

Eastern Kentucky University

Encompass

Honors Theses

Student Scholarship

Spring 5-6-2022

COVID-19 and Executive Functions

Shannon Ackerman

Eastern Kentucky University, shannon_ackerman4@mymail.eku.edu

Follow this and additional works at: https://encompass.eku.edu/honors_theses

Recommended Citation

Ackerman, Shannon, "COVID-19 and Executive Functions" (2022). *Honors Theses*. 881.
https://encompass.eku.edu/honors_theses/881

This Open Access Thesis is brought to you for free and open access by the Student Scholarship at Encompass. It has been accepted for inclusion in Honors Theses by an authorized administrator of Encompass. For more information, please contact Linda.Sizemore@eku.edu.

COVID-19 and Executive Functions

Honors Thesis
Submitted
In Partial Fulfillment
Of The
Requirements of HON 420
Spring 2022

By
Shannon Ackerman

Faculty Mentor
Dr. Adam Lawson
Department of Psychology

Abstract

COVID-19 and Executive Functions

Shannon Ackerman

Dr. Adam Lawson

Department of Psychology

“COVID brain,” a term coined by those who survived COVID-19 and still feel the lasting effects, ultimately raises the question of what COVID-19 is doing to the brain, specifically the executive functions. There have been little to no studies done to examine the relationship between post-COVID-19 and the brain. The current study examines whether COVID-19 leaves a long-lasting effect on processing speed, even after the person has recovered from the virus. In the laboratory setting, participants are expected to take the n-back task and the Stroop test to measure their executive functions, specifically their processing speed. The expected findings will be that participants who have had COVID-19 will have a slower processing speed compared to the participants who did not have COVID-19. The examination of the association between COVID-19 and processing speed could imply that COVID-19 is not just a respiratory disease, but also targets executive brain function. Further research could imply that post-COVID cases should be evaluated further by neuropsychologists and neurologists.

Key Words: Coronavirus Disease, COVID-19, Selective Attention, Stroop Task, Working Memory, n-back Task, Executive Function, Event-Related Potentials

Contents

COVID-19 and Executive Functions	6
COVID-19 Effects on Attention and Memory Systems	7
Understanding Attention Via the Stroop Task	8
Understanding Working Memory Via the n-back Task	9
Experiment 1	13
Method	13
Participants	13
Stroop Task	13
n-Back 2-back task	14
Data Analyses	15
Results	15
Table 1	17
Figure 1	18
Table 2	19
Experiment 2	20
E-prime Stoop Computer Task	21
Procedures	21
EEG & ERP Data Analyses	22
Results & Discussion	23
General Discussion	23
Figure 2	24
Limitations	26
Challenges to Data Collection & Analyses	26
Future Directions	28
References	29
Appendices	36
Appendix A	36
Appendix B	37
Appendix C	38

Appendix D.....	40
-----------------	----

List of Figures

Table 1. Independent Sample t-Test results are taken from the n-back 2-back task, between the COVID-19 group and the vaccination group that created in the Jamovi software system. This was done in Experiment 1.

Figure 1. Representing the vaccination versus the non-vaccination group on a scale of reaction time and accuracy from the n-back 2-back task that was created in Jamovi software system. This was done in Experiment 1.

Figure 2. The Stroop task analysis was done through an ANOVA in Jamovi, to show if there was significance between reaction time and accuracy. There was also a cross-examination in the Stroop task to see if the color condition and vaccination group also showed significant results. This was performed in Experiment 1.

Figure 2. Shows the ERP average of every participant from Experiment 2 within 8 electrodes.

Acknowledgements

I would like to thank my mentor, Dr. Adam Lawson, for guiding me through this process. His expertise in EEG and ERPs, study design, and article writing was vital to the success of this thesis. Additionally, I would like to extend my gratitude to Colton Grubbs and Rachael Vascassenno, as they were key components in data collection and analysis and were the vessel to make sure this project succeeded. I would also like to thank the honors program at Eastern Kentucky University for allowing me the opportunity to do undergraduate research. My research would not have been possible if not for these people and I am extremely thankful for all their help along the way.

COVID-19 and Executive Functions

Acute Respiratory Syndrome (SARs) SARS-CoV-2, otherwise known as Coronavirus Disease 2019 (COVID-19), is the 7th coronavirus that's been known to infect humans (*J. Czubak et Al 2021*). This form of human coronavirus (HCoV) has caused a global pandemic that resulted in worldwide reactions resulting in economic shutdowns. The COVID-19 outbreak originated in Wuhan, China in November of 2019. COVID-19 is currently thought to be the most contagious form of HCoVs (Human coronaviruses) because of its high transferability rate from human-to-human contact via air droplets (enter citation).

Coronavirus Disease 2019 is a disease characterized by severe SARS that is highly contagious (*Pantelis et al. 2020*). This disease comes with an abundance of symptoms that range depending on the nature of the illness. Symptoms range from a mild cold to even death, with the most common symptoms begin a fever, headache, cough, or chills. In late March of 2020, COVID-19 started attacking the olfactory and gustatory cortexes, resulting in the loss of taste and smell, the most prominent symptom. This eventually raised the question of whether COVID-19 was just a respiratory disease, or if it has any other potential side effects. Nevertheless, as more people started recovering from COVID-19, some started feeling lasting symptoms.

COVID-Brain which was coined by those who feel the lasting effects raises the question of whether COVID-19 still lingers even after recovery (*Egbert et al 2020*). Many of those who recovered from COVID-19 started feeling long-term effects of COVID-19, such as fatigue, difficulty remembering things, weakness, pins, and needles in limbs, dizziness, confusion, and in severe cases psychosis or even seizures. However, the symptomology is still expanding.

The broad symptomology outlined reflects several cognitive symptoms that relate to attention and memory systems. The purpose of this thesis is to better understand the potential long-term effects of COVID-19 on such cognitive functions.

COVID-19 Effects on Attention and Memory Systems

There are many long-term neurological manifestations of COVID-19. The two primary cognitive functions this study focuses on are attention and memory. The reason is that attention and memory are the core components of cognition and decline with normal aging (*Jaio et al 2015; Waltz et al 2021*). However, if pathology, such as Alzheimer's, traumatic brain injury, or other diseases of the brain, these cognitive processes can be significantly impaired.

