHO guidelines (Organization, 2020). Moreover, health experts have indicated the potential need for COVID-19 face coverings through 2022 (Crist, 2021). Whereas some countries report that mask use is ~80\% or higher (Jang et al., 2020) concern have been raised that lung function and pulmonary gas exchange are compromised by mask wearing to the extent that they produce arterial hypoxemia and hypercapnia during high intensity exercise resulting in exercise intolerance in recreational exercisers. This study therefore aimed to investigate the effects of a surgical, flannel or horizontal-fold N95 masks on cardiorespiratory responses to incremental exercise.

Methods: This investigation studied 11 adult males and females at rest and while performing progressive cycle exercise to exhaustion. We tested the hypotheses that wearing a surgical (S), flannel (F) or horizontal-fold N95 mask compared to no mask (control) would not promote arterial deoxygenation or exercise intolerance nor alter primary cardiovascular variables during submaximal or maximal exercise.

Results: Despite the masks significantly increasing end-expired peri-oral %CO\textsubscript{2} and reducing %O\textsubscript{2} each ~0.8\%–2\% during exercise (P < 0.05), our results supported the hypotheses. Specifically, none of these masks reduced sub-maximal or maximal exercise arterial O\textsubscript{2} saturation (P = 0.744), but ratings of dyspnea were significantly increased (P = 0.007). Moreover, maximal exercise capacity was not compromised nor were there any significant alterations of primary cardiovascular responses (mean arterial pressure, stroke volume, cardiac output) found during sub-maximal exercise.

Conclusion: Whereas these results are for young healthy recreational male and female exercisers and cannot be applied directly to elite athletes, older or patient populations, they do support that arterial hypoxemia and exercise intolerance are not the obligatory consequences of COVID-19-induced mask-wearing at least for cycling exercise.

The premise for concerns surrounding arterial hypoxemia and impaired exercise capacity have largely been based on earlier, pre–COVID-19 reports using a specialized breathing apparatus, which may not be an appropriate surrogate for the types of face coverings used against COVID-19. For instance, the work of Schulte (1964), which evaluated the effects of a respiratory muscle training device that purposefully increases breathing resistance and can reduce effective inspired O\textsubscript{2} to 17 \% (from ~20.94 \%), is often referenced when discussing the potential effects of N95 facemasks (Davis and Tsen, 2020; Schulte, 1964). In contrast to COVID-19 recommended masks, the respiratory muscle training masks are specifically designed so that the wearer “dials in” a very high breathing resistance that is specifically intended to overcome the ability of the respiratory muscles to elevate
ventilation sufficiently to regulate alveolar and thus arterial CO₂ pressures (PCO₂). As such, they induce a state of hypventilation that drives down alveolar PO₂. Therefore statements made during the COVID-19 pandemic stating that the standard N95 mask reduces the inspired O₂ causing “...headache, lightheadedness, drowsiness, muscular weakness, dyspnea on exertion, nausea and vomiting” (Davis and Tsen, 2020; Schulte, 1964) or that the increased inspiratory and expiratory resistance for greater than 10 min causes “...increased lactate levels, fatigue and impaired physical work capacity.” (Álvarez-Herms et al., 2018; Davis and Tsen, 2020), based on non-N95 specialized breathing apparatus may not be accurate.

Recent work Lassing et al. (2020) and Fikenzer et al. (2020) have revealed significant exercise performance impairments with surgical and N95 masks during exercise (Fikenzer et al., 2020; Lassing et al., 2020). However, these two studies superimposed a spirometry mask on top of each COVID-19 mask, resulting in a relatively leak-proof seal that is at odds with the fitting of COVID-19 masks in real-world setting and thus may not accurately reflect what occurs with normal mask wearing. This is a critical point since the interaction between each face mask and the spirometry valve assemblies required for pulmonary gas exchange measurements will have markedly variant resistances, dead-space and other qualities that impact the subject’s breathing pattern, total ventilation, cardiopulmonary function, gas exchange, and facial skin temperature (Askanazi et al., 1980; Cerretelli et al., 1969; Scarano et al., 2020). This becomes more evident when compared to the recent work by Epstein et al. (2021) which revealed that wearing an N95 facemask, without the additional spirometry mask, during incremental exercise did not alter peak exercise workload, but did increase end-tidal CO₂ compared to a non-mask control (Epstein et al., 2021). Using a similar incremental exercise protocol, Shaw et al. (2020) evaluated the effects of surgical and cloth masks alone on arterial oxygen saturation and muscle tissue oxygenation levels (Shaw et al., 2020). They revealed that wearing a mask had no effect on exercise performance, arterial oxygen saturation, tissue oxygenation index. These initial formative studies have provided some of the first evidence regarding the physiological response to exercise with COVID-19 face coverings, but given the conflicting findings and controversy surrounding this topic (Fikenzer and Lauß, 2020a, b), highlights the need for additional work. Moreover, given that increase in the work of breathing, which may occur with mask wearing, can alter cardiovascular responses to exercise (Harms et al., 1997), evaluation of the cardiac responses to different COVID-19 masks is warranted. Therefore, we tested two hypotheses. Namely, for recreational exercisers, that despite modest effects on “expired” O₂ (decrease) and CO₂ (increase), wearing a surgical, flannel or vertical-fold N95 mask would: 1. Have little or no impact on arterial oxygenation (i.e., <3% decrease in arterial O₂ saturation from rest, (Dominelli et al., 2013; Harms et al., 2000)) or exercise tolerance. 2. Not alter primary cardiovascular variables (heart rate, cardiac output, blood pressure) during submaximal or maximal exercise. In addition to these hypotheses, the present investigation experimentally tested the resistance to flow across each mask at physiologic flow rates.

