The Effects of Wearing a 3-Ply or KN95 Face Mask on Cerebral Blood Flow and Oxygenation

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Background: The SARS-CoV-2 virus has impacted life in many ways, one change being the use of face masks. Their effect on MRI-based measurements of cerebral oxygen levels with quantitative susceptibility mapping (QSM) and cerebral blood flow (CBF) is not known.

Purpose: This study investigated whether wearing a face mask leads to changes in CBF and cerebral venous oxygen saturation measured with MRI.

Study Type: Repeated-measures cohort study.

Population: A total of 16 healthy volunteers (eight male, eight female; 22–36 years) were recruited for the 3-ply study. Ten of the 16 participants (five male, five female; 23–36 years) took part in the KN95 study.

Field Strength/Sequence: A 3 T, single-delay 3D gradient-and spin-echo pseudo-continuous arterial spin labeling (pCASL) scan for CBF quantification, and gradient-echo for QSM and oxygenation quantification.

Assessment: Gray matter CBF and magnetic susceptibility were assessed by masking the pCASL CBF map and the QSM map to the T_1-weighted gray matter tissue segmentation. Venous oxygenation was determined from venous segmentation of QSM maximum intensity projections.

Statistical Tests: Paired Student's t-tests and Cohen's d effect sizes were used to compare the face mask and no face mask scans for gray matter CBF, gray matter magnetic susceptibility, and cerebral venous oxygen saturation. Standard t-tests were used to assess whether the order of scanning with and without a mask had any impact. A statistical cut off of $P < 0.05$ was used.

Results: The 3-ply masks increased gray matter CBF from an average of 43.99 mL/(100 g*min) to 46.81 mL/(100 g*min). There were no significant changes in gray matter magnetic susceptibility ($P = 0.07$), or cerebral venous oxygen saturation ($P = 0.36$) for the 3-ply data set. The KN95 masks data set showed no statistically significant changes in gray matter CBF ($P = 0.52$) and magnetic susceptibility ($P = 0.97$), or cerebral venous oxygen saturation ($P = 0.93$).

Data Conclusion: The changes in blood flow and oxygenation due to face masks are small. Only CBF increased significantly due to wearing a 3-ply mask.

Evidence Level: 2

Technical Efficacy: Stage 3

During the COVID-19 pandemic, face masks have been mandated or at least recommended in large parts of the world, as they help contain the spread of COVID-19.[1–3] While the benefits of masks are largely undisputed within the scientific community, some people are concerned that face masks negatively affect the brain's oxygen supply.[4,5] However, since wearing a face mask results in re-breathing of some of the CO_2-enriched exhaled air, and since CO_2 is a strong

vasodilator, cerebral blood flow (CBF) and therefore oxygen supply to the brain should not decrease but may even show a small increase due to wearing a face mask.[4,6] Increasing the CO_2 concentration in the inhaled air to 5%, for example, can lead to a rise in CBF by up to 50%.[6] Blood flow can be measured with MRI using arterial spin labeling (ASL), where the signal of inflowing blood is labeled with a radiofrequency pulse in the neck region.[7] Changes in blood oxygenation can be detected by measuring the magnetic susceptibility (χ) of the blood vessels or tissues via the phase of gradient echo MRI scans.[8] The more oxygenated the blood, the less paramagnetic it is, relative to the surrounding tissue.[9] The aim of this study was to test whether the wearing of face masks affects MRI-based measurements of cerebral blood flow and oxygenation.

