Medical Engineering and Physics 98 (2021) 50–56

Contents lists available at ScienceDirect

Medical Engineering and Physics

journal homepage: www.elsevier.com/locate/medengphy

What do masks mask? A study on transdermal CO_2 monitoring

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ARTICLE INFO

Keywords:
COVID-19
Carbon dioxide
Facemask
non-dispersive infrared
Personal protective equipment
Transdermal monitoring

ABSTRACT

Medical professionals have complained of extreme discomfort and fatigue from continuous wearing of N95 respirators (N95) overlaid with surgical masks (SM) and face shields (FS) during COVID-19 pandemic. However, there are no reports on the effect of face coverings on transdermal CO_2 ($TrCO_2$) levels (a measure of blood CO_2) during moderate activity. In this study, real-time monitoring of $TrCO_2$, heart rate and skin surface temperature was conducted for six subjects aged 20–59 years with and without wearing personal protective equipment (PPE). We initially studied the effect of wearing PPE (N95+SM+FS) at rest. Then, the effect of moderate stepping/walking activity (120 steps per minute for 60 min) while wearing PPE was evaluated. In addition, we investigated the effect of exercising intensity with different masks. We observed a significant difference ($p < 0.0001$) in $TrCO_2$ levels between without and with PPE during moderate exercise, but not while resting. $TrCO_2$ levels were correlated to exercise intensity independently with masking condition and breathability of masks. For the first time, we present data showing that a properly fitting N95 worn along with SM and FS consistently leads to elevated $TrCO_2$ under moderate exertion, which could contribute to fatigue over long-term use.

1. Introduction

The ongoing pandemic has led to widespread implementation of mandates to wear masks especially in indoor public spaces. The WHO has similarly recommended when and how to use facemasks [1] on a daily basis, which has led to mask wearing in situations not previously considered. Recent studies have claimed that community use of facemasks and implementation of mandates [2] resulted in more than 200, 000 COVID-19 cases being averted by May 22, 2020, and modelling studies [3] on universal masking forecast to save an additional 129,574 lives from September 22, 2020 through the end of February 2021. Medical professionals have routines adopted face-shields in addition to double-masking. Double-masking for the general public has been recommended as COVID-19 variants have emerged.

Even as clarity on the efficacy of facemasks in inhibiting airborne transmission of COVID-19 is emerging, [4] a Danish randomized controlled trial has found that wearing of a surgical mask (SM) in a community with modest infection rates did not reduce the infection rate by more than 50% [5]. There is even more ambiguity regarding blood gases, specifically the impact on gas exchange of carbon dioxide (CO_2) and oxygen (O_2) imposed by facemasks, under moderate exertion. A recent meta-review reported the effects of different facemasks and the cardiorespiratory response to physical activity, which suggested that dyspnea might increase and modify apparent effort with activity. However, it was concluded that the effect on blood gases imposed by facemasks during physical activity is trivial and negligible to detect, even while performing vigorous exercise [6]. Another study has presented no significant changes in gas exchange, O_2 saturation or CO_2 levels with the use of SM even in subjects with severe lung impairment [7]. Further, in a small crossover study, no decline in O_2 saturation was observed in older participants wearing a 3-layer nonmedical facemask [8]. Additionally wearing a mask for an average of 90 min during a flight-training mission does not appear to increase CO_2 retention in the body or the ability to attain O_2 [9].

However, study on the use of FFP-2 respirator with SM cover by healthcare workers during this COVID-19 outbreak has been found to

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https://doi.org/10.1016/j.medengphy.2021.10.013
Received 22 July 2021; Received in revised form 15 October 2021; Accepted 24 October 2021
Available online 27 October 2021

significantly increase the end-tidal CO_2 and fractional inspired CO_2 pressure values, without any disease while in resting position [10]. Another study also showed CO_2 in mask increase with facemasks but remains below short-term National Institute for Occupational Safety and Health limits [11]. More comprehensive studies need to be undertaken for drawing meaningful conclusions in light of certain other studies that claim facemasks reduce O_2 availability, prevents exchange of CO_2 and results in hypercapnic and hypoxic conditions while exercising [12,13]. Close monitoring of respiratory status is critical, especially since there has been an increase in the use of respirators with high filtering performance, (i.e., N95-type), that are also associated with several concerns relating to physiological effects [14], including silent hypoxia and poor oxygenation [15] during early stages of COVID-19. Despite vaccination rates steadily increasing, experts are suggesting that mask wearing continue for everyone and certainly for frontline workers.