2. Methods

2.1. Participants

Eleven healthy, recreationally active participants (5 men and 6 women, age 30 ± 11 yrs [mean ± SD], height 175 ± 11 cm, body mass 73.0 ± 12.9 kg) who were experienced with laboratory exercise testing and maximal exercise tests completed the experiments. Sample size was estimated using a population mean ± SD of 98 ± 2 and 100 ± 5 for percentages of SpO2 and peak power, with α = 0.05 and β = 0.1, to detect a 3% and 6% decrease, respectively (Rosner, 2011). The number of subjects required to show a 3% decrease in SpO2 = 7 and 6% decrease in peak power = 16. Importantly, a 3% decrease in SpO2 has been defined in the literature as the definition of exercise-induced arterial hypoxemia (Harms et al., 2000). Participants were free from known cardiovascular, pulmonary, or metabolic disease and were non-smokers as determined from a health history questionnaire. All procedures were approved by the Institutional Review Board of Kansas State University (#9954) and conformed to the standards set by the Declaration of Helsinki. Written informed consent was obtained from all participants. Subjects were instructed to abstain from vigorous activity 12 h. prior and caffeine and food consumption 2 h. prior to the scheduled testing times. A minimum of 24 h. was mandated between each test with all test performed at a similar time of day (±3 h).

2.2. Facemasks

Surgical mask (USA ASTM F2100): Size: 3.7 × 6.9 in. (9.5 × 17.5 cm), mass: 3.2 g. Dead space: depends on wearer and fitting, estimated <40 mL. Kunshan jiehong (Kunshan City, China) disposable 3-layer face masks feature an inner and outer layer of spun-bond polypropylene, and a middle filter layer made of melt-blown polypropylene. These materials are the industry standard for disposable 3-ply facemasks. They provide level 1 protection with filtration >95 % for 3 μm and 0.1 μm particles. Pore size is 0.1 μm. Flannel facemask: Champion (Rural Hall, North Carolina, 50 % cotton, 50 % polyester, 2 layers, ~30 stitches/in). Size: 5.5 × 8.5 in. (14 × 19 cm), mass: 17.3 g. Dead space: depends on wearer and fitting, estimated <40 mL. Authorized by the Federal Drug Administration (not FDA cleared or approved) under an Emergency Use Authorization for use by health care professionals as personal protective equipment under section 564(b)(1) of the Act, 21 U.S.C. Section 360bb-3(b)(1). N95 NIOSH approved 1570 respirator: Horizontal-fold, non-valved. Size: 7 × 7.75 in. (19 × 20 cm), mass 10.0 g. Dead space: depends on wearer and face shape (140 mL + 15 for subjects herein, measured by water displacement). Dukal Corp (Ronkonkoma, New York). Provides >95 % filter efficiency for particulate oil-free aerosols 0.3 μm. Bacterial filtration efficiency 99.9 %. By comparison, the dead space for the standard Hans-Rudolph (adult – large) two-way non-rebreathing valve and mask assembly is 123.5 mL (https://www.rudolphkc.com/pdf/691151%2021215%20K.pdf). The resistance to flow across each mask material was determined at constant flow rates of 24, 48, 72 and 96 L min⁻¹ through a Medgraphics pneumotachograph, which allowed for real-time evaluation of flow (Fig. 1A). Measurements of the differential pressure on the down- and up-stream side of each mask were taken using a pressure manometer and used to calculate resistance.

2.3. Study design

A randomized cross-over study design was utilized in which participants completed a series of exercise tests while wearing a surgical mask, flannel facemask, and N95 respirator (described below), or no face covering (control). All masks were securely fastened by a trained member of the laboratory according to manufacturers’ specifications and Centers for Disease Control and Prevention (CDC) recommendations. All testing procedures were performed in a temperature-controlled laboratory (21–22 °C), with all participants in a well hydrated state and having abstained from vigorous activity for 24 h prior to testing. At least 48 h was given between adjacent testing sessions.