Methods

Participants

The study was approved by the University of British Columbia Clinical Research Ethics Board. All volunteers gave written, informed consent and were required to answer a COVID-19 questionnaire at the time of booking and upon arrival for the MRI scanning appointment. Participants were recruited with the inclusion criteria of being 18 years of age or older, no contraindications for MRI, and no underlying health conditions. The participants were scanned on a 3 T MR system (Ingenia Elition; Philips Medical Systems, Best, The Netherlands) with and without a 3-ply procedural mask with ear loops (American Society for Testing and Materials [ASTM] level 3). Half of the recruited participants were scanned with the face mask first and the other half were scanned with the face mask second. The participants were recontacted and those who agreed to return for a scan with the KN95 mask (similar to the European FFP2 mask) were rescanned approximately 4 months later with the same scanning parameters and procedures. The metal nose strips were removed from the masks prior to scanning and the masks were taped to the skin left and right of the nose to mimic the effect of the nose strip. When donning and doffing face masks the subjects were removed from the scanner but remained lying down. The time between donning or doffing the mask and the ASL scan was at least 8 minutes.

Scanning Procedures

A 3D T_1-weighted scan (repetition time [TR] = 1.7 msec, echo time [TE] = 3.55 msec, flip angle = 8°, voxel size = $1 \times 1 \times 1$ mm^3, scan duration = 3 min 42 sec), a 3D gradient-and-spin-echo pseudo-continuous arterial spin labeling (pCASL) scan (TR = 4234 msec, TE = 10.61 msec, postlabeling delay = 2000 msec, label duration = 1800 msec, background suppression on, voxel size = $3 \times 3 \times 6$ mm^3, scan duration = 5 min 26 sec), and a 3D gradient echo scan

(TR = 28.4 msec, TEs = 6,12, 18, 24 msec, flip angle = 15°, voxel size = $0.69 \times 0.69 \times 0.69$ mm^3, scan duration = 6 min 28 sec) were acquired.

During scanning, pulse oximetry was performed and SpO_2 measures were taken during each of the two ASL scans.

Data Processing

All images were visually inspected for motion and artifacts (inspected by A.F. <1 year of experience). CBF maps were calculated using the FSL BASIL toolbox with partial volume correction, using the 3D T_1-weighted image for structural information and the BASIL default partial volume threshold of 0.7 for the gray matter masking.[10,11] The average gray matter CBF was computed in the native pCASL space. Quantitative susceptibility maps (QSM) were computed from the fourth echo of the 3D gradient echo scan using the rapid two-step dipole inversion algorithm after Laplacian phase unwrapping and background removal using an in-house Matlab implementation of the V-SHARP method.[12–14] The QSM images were registered to the corresponding 3D T_1-weighted scan using FMRIB's Linear Image Registration Tool (FSL FLIRT).[15] A gray matter mask for the QSM analysis was computed from the 3D T_1-weighted scan using FMRIB's Automated Segmentation Tool (FSL FAST) with a threshold value of 0.9.[16] The gray matter QSM average values were computed in T1-weighted space. See left of Fig. 1 for an example slice of full unregistered CBF map. Slices inferior of the red nuclei were excluded from QSM analysis, as these brain regions are prone to artifacts from background field inhomogeneities.[9,17] The location of the red nuclei and the slices to be excluded were determined by A.F. (<1 year of experience) and confirmed by A.R. (20 years of experience). The nonregistered QSM images were also analyzed using blinded manual segmentation of a maximum intensity projection through the stack of slices that contains the internal cerebral, the anterior septal, and the thalamostriate vein. The slices to be included in the maximum intensity projection were defined by A.F. and confirmed by A.R. (20 years of experience). The venous portions that were segmented (defined by A.F. and confirmed by A.R. with 20 years of experience and C.B. with 10 years of experience) varied between each participant depending on the variable venous anatomy; however, the segmented sections were consistent between face mask and no mask scans.[18] Each segmentation contained portions of the internal cerebral vein, anterior septal vein and thalamostriate vein. The reason we chose to include the deep brain veins in this segmentation as opposed to cortical veins is due to erosion of veins at the surface of the brain during the QSM processing.