In the current study, we present the results from real-time measurement of transdermal CO_2 ($TrCO_2$) levels during exercising and resting conditions, while wearing PPE face coverings. The transdermal measurement approach was chosen as it is non-invasive and the face covering would not be impeded. It has also been previously validated to be reflective of blood CO_2 levels [16]. Usage of the word 'exercise' in this study implies moderate activity/execution of routine tasks. Our study has broad implications related to health and wellbeing, especially during this COVID-19 pandemic. However, our findings are more pertinent to healthcare workers, due to their constant usage of single-use N95 together with SM and patterns of exertion. For the first time, we present that a properly fitted PPE, specifically an N95 worn along with a SM consistently leads to elevated CO_2 under moderate exertion, which could contribute to fatigue. The intent of our article is to understand the physiological effects of mask wearing, and to spur better mask designs and positive ventilation to ameliorate deleterious effects of prolonged mask wearing. In addition, we demonstrate a path towards a wearable transdermal CO_2 sensor.

2. Experimental section

2.1. Systems and experimental design

$TrCO_2$ emission rate could be influenced not only by using PPE but also by other factors. To take these effects into account, room temperature (RT) and relative humidity (RH) sensors (GSP-6, Elitech, USA) were installed in the experimental environment, and subjects wore a skin surface temperature (SST) sensor (GSP-6) and a $TrCO_2$ sampler on the inner side of the forearm, along with a heart rate (HR) sensor (H1, Polar, Finland) on the chest (Fig.1A). Fig. 1B shows a simplified diagram of previously developed rate-based $TrCO_2$ measurement system [17]. The system automatically repeats a purging process with pure N_2 aeration for 30 s and recirculation for 60 s. During recirculation, CO_2 continuously diffuses across the skin through the contacting aperture of the sampler using N_2 as the carrier. The CO_2 concentration in the recirculated N_2 increases according to various parameters, including blood CO_2 concentration. $TrCO_2$ emission rate can hence be monitored every 90 sec in real-time. In this system, a new design of the $TrCO_2$ sampler with a spiral channel was adopted to improve the efficiency of $TrCO_2$ extraction without heating the skin (Fig. S1). Fig. S2 presents the collection arrangement used to obtain the preliminary results which demonstrate good stability of the system. We used this experimental platform to perform a two-pronged study: static and dynamic measurements, as presented in Fig.1C. The static study examined the effect of PPE wearing on $TrCO_2$ under stable conditions. In contrast, the dynamic study examined the effect of PPE wearing upon significant changes in activity, imitating work and exercise.

This study was authorized by the Institutional Review Board at the University of Maryland, Baltimore County (Protocol Number 89) was in accordance with the latest version of the Declaration of Helsinki. Healthy volunteers (five male and one female) were enrolled in this study after obtaining a written informed consent. Table S1 provides the details on the subjects obtained using a questionnaire prior to conducting the experiments. Age (in years) and BMI (kg/m^2) differed by 38.7 ± 14.5 and 24.8 ± 5.5, respectively (mean $\pm$ SD). Data analysis was performed using R software (cran.project.org) version 4.0.0. The PPEs