Participants first completed four incremental ramp exercise tests to exhaustion on a cycle ergometer (Lode, Groningen, Netherlands), under each experimental condition. Following a 2 min resting baseline and 2 min unloading cycling, the power output was progressively increased at a rate of 20 W/min until the participant could not maintain the pedal cadence of 60 rpm for 5 consecutive revolutions despite verbal encouragement. Pedal cadence was maintained constant because pedal cadence can affect ventilatory, cardiac, and pulmonary gas exchange responses during incremental exercise (Broxterman et al., 2015). Participants were blinded to power output and test duration. Seat height was recorded for the first test and reproduced for all subsequent tests.
continuously monitored for any movement artifacts and these were processed with the Modelflow method, incorporating age, height, and weight, to obtain measurements of stroke volume and cardiac output. This method provides a reliable estimate of the relative changes in stroke volume and cardiac output during exercise in healthy men and women but cannot be used to provide absolute values unless corrected to a standard method (Sugawara et al., 2003). As such, only the change in these variables relative to rest is reported. Borg ratings of perceived exertion and dyspnea were recorded at each minute of exercise as previously described (Borg, 1982; Mancini et al., 1992). A 6–20-point Borg dyspnea scale, versus the modified 10-point version, was used to allow for greater fidelity in identifying different levels of perceived dyspnea between conditions. Subjects were well versed in using these scales to assess exertion and dyspnea.

Since the interaction between each face mask and the mouthpiece–breathing valve assemblies required for pulmonary gas exchange measurements will have markedly variant resistances, dead-space and other qualities that impact the subject’s breathing pattern, total ventilation, cardiopulmonary function and gas exchange (Askanazi et al., 1980; Cerretelli et al., 1969) as well as facial skin temperature (Scarano et al., 2020), gas exchange measurements were not performed. Compound by the fact that the devices used to measure ventilatory variables may themselves induce alterations in the measurement of tidal volume, breathing frequency and thus ventilation (Gilbert et al., 1972), a critical aspect of this study is the absence of mouthpiece–breathing valve assembly placed over each respective facemask. Since the primary goal of this work is to provide real-world ecologically valid results that translate to individuals wearing only a facemask, this represents a key aspect of the study design. Peak exercise workload was used as the primary variable for exercise capacity.

**Peri-oral End-Expired CO₂ and O₂.** In a subset of individuals (n = 5, 3 F/2 M, Age: 24.8 ± 1.6 yr, 175.7 ± 9.6 cm, 71.7 ± 13.4 kg) additional sub-maximal exercise tests were performed to evaluate changes in expired peri-oral CO₂ and O₂. Experiments could only be performed in a sub-set due to equipment availability. Within 1 week of completing the ramp tests, each participant returned to the laboratory to perform measurements at rest and during ~3 min of constant-load cycling exercise at 95 W and 127 W (Monark, Ergomedic 828E, Varberg, Sweden) under each experimental condition whilst wearing a nose clip. The order of these tests was randomized. These work rates were chosen as they are associated with MET ranges of 5–7 METs that are common for moderate-to-heavy physical activities (Ainsworth et al., 2011). The short duration was selected purposefully to capture the primary component and avoid development of a slow component in those subjects who may have been > GET at the higher work load. This strategy has been used previously (Poole et al., 1992). During each test, HR and arterial O₂ saturation were measured by pulse oximetry (Proven, OXI-27BL, Beaverton, Oregon) while expired O₂ and CO₂ were measured using Ametek Applied Electrochemistry Inc., CD-3A and S-3A/I analyzers (Oak Ridge, Tennessee) calibrated using precision gasses that spanned the expected range of measured values. These analyzers are accurate to within ±0.01 % (O₂) and 0.02 % (CO₂) with response times of 100 ms for O₂ and 25 ms for CO₂ to 90 % final response with a sensitivity of 0.001 % over the ranges measured. For the constant-load exercise tests performed herein breath-to-breath variation is typically <10 % of the room air to peri-oral end-exhaled value. With 10 breaths averaged to provide final values as presented the coefficient of variation (CV) on repeated analyses within condition (i.e., control or masked) was 5% (O₂) and 4% (CO₂) of the delta from inspired to peri-oral end-tidal giving absolute values for CV of 0.025 % (O₂) and 0.016 % (CO₂).

Breathing frequency was determined by timed (30 s interval) observation. To measure the expired gas concentrations exhaled “mask” gas was sampled between the subject’s chin and lower lip at 0.5 L/min and end-expired CO₂ was detected automatically and the corresponding end-expired O₂ recorded at that precise time. This procedure collected principally, but not exclusively, the expired flow stream and could be

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**Fig. 1.** Illustration of experimental set-up for evaluation of the resistance to flow across each mask (A). The pressure difference across each mask for multiple flow rates demonstrates that a substantial difference exists for all masked conditions compared to control, with the greatest difference for the N95 mask (B). Calculation of resistance at 48 L min⁻¹ revealed a higher resistance to air flow for all masks (C).

During each ramp test, arterial O₂ saturation (SpO₂) was measured continuously via two independent pulse oximetry units (Datex Ohmeda (GE) S/5 Light Patient Monitor and Innovo pulse oximeter, Innovo Medical, Stafford, Texas, U.S.A.). If measurements were more than 3% different the sensors were repositioned. Heart rate was measured via photoplethysmography. Continuous beat-by-beat blood pressure (systolic, diastolic, and mean) was measured via photoplethysmography (Pinometer Pro; Finapres Medical Systems, Amsterdam, The Netherlands). To minimize hand movement artifact during exercise, the right arm was placed on foam padding slightly below heart level on an adjustable stand. In addition, the raw arterial pressure waveforms were

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replicated exactly in the control and mask trials without altering mask geometry or inspiratory/expiratory resistances in any way. We accepted that the expire rate would be contaminated to some degree by room air in the control condition by streaming effects and, in the mask trials, by gas trapping and streaming within the additional dead space. The values of 10 breaths beyond 2 min 30 s of exercise were measured and averaged. Preliminary studies confirmed that the primary measurements had stabilized after 2 min 30 s for these subjects.