Due to presence of the nonvenous tissue in gray matter, the gray matter χ was not converted to cerebral venous oxygen saturation (CS_VO_2); only venous χ from the venous segmentation was converted. Therefore, the QSM image was
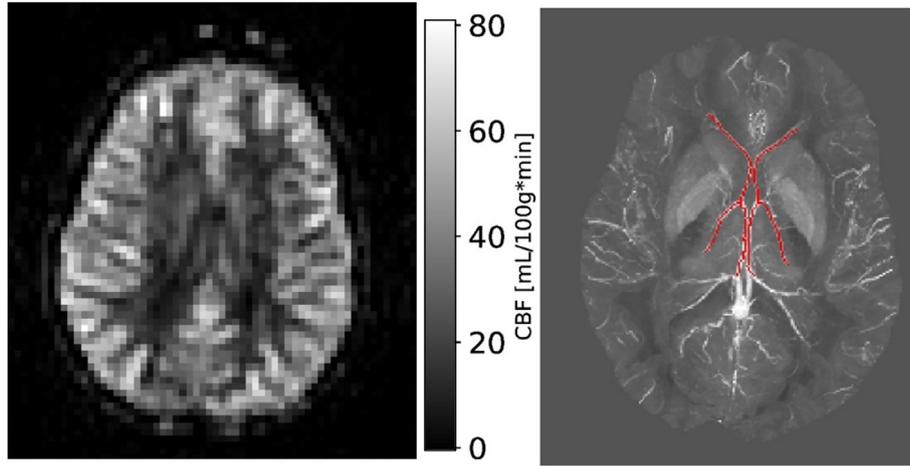
FIGURE 1: Left: Representative slice of full unregistered CBF map. Right: Example of venous segmentation of portions of the internal cerebral vein, anterior septal vein and thalamostriate vein (shown in red) done on the maximum intensity projection of QSM image for one participant's face mask scan.

analyzed in two ways, first as a gray matter susceptibility and second using the venous segmentation to convert to CS_VO_2. The equation used to convert the magnetic susceptibility to CS_VO_2 is

$$CS_VO_2 = 1 - \frac{\chi - \chi_{oxy} \cdot Hct}{\chi_{do} \cdot Hct},$$

where Hct is the hematocrit, χ is the magnetic susceptibility difference between blood and surrounding tissue, χ_{oxy} is the susceptibility difference between fully oxygenated blood and surrounding tissue, and χ_{do} is the magnetic susceptibility difference between fully oxygenated and fully deoxygenated blood. The following literature values were assumed: $\chi_{do} = 4 \cdot \pi \cdot 0.27 \approx 3.39$ ppm, $\chi_{oxy} = 4 \cdot \pi \cdot -0.03 \approx -0.38$ ppm, and Hct = 45%.[19–21]

Statistical Analysis

Data were checked for normality using a Shapiro–Wilk test, and t-tests or Wilcoxon tests were used accordingly. Paired Student's t-tests and Cohen's d effect sizes were used to compare the face mask and no face mask data sets for the CS_VO_2, gray matter χ, and gray matter CBF for both the 3-ply and KN95 scans. Standard Student's t-tests were also used to determine whether there was any statistically difference between participants scanned with a face mask first or scanned without a face mask first. A standard t-test was done to determine whether there were any statistical differences in the 3-ply results between the group who agreed to return for the KN95 and those who did not. A Wilcoxon test was used to compare SpO_2 with and without a face mask. Visual representation of the data was done using R with the raincloudplots package.[22] All MRI data will be shared with interested researchers upon reasonable request. The software for the computation of QSM is freely available at https://

github.com/kamesy. A cut off of ($\alpha = 0.05$) was used for statistical significance.