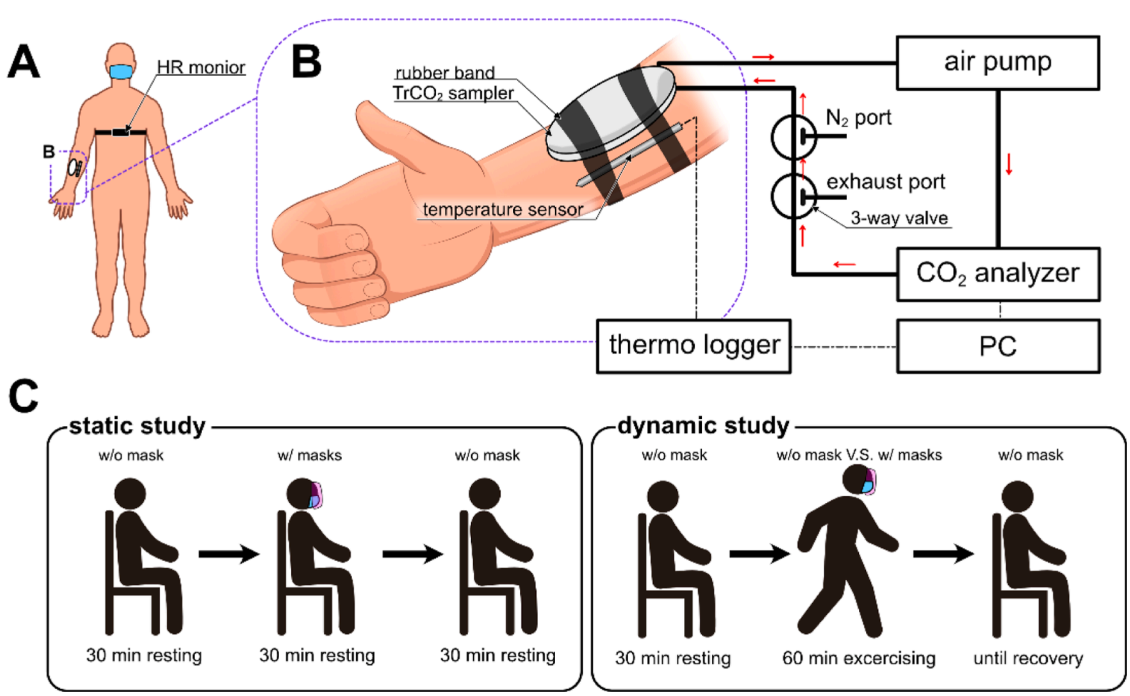

Fig. 1. *Systems and experimental design.* (A) Overview of sensor equipment used for different measurements. (B) Detailed view of sensor head placed on the inner side of the subject's forearm. A $TrCO_2$ sampler connected to the previously reported rate-based transdermal CO_2 analysis system. (C) Two types of experimental conditions were used to investigate the effect of masks on CO_2 levels in the body.

used in this study (Fig. S3) along with other experimental methods are described in the supplementary appendix. During the scheduled experiments conducted in triplicates, the six subjects were first provided with testing instructions, familiarized with the collection system and provided with quantitative fit-tested respiratory devices. The subjects maintained similar diet and fluid intake during all the testing phases of the study.

2.2. Static study

In this study, experiments were initiated within 2 h of the subjects' meals. The study subjects first rested on a chair with the wearable sensors on and without a mask for 30 min. They were then asked to wear N95 (3 M, USA) overlaid with a SM, a face shield (FS) and asked to rest on the chair for 30 min. Finally, the subjects were asked to remove the PPE and continue to rest on the chair for another 30 min. Data acquiring frequency for each of the parameters was as follows: 0.01 Hz for $TrCO_2$ emission rate, 1 Hz for HR, and 0.1 Hz for RT, RH, and SST. These experiments were done in triplicates and each of the subjects completed the experiments on separate days.

2.3. Dynamic study

In this set of experiments, the diet conditioning of the study subjects was the same as in the case of the static study. Here, the study subjects first rested on a chair with the wearable sensors and without wearing a mask for 30 min. In the second phase involving exercise, the subjects were asked to maintain a step rate of 120 steps per minute (spm, audio click) for 60 min. The exercising phase had two patterns: controls (without PPE) and while wearing N95 overlaid with SM and FS. The mask-fitting check was manually done by the subject, and then visually inspected by the investigators. Finally, the subjects sat on the chair for 60 min without a mask for both patterns of the exercising phase. Armpit temperature (AT) and oxygen saturation (SpO2) was measured every 10 min in addition to data acquisition from the other sensors, as described in the static study design. Each subject performed two sets of experiments (exercising phase without and with masks) per day. The order of exercising patterns was randomized. The complete protocol was implemented for three days with at least one rest day in between.

3. Results

3.1. Effect of wearing PPE on $TrCO_2$ and HR while resting

Fig. 2A shows the typical time course variation of $TrCO_2$, HR, RT, RH, and SST parameters. We have defined the three 30 min phases concerning before, during, and after PPE wearing as P1, P2, and P3, respectively. The environmental parameters, HR, and SST were observed to be stable through the 1.5 h of experiments. $TrCO_2$ rate fluctuated negligibly, but this is attributed to the diurnal fluctuation observed in Fig. S2. There are no significant differences in both $TrCO_2$ and HR parameters with confidence intervals of 95% (Fig. 2B). Moreover, we did not observe any differences in other study subjects beyond individual differences.

3.2. Time course studies on $TrCO_2$ emission rate without and with PPE during rest and moderate activity

The supplemental video 1 shows the record of one experiment pertaining to Section 3.4 for reference. The only PPE wearing condition and stepping rate is differed from the experiment in this section. Fig. 3A and B present the variation in $TrCO_2$ rate, HR, RT, RH, SST, and AT overtime when exercising without PPE (control) and with concurrent wearing of N95, SM, and FS. The two sets of experiments were conducted on the same day with a study subject. P1′, P2′, and P3′ are phases of resting before exercise without PPE, during exercise, and resting after exercise without PPE, respectively. Subjects performed 120 steps per minute (spm) of stepping exercise during P2′ without (Fig. 3A) and with PPE (Fig. 3B). RT and RH were similar during each experiment. AT was stable in both of these conditions throughout the experiment. SST decreased on cooling due to sweat vaporization that occurred during P2′. $\Delta TrCO_2$ and ΔHR were defined as the difference between the minimum value obtained in the 0–30 min range and an average value of 80–90 min. $TrCO_2$ emission rate began to increase approximately 10 min later, after the onset of stepping, and was observed in both conditions to converge to a nearly plateau value during P2′ and then recovered to baseline in P3′.