2.4. Statistical analyses

For all statistical analyses, the Prism (version 7.04, Graphpad software, INC., La Jolla, CA) data analysis software package was utilized. The effect of each facemask condition on peak exercise responses (peak power, SpO₂, dyspnea, HR) were assessed using one-way repeated measures ANOVA with Dunnet’s post hoc-analysis. Sub-maximal exercise responses were assessed via two-way repeated measures ANOVA (condition × workrate) with Dunnet’s post hoc-analysis. In cases were the assumption of sphericity was violated Geisser-Greenhouse correction was performed. All primary outcome variables were normally distributed as determined using the Homomorov-Smirnov normality test. Moreover, for the ANOVA test herein the following assumptions were made: 1. Each group sample is drawn from a normally distributed population. 2. All populations have a common variance. 3. All samples are drawn independently of each other. 4. Within each sample, the observations are sampled randomly and independently of each other. 5. Factor effects are additive. To minimize the chances of a type II error due to a modest sample size, effect sizes were calculated as Eta squared (η²) for primary comparisons, which provides information on the magnitude of the difference between the groups. The threshold values for η² were defined as small, moderate, and large effects as 0.01, 0.06, and 0.14, respectively (Lakens, 2013). Spearman correlation coefficients were used to assess the relationship between dyspnea and HR. Data are presented as mean ± SD unless otherwise stated.

3. Results

The resistance to flow across each mask material at physiologic flow rates is illustrated in Fig. 1B. The pressure drop increased linearly with flow. There was a noticeable difference in the pressure drop and calculated resistance (Fig. 1C) to air flow caused by all masks relative to a non-masked control, with a markedly higher resistance for the N95. Note that the non-masked control resistance was determined across the standard Medgraphics exercise testing pneumotachograph. By comparison, the differential pressure for the standard Hans-Rudolph (adult – large) two-way non-rebreathing valve and mask assembly at a flow rate of 100 L/min is 2.1 cmH₂O (https://www.rudolphkc.com/pdf/691151%201215%20K.pdf).

3.1. Ramp exercise: rest and submaximal work rates

At rest, MAP (P = 0.923, η² = 0.04), HR (P = 0.213, η² = 0.02), SpO₂ (P = 0.422, η² = 0.03), and dyspnea score were not different across all conditions. Fig. 2 illustrates the submaximal responses during the ramp exercise test. Ratings of dyspnea were significantly higher during the submaximal work rates of the ramp test for all mask types compared to the no mask condition (P < 0.0001, η² = 0.083). During exercise there was a main effect on HR across conditions (P = 0.041, η² = 0.009), with surgical and N95 masks eliciting a higher HR compared to the no mask condition at all submaximal work rates above 60 W. However, this increase was less than 10 bpm in all instances, but was not present at maximal exercise (P = 0.667, η² = 0.006). The difference in dyspnea significantly correlated with the difference in HR between no mask and N95 conditions at 120 W (P = 0.038, R² = 0.4). Submaximal exercise SpO₂ was not different across conditions (P = 0.087, η² = 0.053). Rating of perceived exertion was not different.
across conditions (P = 0.286). During exercise the MAP (P = 0.897, \( \eta^2 = 0.004 \)), SV (P = 0.576, \( \eta^2 = 0.017 \)), and CO (P = 0.831, \( \eta^2 = 0.003 \)) responses were not altered by the presence of any of the face masks.

3.2. Ramp exercise: maximal work rate

Fig. 3 illustrates that SpO\(_2\) at peak power (P = 0.623, \( \eta^2 = 0.01 \)) was not different across conditions. Moreover, the absolute change in SpO\(_2\) from baseline to peak power was also not different across each mask condition (P = 0.744, \( \eta^2 = 0.005 \)). HR at peak power was not different across conditions (P = 0.667, \( \eta^2 = 0.006 \)). At peak exercise, the magnitude of dyspnea was significantly increased for the N95 (P = 0.011) facemask compared to the no-mask control, but not the flannel (P = 0.104), or surgical (P = 0.110) facemasks compared to the no mask control (\( \eta^2 = 0.369 \)). RPE was not different among conditions. Importantly, the present investigation included healthy men and women with a range of maximal exercise capacities (range: 168–328 W; 2.42–5.57 W/kg). Absolute peak power from the no-mask control was not different compared to the flannel (P = 0.246), surgical (P = 0.168), or N95 (P = 0.077) conditions (Fig. 3). Similarly, peak power normalized to body mass in the no-mask control was not different compared to the flannel (P = 0.271), surgical (P = 0.229), or N95 (P = 0.071) conditions.