Working memory is often understood as a mental workbench. Working memory is an active process where objects can be manipulated, and calculations can be performed which allows individuals to navigate everyday life and solve problems. One of the effects of long-COVID has been its implications on memory (*Zhao et al 2022*). One potential theory is that COVID-19 increases inflammation in the brain after recovery from the virus, however, the downstream effect of inflammation of biological processes is an avenue for exploration—especially as it pertains to cognitive functioning (*Klein et al 2021*).

Coronavirus Disease 2019 is classified as a respiratory disease. Respiratory diseases have been shown to cause alterations in working memory. A study by *Lv et al (2020)* on Chronic Obstructive Pulmonary patients were shown to have alterations with their working memory by using the n-back task. Using magnetic resonance imaging (MRI), their participants had a reduction of grey matter in the dorsolateral prefrontal cortex (PFC).

Attention and memory can be heavily integrated. However, attention can be defined as the concentration or awareness of a singular stimulus, while ignoring the surrounding salient.

Long-COVID sufferers found that even the slightest severity of the symptoms could have significant neurological impacts, especially in attention (*Pilotto et al 2021*). In a study by *Dondaine et al (2022)* the researchers found that participants who had received oxygen therapy while they had COVID-19 had difficulties with attention according to the Conners Continuous Performance Test (CCPT 3).

Understanding Attention Via the Stroop Task

Post-COVID has a variety of symptoms, however, fatigue accounts for the majority (*Ceban et al 2022*). Fatigue is an umbrella term that can affect executive functions such as memory, cognitive performance, and attention. Fatigue has been known to be a primary cause of attentional problems. To assess this reported fatigue, we utilized the Stroop test. The Stroop test is a well-known measure of attention that has been cited in thousands of prior studies.

The Stroop task is a measurement of attention by assessing cognitive interference and task performance (*Ménétré et al (2019)*). There is considerable research that examines COVID-19 and the Stroop test, but many studies examined opinions about COVID-19, and not the cognitive effect of COVID-19 (e.g., *Arias et al 2020; Maggio et al 2021; Ypsilanti et al 2021*). These studies showed reactions to the pandemic. There was only one study that assessed COVID-19 symptoms using the Stroop test (*Ortelli et al 2021*).

In a study done by *Ortelli et al., (2021)* the participants would perform the Stroop task and did 324 trials under three different conditions; two of the conditions were congruous while the third one was an interference condition. The participants were measured by seeing if they could inhibit their interference.

In this study, they found that their post-COVID participants who took the Stroop task had a significantly longer reaction time ($p < 0.015$) as opposed to their healthy control subjects.

Understanding Working Memory Via the n-back Task

The N-Back task is a neuropsychology test that measures working memory, storage, and retrieval processes (*Kimura et al 2021*) often inhabited in the dorsolateral prefrontal cortex (DLPFC). Working memory is the immediate conscious processing of information to perform executive tasks. This test was only used for the first two studies out of the three studies that took place. This version of the N-Back task was the 2-back task, that was pre-made on PsyToolKit. The participants would recall a previously shown letter after being presented with two new letters (*Stoet 2017*).

One of the effects of long-COVID has been its implications on memory (*Mazza et al 2021; Zhao et al 2022*). A study done by *Jaywant et al (2021)* found that 81% of their post-COVID-19 patients that required in-patient rehabilitation had cognitive deficits. Participants in this study took the Brief Memory and Executive Test (BMET), which is a rapid cognitive screening tool to assess impaired cognitive functions and Alzheimer's disease. The study found that working memory was highly impaired.

The current thesis examined the potential for attention and memory effects from having COVID-19 using the Stroop test and n-back test, respectively. There were two experiments performed in this thesis. Experiment 1 was an online and at-home behavioral study conducted using the N-back task and Stroop test through PsyToolKit. After the presentation of the two assessments, the participants took a short demographic survey. Those who answered that they tested positive for COVID-19 filled out a COVID-19 Health Survey which assessed their time with COVID-19 and their symptomology and whether if they still struggled with COVID Brain.

Experiment 2 was a small physiological experiment. An electroencephalography study was done in combination with the Stroop task. After the examination, each participant was asked

to fill out the same demographic survey as in Experiment 1. Participants who answered that they had tested positive for COVID-19 were then given a COVID-19 Health Survey to fill out just like in Experiment 1. Thus, the differences in the two experiments were that Experiment 1 assessed behavioral data (accuracy & response time) with two tasks, and Experiment 2 assessed behavioral and electroencephalography data in one task (Stroop).

The Stroop color-word test is a neuropsychological test that measures attention, performance, and cognitive interference (*Periáñez et al 2020*). There were two versions being used: one was a premade version by PsyToolKit and the other was created through the BioPac Acqknowledge Data Analysis System. The PsyToolKit version was used for Experiment 1, which collected behavioral data. In the PsyToolKit version, the participants were presented the name of a color and were asked to respond to the print color by using the first letter of the color print name (*Stoet 2017*).

The second version of the Stroop task, being BioPac Acqknowledge Data Analysis System that was used in Experiment 2 was used for physiological data. The participants still had to respond to the ink text of the color name presented to them. The stimuli would be presented in the middle of the screen and the participant would be given the choice of two colors to respond to in the right and left corners and to press “q” or “p” to correspond with their response. This was presented while the participant is hooked up to an Electroencephalography (EEG) cap.

The EEG is a non-invasive, macroscopic neurophysiological measurement of electrical activity on the surface of the scalp (insert citation). The EEG was used to decipher event-related-potentials (ERPs), to look at the time dynamics of the brain of the participants in response of the Stroop task (insert citation). The calculations were done in Excel and the final data analysis was

executed in Jamovi. The calculations were done in Excel and the final data analysis was executed in Jamovi.

There are many respiratory infections and diseases that can have harmful neurological effects. Chronic obstructive pulmonary disease was shown to affect cognitive functioning and working memory due to brain hypoxia (*Ly et al 2020*). Encephalomyelitis could result from COVID-19, as it can be triggered by a viral infection (*Paul et al 2021*). Encephalomyelitis is the demyelinating disease of the brain and spinal cord (*Poyrazoğlu et al 2022*).

The exchange of positive and negatively charged ions between cell membranes enables neurons to communicate. This exchange of energy is propagated by neurotransmitters, small chemical substances that serve as messengers between neurons. The nerve conduction velocity measures the speed of electrical impulses through the nerves and can show nerve damage.