3.3. Effect of wearing PPE on $TrCO_2$ in different study subjects while exercising moderately

Five subjects showed significant differences in $TrCO_2$ emission rate between the non-masked and masked (N95+SM+FS) conditions

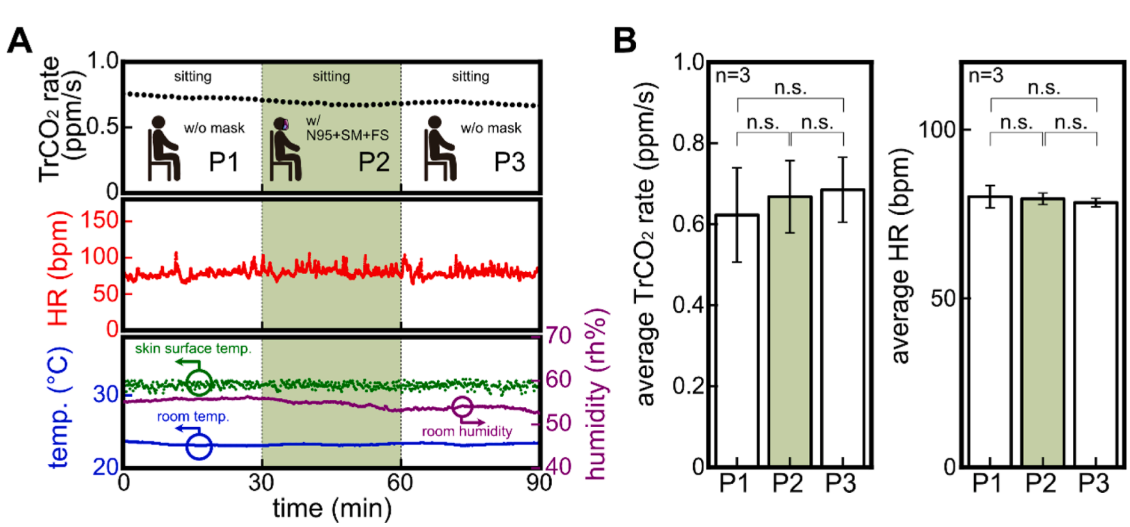

Fig. 2. *Effect of PPE on $TrCO_2$ rate and vitals while resting.* (A) A typical variation in $TrCO_2$ and vitals over time in static conditions observed without and with PPE-N95, SM, and FS. P1, P2, and P3 represent the data before, during, and after PPE wearing, respectively. (B) Comparison of the average $TrCO_2$ emission rate and HR in each of the phases. n.s.: no significant difference.