3.3. Constant-load submaximal exercise

The constant-work load exercise bouts at 95 and 127 W, substantially confirmed the lack of effect of wearing any mask on cardiovascular control (Table 1), with the exception of HR at 95 W, which was significantly elevated above the no mask condition only for the surgical mask (i.e., 129 \pm 25 vs. 119 \pm 18 bpm, P < 0.05). With respect to peak respiratory rate, there was a significant increase for both the surgical and flannel masks at rest and the flannel mask only at 95 W. SpO\(_2\) did not change significantly from the no mask condition either at rest or for either work rate for any mask. For all measurements made, the greatest effect of the masks was on the end-expired peri-oral gas concentrations where the surgical mask decreased peak O\(_2\)\% and increased peak CO\(_2\)% significantly at rest and the N95 significantly increased peak CO\(_2\)% at rest. During exercise, however, each mask consistently and significantly decreased end-expired perioral O\(_2\) and elevated CO\(_2\) between \( \sim 0.8–2\% \) compared with the resting no-mask condition.

4. Discussion

The principal original findings of this investigation support our hypotheses that wearing either the surgical, flannel or N95 mask at rest and during submaximal and maximal exercise did not induce arterial hypoxemia, compromise maximal cycle exercise capacity nor substantially impact major cardiovascular exercise responses. This was true despite the significant elevation of peak end-expired peri-oral CO\(_2\) and depression of O\(_2\) within the mask of 0.8–2 %. However, despite the intransigence of arterial O\(_2\) saturation, subjects rated their dyspnea significantly higher during mask wearing.

The importance of this issue cannot be overstated. The U.S. and the World population is facing an unprecedented challenge to health and longevity. Regular physical exercise avoids, and inactivity promotes, a deterioration in cardiovascular health (Chakravarthy and Booth, 2003) that, over time, contributes to an elevated cardiovascular disease risk (Pecanha et al., 2020). If mask wearing is perceived as noxious or contraindicated for healthy or patient populations, especially during exercise, an unavoidable consequence will be greater home isolation (quarantine), decreased physical activity and the health deterioration sequelae (e.g., reduced maximal O\(_2\) uptake (Nolan et al. 2018) and, impaired insulin sensitivity and metabolic health (Krogh-Madsen et al., 2010; Mikus et al., 2012; Thyfault and Krogh-Madsen, 2011)). Moreover, low cardiorespiratory fitness accounts for more overall deaths than hypertension, smoking, high cholesterol and diabetes (Blair, 2009). A telling exemplar from Fitbit Inc. data demonstrates that, for the week ending March 22 (2020) average step counts, for over 30 million people, in most countries monitored, decreased significantly (up to 38 %) relative to 2019 (News, 2020; Pecanha et al., 2020). Given this scenario it is
imperative that the impact of mask wearing be scientifically evaluated and health experts, public health officials, exercise specialists and scientists as well as the broader public have access to accurate data to guide public policy.

4.1. Dyspnea and rating of perceived exertion (RPE)

Dyspnea is the result of integration among multiple factors, including central command, feedback from a variety of receptors throughout the respiratory system as well as the inspiratory pressor response which may increase both dyspnea and RPE (i.e., Borg-dyspnea and Borg-legs, Romer et al., 2006a, 2006b Parshall et al., 2012; de Morree and Marcora, 2015; Laviolette and Laveneziana, 2014). While hypoxia and elevated $\text{PCO}_2$ can increase the intensity of dyspnea, the unchanged $\text{SpO}_2$ suggests that other factors may be involved in mediating the increased dyspnea with mask wearing during exercise. Specifically, increased central command related to the inspiratory pressor response (higher ventilatory resistance) in combination with psychological factors as related to peri-oral (lips and surrounding skin) temperature elevation (Scarano et al., 2020). Wearing surgical and N95 masks while at rest elicits ~0.7–1.9 °C increase in skin temperature, which parallels significant differences in discomfort (Scarano et al., 2020). This is an important finding in that changes in face temperature have been shown to alter levels of dyspnea in clinical populations, suggesting that changes in receptor firing with increased facial temperatures from mask wearing may increase the sensation of respiratory discomfort, particularly during exercise (Parshall et al., 2012; Qian et al., 2019). Our findings of an increased level of dyspnea with each mask during exercise is consistent with previous reports at maximal exercise with surgical masks and FFP2/N95 masks (Fikenzer et al., 2020). Not surprisingly exhaustion corresponds to a high RPE and, depending to a degree on the type of test performed (e.g. constant-load, ramp, submaximal/exhaustive), the RPE and dyspnea ratings may converge towards a high value at exhaustion that may or may not be impacted by increased or decreased work of breathing (see Fig. 3 in Harms et al., 2000).