There is limited experimental data on COVID-19, specifically on COVID brain or Long-COVID, especially in terms of neurophysiological data. Most articles were case studies that evaluated COVID-19 patients looking at participants at the time the participant was actively having COVID-19. There are currently active clinics researching Long-term COVID-19 such as Cedars-Sinai, Mayo Clinic, and the University of Washington.

As the COVID-19 pandemic continues, so does long-COVID/COVID-Brain. The small list of symptoms coined in 2020 has ever since expanded, allowing Long-Covid to affect nearly every function of the body. Some of the other symptoms include parosmia, digestive system problems, mental health problems, or hair loss (*Lopez-Leon et al 2021*).

In this study two hypotheses were formed: 1) People who had COVID-19 would have alterations in executive functions, especially in task performance using working memory and

attention when performing in the behavioral study. 2) People who had COVID-19 would have a slower reaction time than those who did not have COVID-19.

Experiment 1

Experiment 1 examined the impact of COVID-19 on attention and working memory performance with a relatively large sample size using an online approach. Participants performed both the Stroop test and n-back task, along with questions related to COVID-19 to assess whether long-COVID-19 had significant effects on cognitive functions such as attention, performance, and potentially memory.

Method

Participants

This study was approved by the Institutional Review Board (IRB) and all participants gave informed consent prior to taking part in the study. The inclusion criteria were being 18 years old or older and were collected from the Eastern Kentucky University student population. There were 165 participants (146 Female, 19 male), 31 who had tested positive for COVID-19 participants, and 134 who were healthy controls. Three more participants were excluded from the data as their results were less than 60% accurate in both tasks. Those who claimed that they did not test positive for COVID-19 (n = 134) were composed of the Healthy Control group (HC).

Stroop Task

The Stroop test is a task that assesses cognitive interference, processing, and attention (*Vanderhasselt 2009*). The Stroop task was performed twice in this experiment. Once on PsyToolKit (*Stoet 2017*) and a second time using the E-Prime software system (*Schneider et al, 2012*). The assessment on PsyToolKit was used to evaluate behavioral data and was taken as an “at-home-assessment.” The E-Prime Stroop test was used to collect physiology data, as the participant was hooked up to the electroencephalogram (EEG),

In Experiment 1, the participant is given four color names (red, green, blue, and yellow). The color names are in different print colors, and the participants must respond to the print

colors, and press the correlating buttons to match the print colors. For instance, if the color name green appears and is printed in red, the participant will press the button “r” for red.

In Experiment 2, the participant would perform the task like the Stroop test performed on PsyToolKit. However, instead of pressing the first letter that corresponds to the color ink text, the actual name of the color ink text and the name of the color would appear to either the bottom left or right of the screen. The participant would either select the key “Q” or “P” to correspond to the color/color-ink text that would appear on the screen.

Using the E-Prime software, the Stroop test being performed had two conditions where there was the different color condition and the same color condition. Each participant had 90 trials each, and of the 90 trials, 4 of the trials were for blinking so that the EEG was working correctly.

n-Back 2-back task

The n-back task is a performance task that is used to measure working memory, attention, and cognitive functioning (*Wang et al 2019*). The N-Back Task performed on PsyToolKit (*Stoet, G. 2017*) consists of 15 visual stimuli (A, B, C, D, E, H, I, K, L, M, O, P, R, S, and T) which were presented for 2000 milliseconds each. The participants would get 3 seconds to respond, and a stimulus is presented every 3000 milliseconds. There were 3 blocks of each 25 trials. If the stimulus matched the letter from 2 trials previously, the participant would press the “m” button—a green box would then appear around letting the participant know they got the answer correct. If the participant pressed the “m” button because the letter from 2 trials ago was different, a red box will appear letting the participant know there was an error. If the participant did not press the “m” button but they should have because the letter from 2 trials ago was the same, a red box will

appear because the participant missed the time slot, and it will be marked as an error. The N-back task was later dropped from the electroencephalography (EEG) study.

Data Analyses

If the participant had less than a 65% accuracy score (ACC) on their Stroop false data score and/or correct data score, their data would be excluded from the study. Of the 165 participants, 4 participants fit this criterion and were excluded from the study. If the participant had a Response time (RT) that exceeded over 2000ms (2 seconds) their data would also be excluded from the study.

Results

An Independent Sample t-Test was conducted to measure the difference between the groups that tested negative for COVID-19 and the HC group (see Table 1). There was also an Independent Sample t-Test conducted between the vaccination groups. These measures assessed the accuracy and the reaction. There was no significance between the COVID-19 and HC groups. N-back ACC statistic 0.279 ($p < 0.05$). N-back RT statistic 0.134 ($p < 0.05$).

For all participants, the reaction time was faster for the no-match than for the match (*See Figure 1*). However, the accuracy was lower than the match. With the 2-back reaction time, the data contradicts itself. The overall reaction time of those who are unvaccinated is lower than that of those who are vaccinated. However, the actual match vs no match shows that the vaccinated participants had a slower reaction time for the match than those who are non-vaccinated, however, it is marginal. For no match, the vaccinated participants had a faster reaction time than those not vaccinated.

A repeated measures Analysis of Variance (ANOVA) was conducted with Color Match (Yes, No) serving as the repeated measure and COVID-19 History (Negative, Positive) serving

as the between-group variable. This analysis approach was conducted for accuracy and response time measures. Like prior studies, participants were both more accurate and faster in the Color Match condition than in the Non-color Match (*see Table 2*).

Table 1

2-Back Task Independent Samples T-Test Results

	df	T	<i>p</i>	Cohen's d
COVID-19 Group				
Accuracy	153	1.09	0.279	0.218
RT	153	1.51	0.134	0.303
Vaccination Group				
Accuracy	153	1.28	0.201	0.218
RT	153	2.01	0.046	0.342