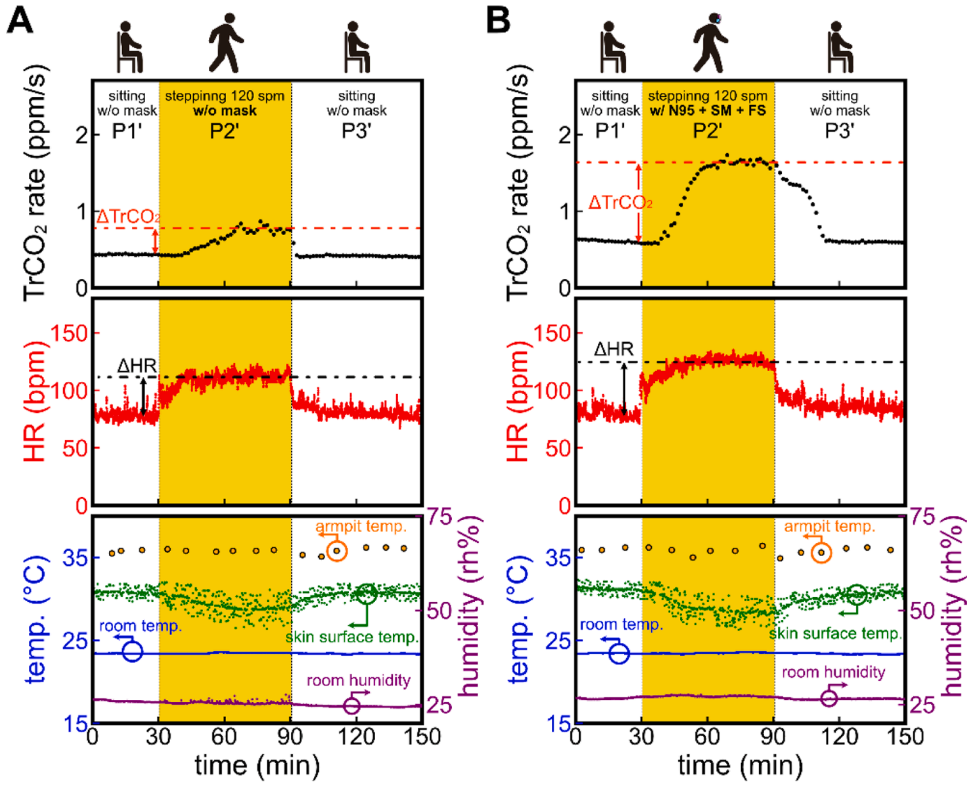

Fig. 3. *Time course studies on $TrCO_2$ emission rate, HR, RT, RH, SST, and AT in the dynamic study at 120 spm.* (A) Data from trial without PPE; (B) Data from trial while wearing PPE-face coverings, N95 overlaid with SM and FS during P2′. $\Delta TrCO_2$ and ΔHR were defined as the difference between minimum value of 0–30 min range and average value of 80–90 min.

(Fig. 4A–E). Note that experiment for subject 5 was conducted only once. Only subject 6 did not show any variation in $\Delta TrCO_2$ levels in both conditions (Fig. 4F). We have however not discarded the results from subject 6, as this is a first study of its kind and necessitates an in-depth understanding of the complex phenomena involved. Similar trends in variation in $\Delta TrCO_2$ levels was observed (with the exception of subject 6): $\Delta TrCO_2$ increased with a time delay from the start of exercise in both conditions, and the ascent rate of $\Delta TrCO_2$ without PPE was slower than with PPE, and the maximum value attained was also lower in this case. The shape of the curve and values of $\Delta TrCO_2$ differed among the five subjects. Fig. 4G shows differential curves of $\Delta TrCO_2$ levels between both conditions on the same day. The mean and SD between 80–90 min of those differences among subjects 1–5 were 0.52 ± 0.09 ppm/s, and the coefficient of variation was 17.5%. Significant differences were observed as results from *t*-tests that were performed using the $\Delta TrCO_2$ emission rate without and with PPE for each study subject (Fig.4H). Moreover, a significant difference was also observed when a *t*-test was performed on the complete data set (six subjects, thirty-two experiments), including the data from subject 6, where no variation was observed. The mean ± SD of $\Delta TrCO_2$ values without and with PPE were 0.29 ± 0.25 and 0.71 ± 0.43 ppm/s, respectively. The median of each condition was similar to its mean: 0.28 ppm/s for no PPE and 0.70 ppm/s while wearing PPE. The same analysis was applied to HR and SST (Figs. S4 and S5). Briefly, there is no significant difference between non-mask and N95+SM+FS (PPE) on ΔHR and ΔSST values.

3.4. *Effect of types and wearing pattern of PPE on $TrCO_2$*

Fig. 5 presents $\Delta TrCO_2$ emission rate when the PPE type or the overlay pattern was changed. In order to observe small changes, the exercise intensity was fixed at 140 spm, which induces the largest change in $TrCO_2$ (Fig. S6C). The inset pictures on the right in Fig. 5 present images of a subject wearing a PPE under each of the study conditions. $\Delta TrCO_2$ emission rate without PPE, with a cloth mask (CM), and with FS indicated nearly the same value: 0.65 ± 0.05, 0.68 ± 0.07, and 0.63 ± 0.03 ppm/s, respectively. $\Delta TrCO_2$ values with N95-only and SM-only was marginally higher (0.91 ± 0.04 and 1.03 ± 0.05 ppm/s) than that of without PPE, with CM, and with FS. $\Delta TrCO_2$ levels with N95 covered by SM (1.21 ± 0.06 ppm/s) or SM and FS (1.58 ± 0.05 ppm/s) were higher than the $\Delta TrCO_2$ levels of the N95 alone.

4. Discussion

In the resting state, there was no variation in the $TrCO_2$ emission rate, although wearing N95 overlaid with SM and FS (Fig. 2B). Hence, wearing a PPE with higher breathability (e.g., wearing only the N95 respirator) rather than N95 overlaid with SM and FS will definitely not alter the $TrCO_2$ levels while resting. This confirms that rebreathing alone, which can be caused by wearing a PPE, does not seem to have a significant effect on CO_2 concentration.