4.2. Cardiopulmonary responses

Accounts of increased HR whilst mask wearing are largely anecdotal (Times, 2020), but do support the reported elevated HR by 8–10 bpm during submaximal exercise herein. This directional change, but often of less magnitude, is supported in the peer reviewed literature and may reflect stimulation of the trigeminal reflex resulting in a mild tachycardia at rest and during activity/exercise (Laird et al., 2002; Li et al., 2005). Moreover, laboratory-induced increases in dyspnea elicited with mild inspiratory threshold loading increased resting HR by 8–10 bpm, but in that instance, did not correlate breathing discomfort rating and HR (Nierat et al., 2017). The present study, however, observed a similar increase in HR that did correlate with the increased dyspnea with mask wearing during exercise. In total these findings implicate a putative role for both stimulation of the trigeminal reflex and breathing discomfort in the observed mask-induced elevated HR during submaximal exercise.

That neither arterial oxygenation nor exercise capacity were compromised for our subjects by wearing the N95 (or other) masks is in direct contrast to the assertions of Davis and Tsen (Davis and Tsen, 2020), but in agreement with the recent work of Samannan et al. in which COPD patients did not experience any clinically significant mask-induced changes in $\text{SpO}_2$ during a standard six-minute walk test (Samannan et al., 2020). It is also pertinent that, at the low flow rates achievable in COPD patients, the elevated resistance provided by the mask would be very modest. These findings are critical in that citing work by Sinkule et al. (Sinkule et al., 2013), Davis and Tsen (Davis and Tsen, 2020) stated that wearing the N95 mask whilst exercising at 2 metabolic equivalents (METS) similar to walking slowly (VO$_2$ ~500 mL/min for a 70 kg individual) elevates inspired CO$_2$ to between
3 and 4% above the normal in fresh inspired air (i.e., 0.03–0.04) and decreases inspired O\textsubscript{2} from normal of 20.94 % to 17 %. There are pertinent considerations that suggest Sinkule et al.’s (Sinkule et al., 2013) results, obtained using an automated breathing and metabolic simulator (ABMS, Ocenco, Inc., Pleasant Prairie, WI), are not applicable to humans wearing an N95 or other COVID-19 protective mask as studied herein. Specifically:

1. Had the N95 or other mask evaluated herein reduced inspired O\textsubscript{2} and increased inspired CO\textsubscript{2} as contended by Sinkule et al., we can use the approximate alveolar gas equation to calculate the impact on alveolar and arterial P\textsubscript{O\textsubscript{2}} (P\textsubscript{a}O\textsubscript{2} and P\textsubscript{O\textsubscript{2}}\textsubscript{r}, West, 1990):

\[
P_{a}O_2 = \frac{[Pb – 47\times F\textsubscript{\text{E}}O_2]}{(P_{a}CO_2/R)}
\]

Where Pb is barometric pressure, F\textsubscript{\text{E}}O\textsubscript{2} is inspired O\textsubscript{2} fraction, P\textsubscript{a}CO\textsubscript{2} is alveolar PCO\textsubscript{2} (considered synonymous with arterial PCO\textsubscript{2} in these circumstances) and R is the respiratory exchange ratio (V\textsub{CO\textsubscript{2}}/V\text{O\textsubscript{2}}, ~0.8 on a mixed diet at rest).

Assuming P\textsubscript{a}CO\textsubscript{2} and P\textsubscript{a}CO\textsubscript{2} rise commensurately to ~60 mmHg, P\textsubscript{a}O\textsubscript{2} will fall from its control (non-mask) value ~100 mmHg to only ~30 mmHg! Such perturbations of the arterial blood gases would drive a massive hypercapnic response elevating both respiratory frequency and tidal volume, neither of which were evident grossly in the present simulator (ABMS, Ocenco, Inc., Pleasant Prairie, WI), are not applicable to 2013 ) results, obtained using an automated breathing and metabolic simulator.

2. What would the impact of achieving the levels of arterial hypoxemia (PaO\textsubscript{2}~30 mmHg) and hypercapnia (~60 mmHg) estimated above from Sinkule et al. (4) be? Ventilation increases some 2–3 L/min for each mmHg PaCO\textsubscript{2} rise by elevation of breathing frequency and tidal volume via stimulation of the peripheral (i.e., carotid bodies) and central chemoreceptors (Ainslie and Poulin, 2004; Cormack et al., 1957; Hirshman et al., 1975; Kronenberg and Severinghaus, 1971; Ogoh et al., 2009; West, 1990) and this response is massively potentiated by concomitant hypoxemic stimulation of the carotid bodies (Kronenberg and Severinghaus, 1971; West, 1990). As above, breathing frequency at rest and 97 W (constant-load exercise, Table 1), whilst increased slightly in certain instances (Table 1), did not evidence the substantial tachypnea expected from any massive derangement of blood gases; had such occurred.

3. Unlike rebreathing in a closed system, the small-to-modest dead space increases provided by the mask (~40–140 ml) would only increase the CO\textsubscript{2} load and decrease inspired O\textsubscript{2} very little. Thus, using the upper extreme of the mask end-expiratory partial CO\textsubscript{2} elevation (Table 1) would theoretically increase inspired CO\textsubscript{2} by only ~7.0–10 ml/breath for the N95 (140 ml dead space) and less than 2.0 ml/breath for the surgical and flannel masks. These values would correspond to a mean elevation of only 0.4–1.5 % in inspired CO\textsubscript{2} for the N95 and 0.1–0.4 % for the surgical/flannel masks. In comparison with the estimated 200 ml CO\textsubscript{2}/min at rest and up to ~4,000 ml CO\textsubscript{2}/min or more exhaled during maximal exercise, clearing these tiny additional CO\textsubscript{2} loads would not require substantial additional ventilation compared to the no-mask condition.