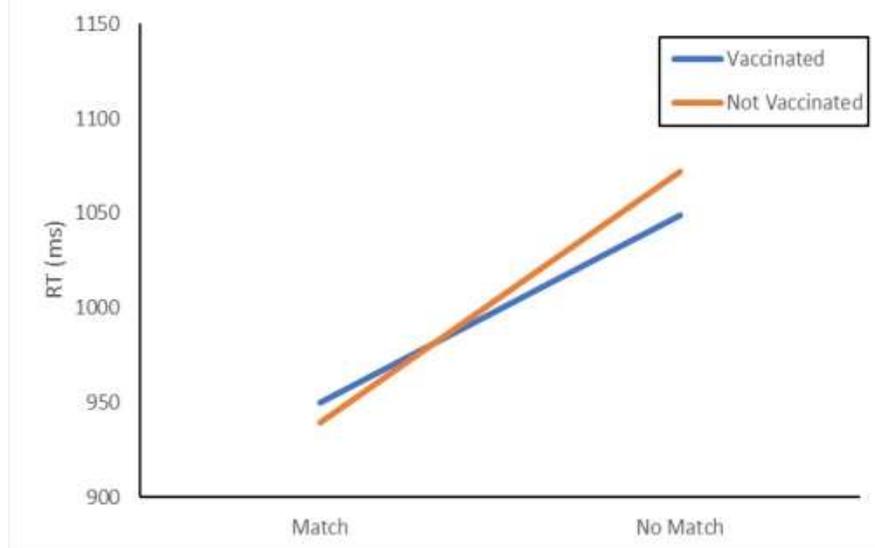
Figure 1

Table 2

Stroop Task ANOVA Results

	df	F	p	η^2_G
COVID-19 Group Accuracy				
COVID-19	1, 152	0.478	0.490	0.002
Color Condition (CC)	1, 152	49.74	<.001**	0.110
CC X COVID-19	1, 152	2.07	0.152	0.005
COVID-19 Group RT				
COVID-19	1, 151	0.907	0.342	0.005
Color Condition (CC)	1, 151	82.762	<.001**	0.073
CC X COVID-19	1, 151	0.628	0.429	0.001
Vaccination Group Accuracy				
Vaccination Group	1,152	0.354	0.553	0.001
Color Condition (CC)	1,152	66.36	<.001**	0.140
CC X Vaccination	1,152	3.31	0.071*	0.008
Vaccination Group RT				
Vaccination	1,151	0.057	0.812	0.000
Color Condition (CC)	1,151	156.94	<.001**	0.127
CC X Vaccination	1,151	3.98	0.048**	0.004

Note. * refers to marginal significance with alpha = .10, ** refers to significance at alpha = .05

Experiment 2

Experiment 2 was conducted to examine psychophysiological data in relation to attention and COVID-19. Electroencephalograms (EEG) were collected and analyzed as Event-related Potentials (ERPs). As in Experiment 1, the Stroop test was utilized to examine attention. The n-back test was not included because

The decision to use event-related potentials (ERPs) in assessment of cognitive functioning in Experiment 2 was due to the excellent temporal resolution offered by EEG (*Burle et al 2015*). Brain activity corresponding to aspects of attentional and perceptual cognitive processes runs on a scale of tens of milliseconds. EEG enables the recording of brain activity one millisecond to the next, allowing precise measurement of time differences among individuals completing cognitive tasks.

The firing of neurons and subsequent exchange of energy generates electrical fields that can eventually reach the surface of the skull and be recorded by external EEG electrodes. For an ERP to be recorded, a large group of neurons must be activated synchronously to generate an electrical field.

As individuals are faced with a task that demands both inhibition of irrelevant information and conscious direction of their attention, large numbers of neurons are activated concurrently in regions associated with executive functions. This increase in activity creates an electrical pulse strong enough in nature to be recorded at the scalp and distinguished from other ongoing brain activity being recorded, creating an ERP.

Method

Participants

Given time and resource constraints, only six participants were collected for Experiment 2. Three participants had a prior diagnosis of COVID-19, and the other three participants were non-COVID-19 controls. Like Experiment 1, all participants were 18 years of age or older and all supplied informed consent prior to beginning the study.

E-prime Stroop Computer Task

Using the E-Prime software, the Stroop test being performed had two conditions where there was the different color condition and the same color condition. Each participant had 90 trials each, and of the 90 trials, 4 of the trials were for blinking so that the EEG was working correctly.

The participants would respond to the ink text of the color name presented to them. The stimuli would be presented in the middle of the screen and the participant would be given the choice of two colors to respond to in the right and left corners and to press “q” or “p” to correspond with their response.

Procedures

In Experiment 2, participants filled out a survey questionnaire that was sent out on social media that asked if they were interested in being part of a study that involved an EEG. 9 participants responded. Each participant was sent a digital sheet that allowed them to fill in a date and time that they were free and send it back to the researcher. Only 6 participants responded. There were 3 non-COVID participants and 3 post-COVID-19 participants.

Participants were given an informed consent sheet and required to sign it before the study was to continue. After reading over the informed consent, the participant was hooked up to the BIOPAC EEG software, using ECI electro gel to insert into electrodes with a blunt needle.

When set up was finished, researchers would leave the room and the participant would take the Stroop task. After the completion of the task, every participant was distributed a demographics survey. The demographics survey asked about the participant's age, sex, race, and COVID vaccination status. The final question on the survey asked if the participant had ever tested positive for COVID-19. If the participant answered that they had suffered from COVID-19, they were distributed a COVID-19 Health Survey. The COVID-19 Health Survey scaled participants' symptoms of when they had COVID and scaled their symptoms of long-COVID.

EEG & ERP Data Analyses

The complexion of ERPs and EEG needs a recording of repeated trials averaged together. Among the 90 trials participants completed, those with eye blinks were removed, and the remaining data was averaged together to create a “grand average”, or event-related potential.

Data was averaged with an epoch of 200ms before the presentation of the Stroop task and 800ms subsequently. This window of time allows for the extraction of small-amplitude voltage fluctuations of brain activity, enabling ERP components such as the P300 to be revealed. A P300 component, for example, signifies an increase in the positive amplitude of approximately 300ms post-presentation of stimuli.

Using the E-Prime software, the Stroop test being performed had two conditions where there was the different color condition and the same color condition. Each participant had 90 trials each, and of the 90 trials, 4 of the trials were for blinking so that the EEG was working correctly.

This would occur while the participants would be hooked up to BIOPAC EEG software, using ECI electro gel to insert into electrodes. We used Cz as a ground, and measured electrodes T3, T4, F7, F8, Fp2, Fp1, Pz, and Fz. In addition, when measuring impedance, the score was always 5 K Ohms \neq 1 K Ohms.