In contrast, during moderate exercise, the $TrCO_2$ emission rate increased even when the subject did not wear a PPE, and a larger increase was induced by wearing N95 overlaid with SM and FS. In our study, we did not use a standard instrument such as an ergometer; however, 120 spm of exercise is in the range of moderate (3 metabolic equivalents; METs) to vigorous (6 METs) exercise [18]. The threshold of exercise intensity at which the $TrCO_2$ levels increase is still debatable on account of large individual differences. Even the CDC has cited the Roberge study that concluded there was no significant difference in pCO_2 after 1 h of mild/moderate exercise while wearing N95 alone and in contrast to N95 overlaid with SM, where 2 out of 10 subjects showed a change in pCO_2 [19,20]. However, $TrCO_2$ levels can increase significantly as a person exercises moderately while wearing N95 overlaid with SM and FS. Sinkule et al. showed that higher concentration in inhaled CO_2 while wearing SM covered N95 compared to N95-only [21]. In our six study subjects, only subject 6 did not show a $TrCO_2$ change

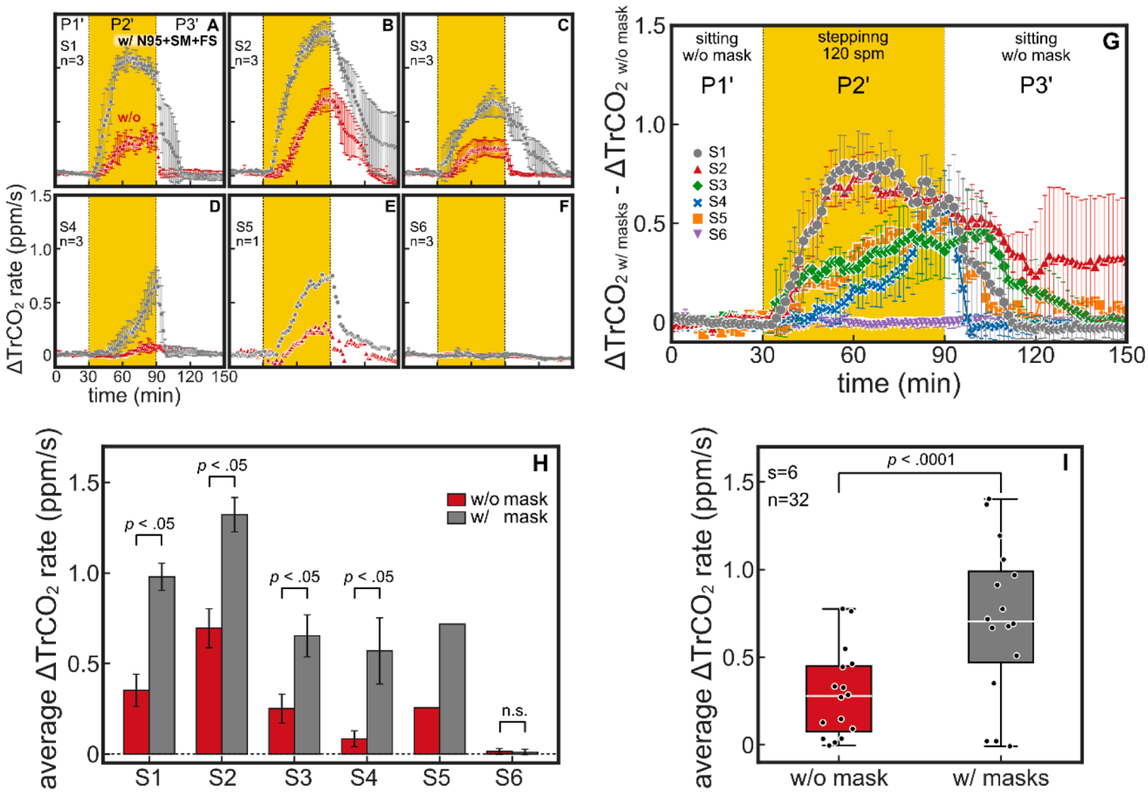

Fig. 4. *Effect of wearing PPE face coverings on TrCO₂ levels during moderate exercise.* (A–F) Time course studies on $\Delta TrCO_2$ without PPE (▲) and while wearing PPE-N95 overlaid with SM and FS (●) in subjects 1–6. $N = 3$ except for subject 5. Each plot and error bar indicates mean value and SD. (G) Comparison of differential values of $\Delta TrCO_2$ emission rate without and with PPE obtained on the same day. There are six curves represented subject 1 (●), subject 2 (▲), subject 3 (◆), subject 4 (×), subject 5 (■), and subject 6 (▼). Each plot and error bar represents mean value and SD that were calculated with experiments performed on different days. (H) Comparison of $\Delta TrCO_2$ emission rate between without and with PPE in each of the subjects with error bars representing SD. Mean value and SD were calculated from the values at 80–90 min in each experiment shown in (A–F). n.s. represents no significant difference. (I) Comparison of $\Delta TrCO_2$ emission rate between without and with PPE using data from all subjects (six subjects, thirty-two experiments). Boxes, white lines, error bars, and subplots (●) indicate quartile range, median, data range, and individual experimental data, respectively.

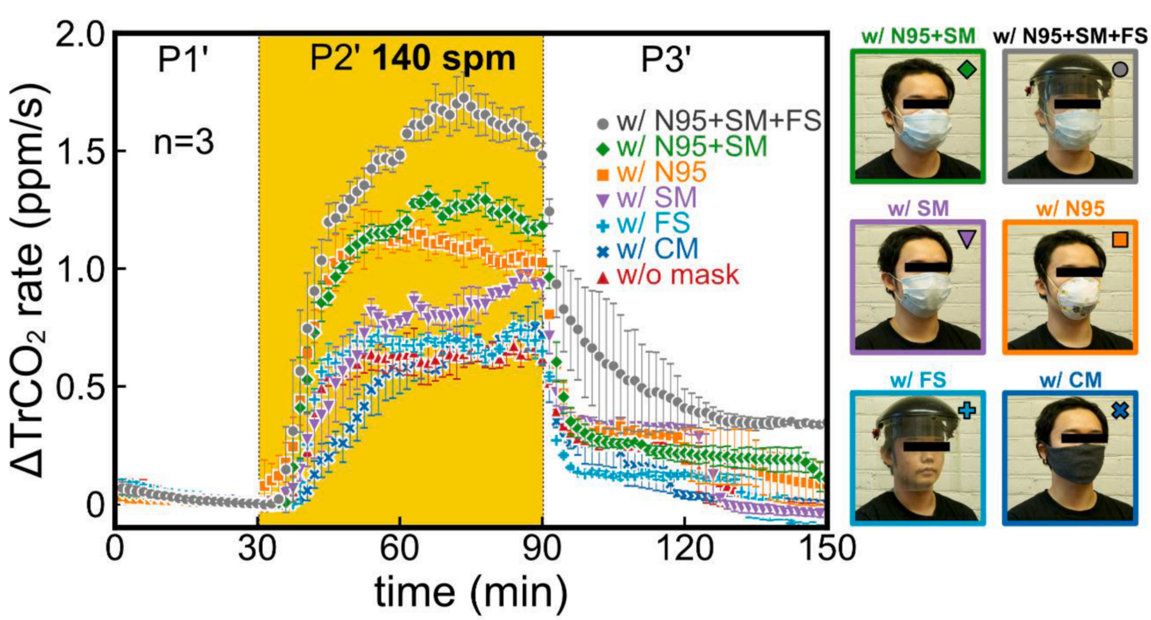