Whereas the young, healthy males and females studied herein are expected to evade a small drop in SpO\textsubscript{2} at maximal exercise related to the Bohr-induced (temperature, acidity) rightward shift in the O\textsubscript{2} dissociation curve, they are far less likely to develop exercise-induced arterial hypoxemia (EIAH) than clinical populations, for example, with COPD or other pulmonary disease (Andrianopoulos et al., 2014; Casa-buri et al., 1991; Wagner et al., 1977). It is true, however, that EIAH can occur without underlying pathology in adults (Dempsey et al., 1984; Dempsey and Wagner, 1995; Dominelli and Sheel, 2019; Powers et al., 1989) and children (Nourry et al., 2004). Furthermore, EIAH may be present in females at far lower metabolic rates than in their male counterparts (Harms et al., 1998a) and reduce VO\textsubscript{2\text{max}} significantly (Harms et al., 2000) thus predating muscle fatigue and exhaustion (Romer and Dempsey, 2006; Romer et al., 2006b). Directly pertinent to the present investigation is that EIAH is both more prevalent and more extreme in highly trained or fitter individuals (Dempsey and Wagner, 1995; Dominelli et al., 2013; Dominelli and Sheel, 2019). Indeed, this population may be far more sensitive to even modest reductions in inspired (and thus alveolar) P\textsubscript{a}O\textsubscript{2} (Gore et al., 1996). For instance, when exercising maximally in a mildly hypobaric chamber (50 mmHg below sea level Pb, i.e., ~710 versus 760 mmHg) equivalent to ~580 m above sea level or inspiring 19.4 % O\textsubscript{2} at sea level, trained male cyclists (VO\textsubscript{2\text{max}}77 ml/kg/min) desaturated to 86.5 %. This desaturation compared with a value of 93.7 % in their untrained counterparts (VO\textsubscript{2\text{max}}51 ml/kg/min) and, crucially, decreased VO\textsubscript{2\text{max}} significantly only in the trained cyclists (see also Lawler et al., 1988). In the present investigation, our subjects included two endurance-trained individuals (>6 h training per week) whose relative maximal work rates (Watts/kg) on the incremental work test exceeded that of the other subjects by almost 50 % (range: 2.42–5.57 W/kg). Despite that the expectation was for these individuals to be extremely sensitive to even small reductions in inspired O\textsubscript{2}%, had such occurred, no mask-induced decreased O\textsubscript{2} saturation or work capacity was evident.

4.3. Work of breathing

Of course, a reduction in arterial O\textsubscript{2} saturation is not the only mechanism by which mask wearing can potentially decrease locomotory muscle O\textsubscript{2} delivery and thus exercise performance. As Harms and colleagues initially demonstrated, increasing the work of breathing by, for example, elevating inspiratory resistance during maximal cycling exercise, elevates leg vascular resistance and lowers blood flow, O\textsubscript{2} delivery and leg VO\textsubscript{2} (Harms et al., 1997; Wetter et al., 1999). These changes, in response to augmented respiratory muscle work, do not elevate cardiac output but, rather, redistribute (or “steal”) blood flow to the respiratory muscles that would normally have gone to the exercising leg muscles (Harms et al., 1998b). As such, during maximal exercise, a 28 % increase in the work of breathing, imposed by adding inspiratory resistance, elicits a ~1.3 L/min reduction in leg blood flow, and decreases maximal exercise capacity (Harms et al., 1997). Unfortunately, we were unable to measure the increased work of breathing induced by the three masks evaluated herein because doing so would have confounded our primary outcomes. However, the absence of any decrement in maximal exercise capacity argues strongly that any increase in the work of breathing had minimal impact on leg muscle(s) perfusion and work capacity.

4.4. Experimental considerations

4.4.1. Statistical power

Our statistical power to detect a 3% decrease in SpO\textsubscript{2} or 5% in peak power was ~0.9. The very low effect sizes reported for SpO\textsubscript{2} peak power, and the cardiovascular variables support the lack of substantial physiological differences with mask wearing in these recreational
exercisers. Sample size calculations based on our findings indicate that a sample size of >250 would be required to detect significant differences for SpO$_2$ (G*Power 3.1.9.2). With respect to SpO$_2$ it is pertinent that these results are for young, healthy active individuals for whom the respiratory system has arguably been considered "overbuilt" for exercise (Dempsey and Johnson, 1992; Dempsey et al., 2003) and in whom the incidence of expiratory flow limitation or arterial hypoxemia attending maximal cycling exercise is expected to be low. That said, the 6 young, healthy active women (54 % of the tested sample size) would be more likely to experience expiratory flow limitation compared to men (Guettet et al., 2007; Guettet and Sheel, 2007). We acknowledge that our results likely do not apply to elite athletes or patient populations, especially the latter with emphysema/COPD or the elderly, in whom pulmonary function limits or is close-to-limiting exercise performance, who do experience expiratory flow limitation, respiratory muscle fatigue and/or erosion of arterial blood gasses during exercise (e.g., Yoshimura et al. (Yoshimura et al., 2014); Kalinov et al. (Kalinov et al., 2019)). Moreover, whereas elite athletes may be more physiologically susceptible to modest increases in breathing resistance from a mask they also demonstrate greater motivation that may diminish performance decrements (Martin et al., 2016).