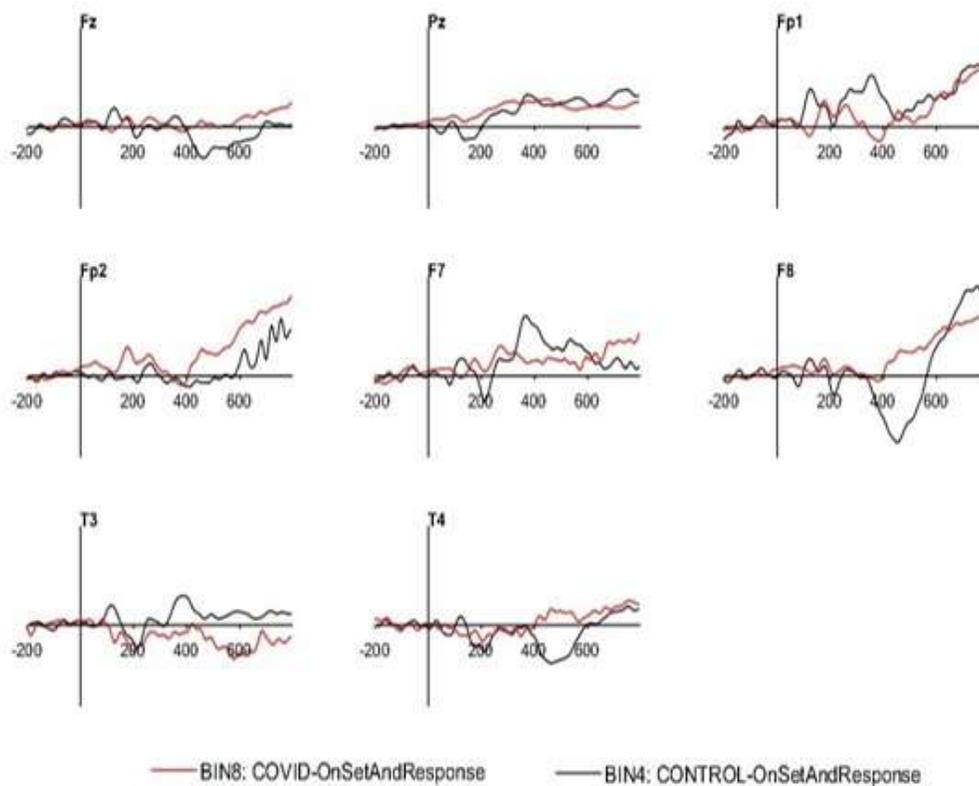
Results & Discussion

The limited number of participants did not allow for statistical comparisons between COVID-19 and control groups. However, visual inspection of ERPs showed promising differences between 400 and 600 milliseconds. These 400 to 600 millisecond areas are called the Late Positive Component (LPC), and this region is known for indexing working memory and attentional processes (*Luck 2005*). These potential results show the potential for psychophysiological research to detect cognitive differences between COVID-19 and non-COVID-19 individuals.

General Discussion

Coronavirus Disease 2019 is characterized by severe acute respiratory infection. It is the 7th human coronavirus currently known and has caused a worldwide pandemic. Previous studies have shown that COVID-19 can be accompanied by cognitive impairments. However, long-COVID is still being studied. Experiment 1 was aimed at evaluating the mental functions of post-COVID-19 participants, using two tasks that focus on attention, processing, working memory, and performance: the N-back task and the Stroop task. Experiment 2 was aimed at evaluating the executive functions of post-COVID-19 participants, using the Stroop task while also having the participants hooked up to the EEG, and analyzing each participant's ERPs.

Figure 2



For Experiment 1, the N-back task was used to measure working memory, attention, and cognitive functioning. Through this task, we measured the accuracy of the responses and the response time given. There was not a significant difference between the COVID group and the HC group in either accuracy or response time. However, there was a significant difference in response time between the participants who were vaccinated and the participants who were unvaccinated ($p < 0.046$).

For Experiment 1, the Stroop task was used to assess cognitive interference, processing, and attention. In this task, we measured the accuracy of false responses (questions the participants got wrong) whether if it was incorrect or missed it by responding too late, furthermore, we measured the accuracy of correct responses or correct but was counted as a 'miss' due to responding too late. Response times were also measured through both false answers and correct answers. All measurements showed no significance between the COVID-19 group and the HC group. All measurements were assessed through Jamovi using an ANOVA.

. Following the two tasks, participants were asked to take a survey assessing age, sex, education, demographics, if they were vaccinated, and if the participant had suffered from COVID-19. If the participant had, a separate survey would open for participants who had tested positive and scaled their symptoms. All participants were females attending Eastern Kentucky University. A correlation-regressions test was run through Jamovi to assess demographics and age. No significance was given, except for vaccination status.

Six participants took part in Experiment 2, and both their behavioral and ERP data were collected and examined. The focus was primarily on learning and developing computerized data analysis programs. In particular, the use of MATLAB software and EEGLab were utilized to transform the raw EEG to ERPs.

The 6 participants' data did not allow for statistical comparisons but did provide the framework for collecting and analyzing data for continuing data collection and analyses past this thesis.

Limitations

There were several limitations to this study. For Experiment 1, this study was done during the COVID-19 pandemic (2020-2021), therefore it was done on each participant's laptop and cannot account for computer error. Furthermore, there were limited COVID participants, and the female to male ratio was significant.

In Experiment 2, our sample size was insufficient for statistical measurement. Furthermore, there is no correct or proper assessment of "Long-COVID" as it has been shown to have a multiorgan impact and is novel.

For both experiments, (1 & 2) one more important limitation is that our non-COVID-19 participants reported never testing positive. However, there could be participants within this group who could have been asymptomatic at one point or another. Moreover, Long-COVID is novel in research and therefore there is not a lot of previous research. This study also does not account for the time of diagnosis of COVID-19 for the post-COVID-19 group. Another limitation is that we cannot limit cognitive function assessments to just the Stroop and N-back task. Despite these tasks being made for cognitive assessments, there are other cognitively demanding tasks that could measure cognitive functioning.