Results

Study Participants

Sixteen healthy participants (eight male, eight female) with a mean age of 26.6 ± 3.5 years (range 22–36 years) were scanned for the 3-ply scans. Of the initial sixteen participants, ten agreed to return for the KN95 mask scans (five male, five female; mean age 26.5 ± 4.1 years with a range of 23–36 years). The SpO_2 group averages were significantly different (determined with a Wilcoxon test). The no mask and 3-ply mask SpO_2 averages were 98% and 97% respectively. For the return participants, the SpO_2 group averages were 98% for both the KN95 mask and no mask scans, and there was no statistically significant difference with a P value of 0.60 for the Wilcoxon test. There were no statistically significant differences in any of the measures between the participant group scanned with a mask first and those scanned without a mask first for any of the metrics (P values ≥ 0.35). No statistically significant differences were seen in any of the 3-ply results for those who agreed to return for the KN95 study and those who did not (P values ≥ 0.21).

Segmentation

An example of the venous segmentation described in the methods is shown in the right of Fig. 1.

3-ply Mask

There was a significant 6.4% increase in average gray matter CBF when wearing a 3-ply mask relative to no face mask in the group of 16 participants (P value of 0.008). The group average gray matter CBF was 43.99 mL/(100 g*min) with a standard deviation (SD) of 8.25 mL/(100 g*min) without the

face mask and 46.81 mL/(100 g*min) with a SD of 8.21 mL/(100 g*min) with the face mask. The effect size for the gray matter CBF with and without a face mask was 0.34. In gray matter, an average χ of 0.0055 (SD of 0.0019) was seen for the 3-ply face mask scan relative to the no face mask scan with an average of 0.0059 (SD of 0.0017). This difference was not statistically significant with a t-test P value of 0.07 and an effect size of 0.23. The segmented veins also showed no statistically significant increase in CS_VO_2 between the 3-ply face mask and the no face mask scans with group averages and SDs of 0.709 (SD of 0.020) and 0.707 (SD of 0.020), respectively. The t-test P value was 0.36 and the effect size was 0.13. The gray matter CBF, gray matter χ, and CS_VO_2 results are represented in the raincloud plots shown in Fig. 2.

KN95 Mask

When wearing the KN95 mask the average gray matter CBF was 48.70 mL/(100 g*min) with a SD of 11.50 mL/(100 g*min) and without a face mask the average was 47.73 mL/(100 g*min) with a SD of 11.11 mL/(100 g*min). The change between the gray matter CBF with and without the KN95 mask was not statistically significant with a t-test P value of 0.52 and an effect size of 0.086. The difference in gray matter χ was not statistically significant ($P = 0.97$ and effect size of 0.0033). Without the face mask, the gray matter χ average being 0.005095 and a SD of 0.002314 and with the mask the average being 0.005103 and a SD of 0.002518. The average CS_VO_2 without the KN95 mask was 0.71 with a SD of 0.020 and the average CS_VO_2 with the KN95 mask was 0.71 with a SD of 0.022. The change in CS_VO_2 with and without the KN95 mask was not statistically significant with a t-test P value of 0.93 and an effect size of 0.014. The raincloud plots for the KN95 mask vs. no mask results are shown in Fig. 3.

Discussion

This study showed that wearing a 3-ply or KN95 face mask resulted in no statistically significant change in the magnetic susceptibility or cerebral oxygenation. The 3-ply mask showed a statistically significant increase in gray matter CBF but no statistically significant changes in gray matter χ or CS_VO_2 values. There have been two other recent studies investing the physiological effect of face masks using different quantification methods. Fischer et al investigated 3-ply and FFP2 (EU equivalent of KN95) using functional near-infrared spectroscopy (fNIRS) and functional diffuse correlation spectroscopy and found both FFP2 and 3-ply masks resulted in statistically significant increases in CBF and cerebral blood oxygen saturation.[23] A blood oxygenation level-dependent (BOLD) fMRI study by Law et al found that wearing a 3-ply mask caused hypercapnia, a significant increase in baseline BOLD signal, and a statistically significant increase in end tidal CO_2.[24] The results of the present study are consistent with the assumed CBF increase as mentioned in Law et al and further supported by the CBF increase determined in the fNIRS study by Fischer et al.[23,24] The magnitude of CBF increase for the 3-ply mask was similar for this study and the Fischer et al study (6.4% GM CBF and 6.2% CBF increase, respectively).[23] However, the changes due to the FFP2/KN95 mask were not significant in our study. Fischer et al found a statistically significant increase of 6.5% for CBF with these masks while there was not a statistically significant change in the present cohort, the reason for this remains unclear but may be due to the different measurement techniques (ASL MRI and fNIRS).