4.4.2. Duration of exercise

A second experimental consideration is the duration of exercise. The exercise bouts evaluated herein were designed to explore the full range of whole-body O$_2$ transport such as can be achieved by the maximal ramp protocol to exhaustion in sufficiently well-motivated subjects (Poole and Jones, 2017). Including resting and baseline measurements, subjects wore each mask for 20–25 min. We did not employ extended (at least beyond 3 min) square-wave exercise protocols which, in the moderate or heavy exercise intensity domains, could have been sustained for far longer durations. Thus, our investigative protocol, whereas it effectively stressed the upper extremities of oxidative demands did not evaluate the effect of mask wearing on endurance capacity per se.

4.4.3. Ecological validity

As detailed in the Methods, to the extent possible, we specifically designed a measurement protocol that did not in-and-of itself change what was being measured. This included avoiding application of a one-way non-rebreathing valve or respiratory mask necessary for determination of ventilatory volumes and flows as well as VO$_2$, VCO$_2$ and respiratory patterns. This is in contrast to recent work by Fikenzer et al. that evaluated physiological variables during incremental exercise with standard spirometry mask placed over the COVID mask in a leak-proof manner (Fikenzer et al., 2020). Similar to our findings they observe no differences in peak arterial PO$_2$ and key cardiovascular variables. However, the translatability of their findings to real settings is limited by the addition of the leak proof spirometry mask, as this combination can substantially alter pulmonary gas exchange efficacy and arterial blood gasses. It may also alter peri-oral temperature, which may exacerbate the intensity of dyspnea compared to wearing each mask in the prescribed manner and as described by the CDC (i.e., not leak proof).

Thus, although the work of breathing (WOB) was undoubtedly increased herein that increase was not sufficient to divert enough cardiac output away from the locomotory muscles to have a major impact on the maximal work rate/exercise tolerance. As mentioned above, Harms and colleagues (Harms et al. J Appl Physiol 82:1573–83, 1997; 85:609–18, 1998; Harms et al. 89:131–8, 2000) previously demonstrated that increasing the WOB via elevated inspiratory resistance reduced leg blood flow (Harms et al., 1997) and maximal exercise tolerance (Harms et al., 2000) significantly but the subjects were able to work at the same “maximal” work rate under all conditions (albeit for different durations). We believe that how the masks tested herein operate at high ventilations is that there is effective leakage of inspired and expired ventilation around the mask periphery: Such that the in vivo resistance may well have been reduced below that presented in Fig. 1 where no leakage was allowed. We believe that this aspect of the study adds ecological validity to the present investigation as this is how the public actually uses these masks.

4.4.4. Different masks

As is evident from the opinions expressed in the literature (Davis and Tsen, 2020), when protective “masks” are considered, there are many different types (e.g., gas masks) and configurations reflecting specific environments for which they are designed. Results from wearing those masks, or even multiple layers of COVID-19 masks, whilst relevant to their particular circumstance should not be confused with the evaluation of the COVID-19 relevant masks evaluated herein.

4.5. Conclusions

The findings that neither arterial oxygenation, maximal exercise capacity nor submaximal cardiovascular responses are compromised by surgical, flannel, or N95 masks worn to help prevent COVID-19 transmission has important implications. Specifically, because physical inactivity and the resultant decrease in cardiorespiratory fitness (e.g., maximal O$_2$ uptake, (Blair, 2009)) and metabolic health (Krogh-Madsen et al., 2010; Mikus et al., 2012; Thyfault and Krogh-Madsen, 2011) are major cardiovascular and all-cause risk factors, any additional road-block or disincentive to exercise conveys a major public health burden. Thus, at least for the young healthy subjects herein, mask wearing does not present a physiological barrier to physical exercise, from a cardiovascular and arterial oxygenation perspective. However the increased dyspnea rating that attended exercising with any of the masks investigated herein, may still present a deterrent to exercise for some individuals. We acknowledge that there is a pressing urgency to investigate the impact of mask wearing on at-risk individuals including the aged and patient populations.

Disclosure statement

We state that this manuscript is not under consideration elsewhere and that the research reported will not be submitted for publication elsewhere until a final decision is made as to the acceptability of the manuscript. There is no financial or other relationship that influenced the outcome of this paper. In addition, this manuscript represents original work without fabrication, fraud or plagiarism and has been read and approved by all authors.

Funding

None.

Declaration of Competing Interest

The authors declare no conflict of interests.

Acknowledgements

The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The authors gratefully acknowledge Mr. Alec Butenas for his contributions to this research.

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