Fig. 5. *Effect of PPE face coverings breathability on TrCO₂ levels.* Time course of $\Delta TrCO_2$ emission rate with various types and overlaying patterns of PPE during 140 spm of stepping exercise: with N95 overlaid with SM and FS (●), with N95 overlaid with SM (◆), with N95 (■), with SM (▼), with FS (+), with CM (×), and without PPE (▲). Each plot and error bar indicates mean and SD calculated with data from triplicate studies.

both without and with PPE (Fig. 4F). This result may also be due to individual differences in tolerance to exercise. This subject particularly was in the habit of playing soccer, a sport with relatively high physical activity. It is hence possible that the subject did not reach the intensity threshold for $TrCO_2$ to increase with 120 spm of exercise. This discussion is supported by the fact that $TrCO_2$ did not increase in subject 1 during the 80 spm exercise without and with PPE (Fig. S6A–C). As a result, on subject-wide comparison (six subjects, thirty-two experiments), there are significant differences between without and with PPE while performing moderate exercise. This is especially since $TrCO_2$ levels can be affected not only by blood CO_2 concentration but also by variation in SST, blood flow, physical condition, and skin conditions, to name a few. ΔSST and ΔHR did not differ significantly between subjects without and with PPE (Figs. S4I and S5I). Further, variations of physical and skin conditions were negated by executing control experiments (exercising without PPE) along with exercising while wearing PPE, on the same day. In principle, non-dispersive infrared (NDIR) CO_2 sensors can be affected by water vapor in gaseous samples, however, a NDIR CO_2 sensor that was used in our study compensated for water vapor interference by measuring the reference signal. In addition, a high correlation between $TrCO_2$ and arterial blood gas pCO_2 was measured by the same rate-based method in the previous study [16], although the sampler geometry was different. These findings suggested that the variations in $TrCO_2$ observed during the experiment correlate with the changes in CO_2 concentration in the body. These results are in correlation with the qualitative assessment on suffocation experienced during the dynamic study by the study subjects (Fig. S7). Note that there was a limit to the number of human subjects we could access during this study. In order to extend these findings to a general conclusion, it would be necessary to investigate with a larger sample size. Another current limiting factor is the fact that it is different from the actual working situation where health care workers have to walk around and speak.