Challenges to Data Collection & Analyses

Both the collection and analysis of EEG data proved challenging during this study. Analysis of EEG data required learning three new applications: AcqKnowledge, E-Prime, and EEGLAB. AcqKnowledge was used to record EEG data from the BIOPAC system. Setup of

AcqKnowledge included specifying proper channels, creating event markers, and analyzing data in real-time to ensure the reliability of data during recording. E-Prime was used to design and develop the Stroop test administered during EEG. Using Visual Basic programming language, a Stroop test was programmed specifically for the EEG portion of the study. E-Prime communicated in real-time with AcqKnowledge to ensure events were marked correctly within a 5-millisecond window for later analysis. EEG data was analyzed in EEGLAB, a popular open-source program used to analyze EEG data. EEG data recorded within BIOPAC AcqKnowledge was exported to a MATLAB format. The exported data was imported into EEGLAB. Individual events, such as target onset, response, and eyeblinks were imported into EEGLAB by importing event information from channel information recorded by AcqKnowledge. Events were then renamed for organization and later used in ERPLAB. EEG data was then cleaned by removing unnecessary channels. ERPLAB, a plugin within EEGLAB, was used to create event-based epochs from EEG data. For example, each onset (presentation of Stroop test) followed by response is a single epoch, therefore approximately 86 individual epochs (representing 86 individual trials) were generated for each participant. These epochs began at -200ms from stimulus onset to 800ms (about 1 second) post-stimulus onset. A moving window peak-to-peak amplitude tool was used to detect potential artifacts during epochs. Epochs that have artifacts such as eyeblinks were removed from subsequent analysis. A high-pass ERP filter was then applied to the remaining epochs for enhanced interpretation. Finally, an event-related potential was generated by computing the average of all epochs together.

It is important to note that individual ERPs were generated for each participant. A total of 8 ERPs were created for each participant, one for each channel. ERPs generated for every participant were then averaged together, separated by COVID vs. Non-COVID groups. Thus, a

total of 16 ERPs are presented in the data: 8 for non-COVID participants, and 8 for positive-COVID participants. These ERPs are presented on a graph depicting 8 unique channels. Each graph has two lines: One for the group who had tested positive for COVID in the past, and one for those who did not.

Future Directions

Coronavirus Disease 2019 is still ongoing and is becoming a part of everyday lives. However, this does not negate the suffering of those who experience long-COVID and have symptoms that impact their everyday lives. Other studies should follow COVID participants from their diagnosis of COVID and follow their symptomology, and have the participants report if they are suffering from long-COVID and its severity. Future studies should also look to see if participants were hospitalized when they had COVID-19. Also, studies should look at participants of various ages as this could greatly influence cognitive function and how COVID-19 could impact the executive functioning.

References

- Almqvist, J., Granberg, T., Tzortzakakis, A., Klironomos, S., Kollia, E., Öhberg, C., Martin, R., Piehl, F., Ouellette, R., & Ineichen, B. V. (2020). Neurological manifestations of coronavirus infections – a systematic review. *Annals of Clinical & Translational Neurology*, 7(10), 2057–2071. <https://doi-org.libproxy.eku.edu/10.1002/acn3.51166>
- Arias, F., Safi, D. E., Miranda, M., Carrión, C. I., Diaz Santos, A. L., Armendariz, V., Jose, I. E., Vuong, K. D., Suarez, P., & Strutt, A. M. (2020). Teleneuropsychology for monolingual and bilingual Spanish-speaking adults in the time of COVID-19: Rationale, professional considerations, and resources. *Archives of Clinical Neuropsychology*, 35(8), 1249–1265. <https://doi-org.libproxy.eku.edu/10.1093/arclin/aaa100>
- Burle, B., Spieser, L., Roger, C., Casini, L., Hasbroucq, T., & Vidal, F. (2015). Spatial and temporal resolutions of EEG: Is it really black and white? A scalp current density view. *International Journal of Psychophysiology*, 97(3), 210–220. <https://doi-org.libproxy.eku.edu/10.1016/j.ijpsycho.2015.05.004>
- Ceban, F., Ling, S., Lui, L. M. W., Lee, Y., Gill, H., Teopiz, K. M., Rodrigues, N. B., Subramaniapillai, M., Di Vincenzo, J. D., Cao, B., Lin, K., Mansur, R. B., Ho, R. C., Rosenblat, J. D., Miskowiak, K. W., Vinberg, M., Maletic, V., & McIntyre, R. S. (2022). Fatigue and cognitive impairment in post-COVID-19 syndrome: A systematic review and meta-analysis. *Brain, Behavior, and Immunity*, 101, 93–135. <https://doi-org.libproxy.eku.edu/10.1016/j.bbi.2021.12.020>
- Czubak, J., Stolarczyk, K., Orzeł, A., Frączek, M., & Zatoński, T. (2021). Comparison of the clinical differences between COVID-19, SARS, influenza, and the common cold: A systematic literature review. *Advances in Clinical and Experimental Medicine: Official*

Organ Wroclaw Medical University, 30(1), 109–114. <https://doi-org.libproxy.eku.edu/10.17219/acem/129573>

Dondaine, T., Ruthmann, F., Vuotto, F., Carton, L., Gelé, P., Faure, K., Deplanque, D., & Bordet, R. (2022). Long-term cognitive impairments following COVID-19: a possible impact of hypoxia. *Journal of Neurology*. <https://doi-org.libproxy.eku.edu/10.1007/s00415-022-11077-z>

Egbert, A. R., Cankurtaran, S., & Karpiak, S. (2020). Brain abnormalities in COVID-19 acute/subacute phase: A rapid systematic review. *Brain, Behavior, and Immunity*, 89, 543–554. <https://doi-org.libproxy.eku.edu/10.1016/j.bbi.2020.07.014>

Jaywant, A., Vanderlind, W. M., Alexopoulos, G. S., Fridman, C. B., Perlis, R. H., & Gunning, F. M. (2021). Frequency and profile of objective cognitive deficits in hospitalized patients recovering from COVID-19. *Neuropsychopharmacology*, 46(13), 2235–2240. <https://doi-org.libproxy.eku.edu/10.1038/s41386-021-00978-8>

Jiao, S.-S., Yao, X.-Q., Liu, Y.-H., Wang, Q.-H., Zeng, F., Lu, J.-J., Liu, J., Zhu, C., Shen, L.-L., Liu, C.-H., Wang, Y.-R., Zeng, G.-H., Parikh, A., Chen, J., Liang, C.-R., Xiang, Y., Bu, X.-L., Deng, J., Li, J., ... Wang, Y.-J. (2015). Edaravone alleviates Alzheimer's disease-type pathologies and cognitive deficits. *PNAS Proceedings of the National Academy of Sciences of the United States of America*, 112(16), 5225–5230. <https://doi-org.libproxy.eku.edu/10.1073/pnas.1422998112>