Note that the gray matter χ values were not converted to CS_VO_2 since there is both vascular and nonvascular tissue.[25] The χ values from the manually segmented venous vessels, however, were converted to CS_VO_2. There was no statistically significant difference between wearing the face mask during the first set of scans or during the second set of
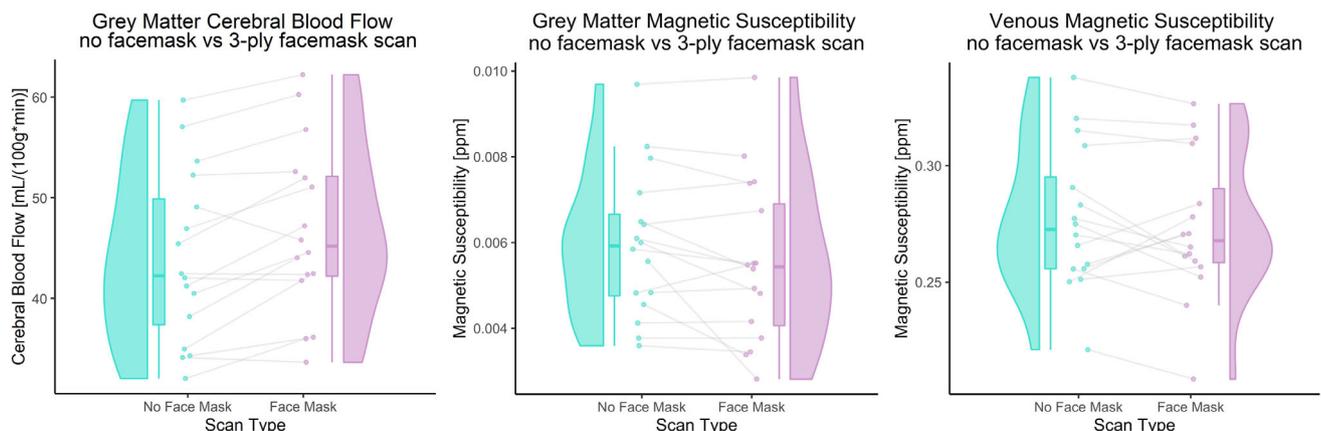

FIGURE 2: Raincloud plots of 3-ply face mask results for the GM CBF results (left), QSM GM results (center), and QSM venous results (right).
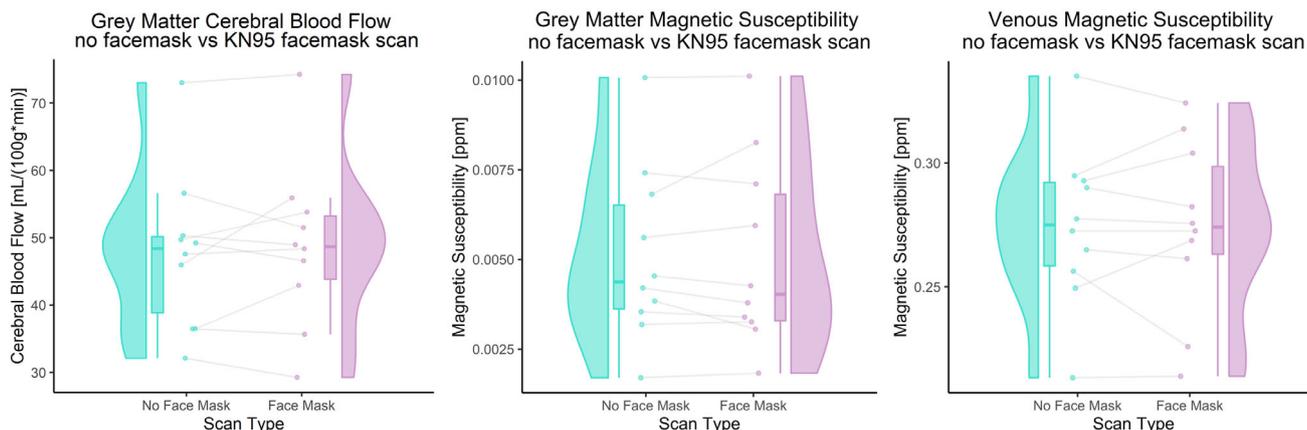
FIGURE 3: Raincloud plots of KN95 face mask results for the gray matter CBF results (left), QSM GM results (center), and QSM venous results (right).