$\Delta TrCO_2$ levels on different types and overlaying patterns of PPE (Fig. 5) correlate well with filtering performance or breathability of PPE [22–25]. There were two interesting observations as seen in Fig. 5: (1) when N95 and SM were layered, the profile of $\Delta TrCO_2$ was similar to when N95 was worn alone; (2) use of the FS alone showed a similar $\Delta TrCO_2$ profile to when PPE were not worn. The differences however became larger when the FS was added to SM covering N95. The first observation in the current study is consistent with the findings of a previous study by Roberge et al. [20] However for the second observation, computational fluid dynamics studies on airflow around the mask would augment the understanding in this arena. It has been shown that exhaled air can easily diffuse beyond the FS into the ambient air when the mask is not worn [26,27]. In contrast, when SM covering N95 was worn inside FS, the mask caused a pressure loss in the exhalation [28–30]. As a result, exhaled air could stay in the vicinity of the masks, and furthermore, the FS could prevent diffusion of the exhaled breath into the ambient environment, which promotes re-inhalation of exhaled air. Note that we observed significant changes in $TrCO_2$ with bag breathing that mainly contributes to re-breathing (Fig. S8). Thus, there is a trade-off between the filter performance and breathability of a mask. Considering variations in $TrCO_2$ levels as in our study and earlier studies that have evaluated the filtering performance of masks, it is likely that SM would be the first choice for the general public when exercising in indoor gyms.

On the other hand, a recent study showed that commercially available powered air purifying respirator that enhance breathability could prevent headache related to PPE [31] induced by hemodynamic alterations [32]. We are confident that our device will support the rapidly advancing research on filter materials [33,34] and designs [35,36] will lead to engineering of ergonomic masks that do not compromise on filter performance and breathability.

Continuous transdermal CO_2 monitoring using a wearable sensor may provide physiological insights that are of value to a number of medical applications and disease states [37]. Our earlier approach is readily amenable to a wearable format (Fig. S9) by modifying a CO_2 sensor previously designed for bioprocess monitoring [38,39].

5. Conclusions

We observed a significant effect on wearing N95 overlaid with SM and FS during moderate exercise/activity on $TrCO_2$ levels, but not while resting. There is however no significant difference in HR and SST while exercising with masks. Individual differences in exercising tolerance affect $TrCO_2$ levels during activity. Hence, having a personal $TrCO_2$ monitor will be a prudent solution to monitor the health of first responders in this pandemic. Given the disadvantages and limitations of the existing technologies, there is clearly a need for the development of new generation devices for rapid and accurate assessment of respiratory status to better guide clinical practice. Further studies are currently underway for a more comprehensive understanding.

CRediT authorship contribution statement

Kenta Iitani: Investigation, Visualization, Project administration, Formal analysis, Funding acquisition, Writing – original draft. **Joel Tyson:** Methodology, Investigation. **Samyukta Rao:** Investigation. **Sai Sathish Ramamurthy:** Project administration, Supervision, Writing – original draft. **Xudong Ge:** Project administration, Supervision. **Govind Rao:** Conceptualization, Project administration, Supervision, Funding acquisition.

Declaration of Competing Interest

None declared.

Acknowledgments

We thank Dr. Yordan Kostov for the design of the instrumentation in connection with the rate-based $TrCO_2$ measurement system. This study is dedicated to first responders who serve and protect while constantly wearing masks.

Funding

This work was supported by NIH, Grant No. 1U01EB021952-01 and Japan Society for the Promotion of Science (JSPS), Grant-in-Aid for JSPS fellows No. JP19J01649.

Ethical approval

This study was approved by the Office of Research Protections and Compliance, University of Maryland Baltimore County.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.medengphy.2021.10.013.

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