Klein, R., Soung, A., Sissoko, C., Nordvig, A., Canoll, P., Mariani, M., Jiang, X., Bricker, T., Goldman, J., Rosoklija, G., Arango, V., Underwood, M., Mann, J. J., Boon, A., Dowrk, A., & Boldrini, M. (2021). COVID-19 induces neuroinflammation and loss of

- hippocampal neurogenesis. *Research Square*. <https://doi-org.libproxy.eku.edu/10.21203/rs.3.rs-1031824/v1>
- Kilner, J. M. (2013). Bias in a common EEG and MEG statistical analysis and how to avoid it. *Clinical Neurophysiology*, *124*(10), 2062–2063. <https://doi-org.libproxy.eku.edu/10.1016/j.clinph.2013.03.024>
- Kimura, T., & Matsuura, R. (2021). Changes in brain activity induced by the N-back task are related to improved dual-task performance. *Behavioural Brain Research*, *396*. <https://doi-org.libproxy.eku.edu/10.1016/j.bbr.2020.112881>
- Kubota, T., Gajera, P. K., & Kuroda, N. (2020). Meta-analysis of eeg findings in patients with covid-19. *Epilepsy & Behavior*. <https://doi-org.libproxy.eku.edu/10.1016/j.yebeh.2020.107682>
- Lopez-Leon, S., Wegman-Ostrosky, T., Perelman, C., Sepulveda, R., Rebolledo, P. A., Cuapio, A., & Villapol, S. (2021). More than 50 long-term effects of COVID-19: a systematic review and meta-analysis. *Scientific Reports*, *11*(1), 16144. <https://doi-org.libproxy.eku.edu/10.1038/s41598-021-95565-8>
- Luck. (2005). *An introduction to the event-related potential technique / Steven J. Luck*. MIT Press.
- Lv, Z., Hu, P., Jiang, Y., Yang, W., Wang, R., Wang, K., & Fan, X. (2020). Changes in Spatial Working Memory in Stable Chronic Obstructive Pulmonary Disease: A Retrospective Study. *BioMed Research International*, *2020*, 7363712. <https://doi-org.libproxy.eku.edu/10.1155/2020/7363712>

- Maggio, M. G., Foti Cuzzola, M., Calatozzo, P., Marchese, D., Andaloro, A., & Calabrò, R. S. (2021). Improving cognitive functions in adolescents with learning difficulties: A feasibility study on the potential use of telerehabilitation during COVID-19 pandemic in Italy. *Journal of Adolescence*, *89*, 194–202. <https://doi-org.libproxy.eku.edu/10.1016/j.adolescence.2021.05.005>
- Mazza, M. G., Palladini, M., De Lorenzo, R., Magnaghi, C., Poletti, S., Furlan, R., Ciceri, F., Rovere-Querini, P., & Benedetti, F. (2021). Persistent psychopathology and neurocognitive impairment in COVID-19 survivors: Effect of inflammatory biomarkers at three-month follow-up. *Brain, Behavior, and Immunity*, *94*, 138–147. <https://doi-org.libproxy.eku.edu/10.1016/j.bbi.2021.02.021>
- Mehta, J. R., Ratnani, I. J., Dave, J. D., Panchal, B. N., Patel, A. K., & Vala, A. U. (2014). Association of psychiatric co-morbidities and quality of life with severity of chronic obstructive pulmonary disease. *East Asian Archives of Psychiatry*, *24*(4), 148–155.
- Ménétré, E., & Laganaro, M. (2019). Attentional reorientation and inhibition adjustment in a verbal Stroop task: A lifespan approach to interference and sequential congruency effect. *Frontiers in Psychology*, *10*. <https://doi-org.libproxy.eku.edu/10.3389/fpsyg.2019.02028>
- Ortelli, P., Ferrazzoli, D., Sebastianelli, L., Engl, M., Romanello, R., Nardone, R., Bonini, I., Koch, G., Saltuari, L., Quartarone, A., Oliviero, A., Kofler, M., & Versace, V. (2021). Neuropsychological and neurophysiological correlates of fatigue in post-acute patients with neurological manifestations of COVID-19: Insights into a challenging symptom. *Journal of the Neurological Sciences*, *420*. <https://doi-org.libproxy.eku.edu/10.1016/j.jns.2020.117271>

- Pantelis, C., Jayaram, M., Hannan, A. J., Wesselingh, R., Nithianantharajah, J., Wannan, C. M., Syeda, W. T., Choy, K. C., Zantomio, D., Christopoulos, A., Velakoulis, D., & O'Brien, T. J. (2021). Neurological, neuropsychiatric, and neurodevelopmental complications of COVID-19. *The Australian and New Zealand Journal of Psychiatry*, 55(8), 750–762. <https://doi-org.libproxy.eku.edu/10.1177/0004867420961472>
- Paul, B. D., Lemle, M. D., Komaroff, A. L., & Snyder, S. H. (2021). Redox imbalance links COVID-19 and myalgic encephalomyelitis/chronic fatigue syndrome. *Proceedings of the National Academy of Sciences of the United States of America*, 118(34). <https://doi-org.libproxy.eku.edu/10.1073/pnas.2024358118>
- Pilotto, A., Cristillo, V., Cotti Piccinelli, S., Zoppi, N., Bonzi, G., Sattin, D., Schiavolin, S., Raggi, A., Canale, A., Gipponi, S., Libri, I., Frigerio, M., Bezzi, M., Leonardi, M., & Padovani, A. (2021). Long-term neurological manifestations of COVID-19: Prevalence and predictive factors. *Neurological Sciences*, 42(12), 4903–4907. <https://doi-org.libproxy.eku.edu/10.1007/s10072-021-05586-4>
- Poyrazoğlu, H. G., Kırık, S., Sarı, M. Y., Esen, İ., Toraman, Z. A., & Eroğlu, Y. (2022). Acute demyelinating encephalomyelitis and transverse myelitis in a child with COVID-19. *The Turkish Journal of Pediatrics*, 64(1), 133–137. <https://doi-org.libproxy.eku.edu/10.24953/turkjped.2020.3385>
- Smith, A. P. (2012). Effects of the common cold on mood, psychomotor performance, the encoding of new information, speed of working memory and semantic processing. *Brain, Behavior, and Immunity*, 26(7), 1072–1076. <https://doi-org.libproxy.eku.edu/10.1016/j.bbi.2012.06.012>