scans, which suggests that blood flow normalizes within minutes of the mask being removed or put on. The larger change for the gray matter χ compared to the venous χ may be due to the impact of cerebral blood volume changes on susceptibility. An increase in CBF can increase overall cerebral blood volume.[26,27] This change in cerebral blood volume together with the actual increase in blood oxygenation would impact the gray matter χ more than only a change in venous χ.[28] On the other hand, since the CS_VO_2 calculation is done using manually segmented venous voxels (i.e. only voxels containing 100% vessel), any changes to cerebral blood volume will not affect the χ of the segmented vessels. Note also that a certain increase in flow does not have to be accompanied by an equivalent increase in oxygenation. For instance, Gagnon et al have measured blood flow and oxygenation in rodents after a forepaw stimulus.[29] They found that an increase in blood flow by 25% is accompanied by an increase in blood oxygenation by about 6%. When simulating the changes in oxygenation based on the vascular architecture and the flow changes, they also found an increase by 6%.

Two potential reasons for the larger percent change found in the 3-ply result when compared to the KN95 result may be that there is a higher CO_2 concentration in the air breathed when wearing a 3-ply mask, or a selection bias in return participants. Since the KN95 face mask has a larger pocket between the fabric and the mouth when compared to the 3-ply face mask, this may mean the KN95 face mask has a lower concentration of CO_2 in the air, but a capnography study would be needed to confirm this. The other possibility of a selection bias may be due to the group of participants who chose to return. While all 16 participants were asked whether they would be willing to return only 10 agreed, which may have introduced a selection bias. Although small, the changes in CBF may influence the results of MRI studies, if mask wearing is not controlled for in study design and data analysis. For example, if participants in a longitudinal study wore a mask during MRI scanning, they should continue to do so at all follow-up MRI scans, even if mask mandates are lifted.

Limitations

One limitation is the use of an assumed hematocrit value. Since hematocrit values for each participant would require blood sample analysis not done in this study, the calculation of CS_VO_2 from the venous magnetic susceptibility used an assumed value of 0.45 for each participant. Additionally, there is a possibility that larger changes to CS_VO_2 may be seen in cortical veins; however, these were not included in the venous segmentation due to the potential for erosion in these regions through the QSM analysis.[30] Gross pathology was ruled out based on a high-resolution 3D T_1-weighted scan, but no other routine MRI/MRA was done to rule out the possibility of vascular abnormalities in the participants. Finally with this being a single site study done using a single vendor 3 T MRI machine on a reasonably small population, confirming the results in a larger population across multiple sites may be a future step from this work.

Conclusion

This study measured the potential impacts of face masks on MRI measurements of cerebral blood flow and oxygenation. The findings from this study were that none of the parameters decreased and that there was a small increase only in CBF with 3-ply masks. This suggests that the use of face masks as a method to contain COVID-19 spread does not negatively impact cerebral blood flow or oxygenation, at least in young healthy individuals. Additionally, the increases in CBF observed in this study suggest that face mask protocols should be kept consistent in MRI studies involving fMRI, ASL, and QSM.

ACKNOWLEDGMENTS

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