- Smith, A. P., Tyrrell, D. A., Coyle, K., & Willman, J. S. (1987). Selective effects of minor illnesses on human performance. *British Journal of Psychology*, *78*(2), 183–188.
<https://doi-org.libproxy.eku.edu/10.1111/j.2044-8295.1987.tb02238.x>
- Schneider, W., Eschman, A., and Zuccolotto, A. (2012). E-Prime User's Guide. Pittsburgh: Psychology Software Tools, Inc.
- Stoet, G. (2010). PsyToolkit - A software package for programming psychological experiments using Linux. *Behavior Research Methods*, *42*(4), 1096-1104.
- Stoet, G. (2017). PsyToolkit: A novel web-based method for running online questionnaires and reaction-time experiments. *Teaching of Psychology*, *44*(1), 24-31
- Vollono, C., Rollo, E., Romozzi, M., Frisullo, G., Servidei, S., Borghetti, A., & Calabresi, P. (2020). Focal status epilepticus as unique clinical feature of COVID-19: A case report. *Seizure*, *78*, 109–112. <https://doi-org.libproxy.eku.edu/10.1016/j.seizure.2020.04.009>
- Walz, J. A., Mani, R., Alnawmasi, M. M., & Khuu, S. K. (2021). Visuospatial attention allocation as an indicator of cognitive deficit in traumatic brain injury: A systematic review and meta-analysis. *Frontiers in Human Neuroscience*, *15*. <https://doi-org.libproxy.eku.edu/10.3389/fnhum.2021.675376>
- Wang, H., He, W., Wu, J., Zhang, J., Jin, Z., & Li, L. (2019). A coordinate-based meta-analysis of the n-back working memory paradigm using activation likelihood estimation. *Brain and Cognition*, *132*, 1–12. <https://doi-org.libproxy.eku.edu/10.1016/j.bandc.2019.01.002>
<https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/electroencephalogram-eeg>

Ypsilanti, A., Mullings, E., Hawkins, O., & Lazuras, L. (2021). Feelings of fear, sadness, and loneliness during the COVID-19 pandemic: Findings from two studies in the UK.

Journal of Affective Disorders, 295, 1012–1023. <https://doi-org.libproxy.eku.edu/10.1016/j.jad.2021.08.031>

Zhao, S., Shibata, K., Hellyer, P. J., Trender, W., Manohar, S., Hampshire, A., & Husain, M.

(2022). Rapid vigilance and episodic memory decrements in COVID-19 survivors. *Brain Communications*, 4(1). <https://doi-org.libproxy.eku.edu/10.1093/braincomms/fcab295>

Zurrón, M., Ramos-Goicoa, M., & Díaz, F. (2013). Semantic conflict processing in the color-

word Stroop and the emotional Stroop: Event-related potential (ERP) correlates. *Journal of Psychophysiology*, 27(4), 149–164. <https://doi-org.libproxy.eku.edu/10.1027/0269-8803/a000100>

Appendices

Appendix A

Demographics Questionnaire for Experiment 1

COVID-19 Demographics Questionnaire

COVID-19 Effects on Mental Functions

1. Have you been vaccinated for the COVID-19 virus?
 - Yes
 - No
2. How many times have you received a COVID test?
 - Never
 - 1-3 times
 - 4-7 times
 - 8+
3. Have you ever *tested positive* for COVID-19 (not including false positives)
 - Yes
 - No
4. Do you have a history of Traumatic Brain Injury (TBI)
 - Yes
 - No

Appendix B
COVID-19 Health Survey for Experiment 1

COVID-19 Health Survey

COVID-19 Effects on Mental Functions

1. How long has it been since you recovered from COVID-19?
 - Six months or longer
 - 3-6 months
 - 1-3 months
 - 1-3 weeks
2. What symptoms did you experience?
 - a.
3. Were you hospitalized for COVID-19?
 - Yes
 - No
4. Do you still experience side effects even though you've recovered?
 - Yes
 - No
5. Did you experience "COVID Brain Fog" (Confusion, fatigue, headaches, loss of short-term memory, psychosis or seizures)?
 - Yes
 - No
6. How often did you experience what is called "COVID Brain Fog"
 - Always
 - Most of the time
 - About half the time
 - Sometimes
 - Never
7. How often does "COVID Brain Fog" interfere with daily life?
 - Always
 - Most of the time
 - About half the time
 - Sometimes
 - Never

Appendix C
Demographics Survey for Experiment 2

COVID-19 Effects on Executive Functions

COVID-19 Demographics Questionnaire

1. How old are you?

- 18 – 25
- 26 – 35
- 36 – 45
- 46 – 55
- 56+

2. What is your biological sex?

- Female
- Male

3. What year are you in college:

- Freshman
- Sophomore
- Junior
- Senior
- Graduate

4. What race/ethnicity do you identify as?

- Native American/ Alaskan Native
- Asian
- Black / African American
- Native Hawaiian / Other Pacific Islander
- Caucasian
- Latinx
- 2 or more
- Other

5. Have you tested positive for COVID-19 (not including false positives?)

· Yes

· No

Appendix D
COVID-19 Health Survey for Experiment 2

COVID-19 Effects on Executive Functions

COVID-19 Health Questionnaire

1. Are you vaccinated for COVID-19?
 - Yes
 - No
2. If you responded yes to the question above, did you receive your vaccination before you tested positive for COVID-19?
 - Yes
 - No
3. Do you have a history of neurological problems?
 - Yes
 - No
4. How long has it been since you recovered from COVID-19?
 - Six months or longer
 - 3-6 months
 - 1-3 months
 - 1-3 weeks
5. What symptoms did you experience?
6. Were you hospitalized for COVID-19?
 - Yes
 - No
7. Do you still experience side effects even though you've recovered?
 - Yes
 - No

COVID-19 severity symptom log

8. How many days were you unable to work (if none, then report 0): _____
9. On a scale of 0 (no symptoms) – 10 (almost died), how would you rate the severity of your symptoms of COVID-19? Provide a number between 0 – 10: _____
10. Did you experience “COVID Brain Fog” (Confusion, fatigue, headaches, loss of short-term memory, psychosis or seizures)?
- Yes
 - No
11. How often did you experience what is called "COVID Brain Fog"
- Always
 - Most of the time
 - About half the time
 - Sometimes
 - Never
12. How often does "COVID Brain Fog" interfere with daily life?
- Always
 - Most of the time
 - About half the time
 - Sometimes
 - Never

